Sandra A. Edwards (State Bar No. 154578)
Joshua W. Malone (State Bar No. 301836)
Farella Braun + Martel LLP
235 Montgomery Street, 17th Floor
San Francisco, CA 94104
Telephone: (415) 954-4400; Fax: (415) 954-4480
sedwards@fbm.com
jmalone@fbm.com

Joe G. Hollingsworth (appearance *pro hac vice*)
Martin C. Calhoun (appearance *pro hac vice*)
Kirby T. Griffis (appearance *pro hac vice*)
William J. Cople (appearance *pro hac vice*)
Hollingsworth LLP
1350 I Street, N.W.
Washington, DC 20005
Telephone: (202) 898-5800; Fax: (202) 682-1639
jhollingsworth@hollingsworthllp.com
mcalhoun@hollingsworthllp.com
kgriffis@hollingsworthllp.com
wcople@hollingsworthllp.com

George C. Lombardi (appearance *pro hac vice*)
James M. Hilmert (appearance *pro hac vice*)
Winston & Strawn LLP
35 West Wacker Drive
Chicago, IL 60601
Telephone: (312) 558-5969; Fax: (312) 558-5700
glombard@winston.com
jhilmert@winston.com

Attorneys for Defendant
MONSANTO COMPANY

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF SAN FRANCISCO

DEWAYNE JOHNSON,

Plaintiff,

vs.

MONSANTO COMPANY,

Defendant.

Case No. CGC-16-550128

Exhibit 1012, Part 1 of 2

AFFIDAVIT AND SWORN REPORT OF SYLVIA D. HALL-ELLIS, Ph.D.

Trial Date: June 18, 2018
Time: 9:30 a.m.
Department: 504

Exhibit 1012 – Part 1 of 2

I, Scott Jeror, Publications Supervisor in the
Policy, Communications and Regulatory Affairs Directorate
of the Pest Management Regulatory Agency of Health Canada,
hereby certify that the attached document,
"Proposed Re-evaluation Decision PRVD2015-01, *Glyphosate*",
dated April 13, 2015,
is a true copy of the original document

Scott Jeror

Signed before me on May 18, 2018

Nicole Levasseur

Proposed Re-evaluation Decision PRVD2015-01

Glyphosate

(publié aussi en français)

13 April 2015

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Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6607 D
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Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide glyphosate, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing glyphosate for sale and use in Canada.

An evaluation of available scientific information found that products containing glyphosate do not present unacceptable risks to human health or the environment when used according to the proposed label directions. As a condition of the continued registration of glyphosate uses, new risk reduction measures are proposed for the end-use products registered in Canada. No additional data are being requested at this time.

This proposal affects the products containing glyphosate registered in Canada. Once the final re-evaluation decision is made, the registrant will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for glyphosate and presents the reasons for the proposed re-evaluation decision. It also proposes new risk reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of glyphosate.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

Health Canada's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health and the environment. Re-evaluation draws on data from registrants, published scientific reports, information from other regulatory agencies and any other relevant information.

In 2010, Health Canada published a re-evaluation work plan for glyphosate (REV2010-02) outlining the focus of this re-evaluation and indicating that the PMRA is working cooperatively with the United States Environmental Protection Agency on the re-evaluation of glyphosate. As part of this re-evaluation, the effect of Polyethoxylated Tallow Amines (POEA) and the metabolite and transformation product Aminomethylphosphonic acid (AMPA) are also included.

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Is Glyphosate?

Glyphosate is a non-selective herbicide registered for post-emergence control of a wide spectrum of weeds including annual and perennial broadleaf and grassy weeds, weedy trees and brush. It is registered under various forms including glyphosate acid, glyphosate isopropylamine or ethanolamine salt, glyphosate mono-ammonium or diammonium salt, glyphosate potassium salt and glyphosate dimethylamine salt. Another form, glyphosate trimethylsulfonium salt, was voluntarily discontinued by the registrant and therefore is not included in the current re-evaluation.

Glyphosate is registered for use on the following Use-Site Categories (USC): Forests and Woodlots, Industrial Oil Seed Crops and Fibre Crops, Terrestrial Feed Crops, Terrestrial Food Crops, Industrial and Domestic Vegetation Control Non-food Sites, Ornamentals Outdoors and Turf.

Glyphosate products are formulated as solutions, pastes or tablets and can be applied using ground or aerial equipment. Some special application techniques are also used.

Health Considerations

Can Approved Uses of Glyphosate Affect Human Health?

Products containing glyphosate acid are unlikely to affect your health when used according to label directions.

Potential exposure to glyphosate may occur through the diet (food and water), when handling and applying the products containing glyphosate, or by entering treated sites. When assessing health risks, two key factors are considered: the levels at which no health effects occur in animal testing and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose at which no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much higher) than levels to which humans are normally exposed when glyphosate products are used according to label directions.

In laboratory animals, glyphosate was of low acute oral, dermal and inhalation toxicity. Glyphosate did not cause skin irritation or an allergic skin reaction. It was severely irritating to the eyes.

Short and long term (lifetime) animal toxicity tests, as well as numerous peer-reviewed studies from the published scientific literature were assessed for the potential of glyphosate to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints used for risk assessment included clinical signs of toxicity and developmental effects. There was no indication that the young were more sensitive than the adult animal. The risk assessment approach ensures that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

The World Health Organization's (WHO) International Agency for Research on Cancer (IARC) recently assigned a hazard classification for glyphosate as "probably carcinogenic to humans". It is important to note that a hazard classification is not a health risk assessment. The level of human exposure, which determines the actual risk, was not taken into account by WHO (IARC). Pesticides are registered for use in Canada only if the level of exposure to Canadians does not cause any harmful effects, including cancer.

Residues in Food and Water

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Potential acute and chronic dietary exposures to glyphosate were estimated from residues of glyphosate and relevant metabolites in both treated crops and drinking water. Exposure to different subpopulations, including children and women of reproductive age, were considered. The acute dietary exposure estimate (in other words, from food and drinking water) at the 95th percentile represents 31% of the acute reference dose (ARfD) for females 13-49 years of age and ranges from 12% to 45% of the ARfD for all other population subgroups. The chronic dietary exposure estimate for the general population represents 30% of the acceptable daily intake (ADI). Exposure estimates for population subgroups range from 20% of the ADI (for adults aged 50 years or older) to 70% of the ADI (for children 1-2 years old). Thus, acute and chronic dietary risks are not of concern.

The *Food and Drugs Act* prohibits the sale of adulterated food; that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose a health risk concern.

Canadian MRLs for glyphosate are currently specified for a wide range of commodities (MRL database). Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specific MRL, are regulated under Subsection B.15.002(1) of the Food and Drug Regulations, which requires that residues do not exceed 0.1 ppm. The current MRLs for glyphosate can be found in Appendix VII of this document. Separate MRLs have been established for the trimethylsulfonium (TMS) cation, the major metabolite of the glyphosate-TMS salt, in/on a variety of commodities. Given that all glyphosate-TMS-containing products have been discontinued, it is proposed that all MRLs for the TMS cation be revoked.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern when used according to label directions.

Residential exposure may occur from the application of products containing glyphosate to residential lawns, and turf (including golf courses). Residential handler exposure would occur from mixing, loading and applying domestic-class glyphosate products. These products can be applied as a liquid by a manually pressurized handwand, backpack, sprinkler can and ready-to-use sprayer.

Residential postapplication exposure may occur while performing activities on treated areas. Treated areas include areas treated by residential handlers as well as residential areas treated by commercial applicators. Exposure would be predominantly dermal. Incidental oral exposure may also occur for children (1 to < 2 years old) playing in treated areas.

For all domestic class products, the target dermal and inhalation margins of exposure (MOE) were met for adults applying glyphosate and are not of concern. Residential postapplication activities also met the target dermal MOE for all populations (including golfers) and are not of concern. For incidental oral exposure, the target oral MOEs were met for children (1 to < 2 years old) and are not of concern.

Non-occupational scenarios were aggregated with background (chronic) dietary exposure (food and drinking water). The resulting aggregate risk estimates reached the target MOE for all uses and are not of concern.

Non-occupational risks from bystander dermal exposure are not of concern.

Bystander exposure may occur when the general public enter non-cropland areas (for example, hiking through forests or parks) that have recently been treated with glyphosate. The resulting risk estimates associated with bystander dermal exposure exceeded the target MOE for all populations and are not of concern.

Occupational Risks from Handling Glyphosate

Occupational risks to handlers are not of concern when used according to label directions.

Risks to handlers are not of concern for all scenarios. Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation, risk estimates associated with mixing, loading and applying activities exceeded target dermal and inhalation MOEs and are not of concern.

Postapplication risks are not of concern for all uses.

Postapplication occupational risk assessments consider exposures to workers entering treated sites in agriculture. Based on the current use pattern for agricultural scenarios reviewed for this re-evaluation, postapplication risks to workers performing activities, such as scouting, exceeded target dermal MOEs and are not of concern. A restricted entry interval of 12 hours is proposed for agricultural sites.

Polyethoxylated Tallow Amines

POEA is a family of several compounds that are used as surfactants in many glyphosate products registered in Canada. No human health risks of concern were identified, provided end-use products contain no more than 20% POEA by weight. All of the currently registered glyphosate end-use products in Canada meet this limit.

Environmental Considerations

What Happens When Glyphosate Is Introduced Into the Environment?

When used according to proposed label directions, glyphosate products do not pose an unacceptable risk to the environment. Labelled risk-reduction measures mitigate potential risks posed by glyphosate formulations to non-target plants and freshwater/marine/estuarine organisms.

When glyphosate is released into the environment, it can enter soil and surface water. Glyphosate breaks down in soil and water and is not expected to persist for long periods of time. Glyphosate produces one major transformation product in soil and water, aminomethyl phosphonic acid (AMPA), which can persist in the environment. Carryover of glyphosate and AMPA into the next growing season is not expected to be significant. Glyphosate and AMPA are not expected to move downward through the soil and are unlikely to enter groundwater.

Glyphosate dissolves readily in water but is expected to move into sediments in aquatic environments. Glyphosate is not expected to enter the atmosphere. Glyphosate and AMPA are unlikely to accumulate in animal tissues.

Certain glyphosate formulations include a surfactant composed of POEA compounds. At high enough concentrations, POEA is toxic to aquatic organisms but is not expected to persist in the

environment. While, in general, glyphosate formulations that contain POEA are more toxic to freshwater and marine/estuarine organisms than formulations that do not contain POEA, they do not pose an unacceptable risk to the environment when used as directed on the label.

In the terrestrial environment the only area of risk concern identified from the available data was for terrestrial plants and therefore spray buffer zones are required to reduce exposure to sensitive terrestrial plants.

Glyphosate formulations pose a negligible risk to freshwater fish and amphibians, but may pose a risk to freshwater algae, freshwater plants, marine/estuarine invertebrates and marine fish if exposed to high enough concentrations. Hazard statements and mitigation measures (spray buffer zones) are required on product labels to protect aquatic organisms.

Glyphosate, AMPA and POEA do not meet all Toxic Substances Management Policy (TSMP) Track 1 criteria and are not considered Track 1 substances. Other than incident reports of damage to plants, there are currently no environmental incident reports involving glyphosate in Canada.

Value Considerations

What is the Value of Glyphosate?

Glyphosate plays an important role in Canadian weed management in both agricultural production and non-agricultural land management and is the most widely used herbicide in Canada.

Glyphosate is an important herbicide for Canadian agriculture, for the following reasons:

- Due to its broad and flexible use pattern and its wide weed-control spectrum, it is the most widely used herbicide in several major crops grown in Canada such as canola, soybean, field corn and wheat. It is also one of only a few herbicides regularly used in fruit orchards such as apple.
- It is the essential herbicide for use on the glyphosate tolerant crops (GTCs) including canola, soybean, corn, sweet corn and sugar beet. The combination of GTCs and glyphosate has been adopted as an important agricultural production practice in Canada.
- It has a wide application window ranging from pre-seeding to after seeding (prior to crop emergence), in-crop, pre-harvest or post-harvest, providing a flexible and effective weed management program.
- It is one of few herbicides that can also be used as harvest management and desiccation treatment.
- Post-harvest stubble treatment with glyphosate allows reduced or zero tillage, which has facilitated the adoption of conservation agriculture that results in improved soil quality.

Glyphosate is also an important weed management tool and is widely used for weed control in non-agricultural land management, such as forestry, industrial areas, and along rights-of-way. It is an effective tool for control of many invasive weed species and is also used in the control of toxic plants such as poison ivy.

Proposed Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of glyphosate, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- To protect workers entering treated sites a restricted-entry interval of 12 hours is proposed for agricultural uses.

- To protect bystanders, a statement indicating to apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal is required.

Environment

- Environmental hazard statements to inform users of its toxicity to non-target species.

- Spray buffer zones to protect non-target terrestrial and aquatic habitats are required.

- To reduce the potential for runoff of glyphosate to adjacent aquatic habitats, precautionary statements for sites with characteristics that may be conducive to runoff and when heavy rain is forecasted are required. In addition, a vegetative strip between the treatment area and the edge of a water body is recommended to reduce runoff of glyphosate to aquatic areas.

What Additional Scientific Information is Being Requested?

There are no additional data requirements proposed as a condition of continued registration of glyphosate products.

Next Steps

Before making a final re-evaluation decision on glyphosate, the PMRA will consider any comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on glyphosate. The PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

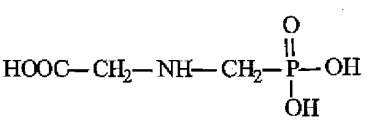
1.0 Introduction

Glyphosate is a non-selective systemic herbicide. As an aminophosphonic analogue of the natural amino acid glycine, glyphosate is classified as a Weed Science Society of America Group 9 herbicide. It disrupts the shikimic acid pathway through inhibition of the enzyme 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase. The resulting deficiency in EPSP production leads to reductions in aromatic amino acids (phenylalanine, tyrosine and tryptophan) that are vital for protein synthesis and plant growth.

Following the re-evaluation announcement for glyphosate, the registrants of the technical grade active ingredient indicated their support to continue registration of all uses included on the labels of end-use products (EPs) containing glyphosate in Canada. Registrants of all Canadian glyphosate products are listed in Appendix I.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common Name		Glyphosate
Function		Herbicide
Chemical Family		Organophosphorus
Chemical Name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	*N*-(phosphonomethyl)glycine
2	**Chemical Abstracts Service (CAS)**	*N*-(phosphonomethyl)glycine
CAS Registry Number		1071-83-6
Molecular Formula		$C_3H_8NO_5P$
Structural Formula		
Molecular Weight		169.1

The purity (in other words, guarantee) of the currently registered technical grade active ingredient is provided in Appendix I.

Identity of relevant impurities of human health or environmental concern include the following:

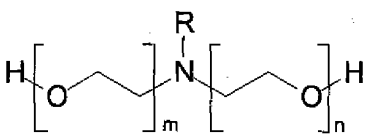
Based on the manufacturing process used, impurities of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	1.31×10^{-2} mPa
Ultraviolet (UV) / visible spectrum	Not expected to absorb at $\lambda > 300$ nm
Solubility in water at 20°C	10.5 g/L (pH 1.9)
n-Octanol/water partition coefficient at 20 °C	Log $K_{ow} < -3.2$ (pH 2-5); $K_{ow} < 6.3 \times 10^{-4}$
Dissociation constant (p*K*a)	2.34 (20°C), 5.73 (20°C), 10.2 (25°C)

2.3 Polyethoxylated Tallow Amines

Polyethoxylated tallow amines (POEA) are surfactants consisting of a family of many compounds. The general structure for POEA is as follows:



In Canada, majority of the currently registered glyphosate end-use products contain the surfactant POEA.

2.4 Description of Registered Glyphosate Uses

Appendix I lists all glyphosate products that are registered under the authority of the *Pest Control Products Act* as of 3 May 2012. A total of 169 products contain glyphosate including 19 technical grade active ingredients, 19 Manufacturing Concentration, 97 Commercial Class end-use products and 34 Domestic Class end-use products. Although glyphosate is registered in various forms, there are no differences in efficacy and toxicity end-points among glyphosate forms. Therefore, the assessments were based on the glyphosate acid form.

Appendix IIa and IIb list all the Commercial Class and Domestic Class uses, respectively, for which glyphosate is currently registered. All uses including uses registered through the PMRA User Requested Minor Use Label Expansion (URMULE) program were supported by the registrants at the time of initiation of re-evaluation and were therefore considered in the health and environmental risk assessments. Under the URMULE program, the data supporting the minor use registrations are generated by a user group or by the Pest Management Centre of Agriculture and Agri-Food Canada.

Uses of glyphosate belong to the following use site categories: Forests and Woodlots (Use-Site Category (USC 4), Industrial Oil Seed Crops and Fibre Crops (USC 7), Terrestrial Feed Crops (USC 13), Terrestrial Food Crops (USC 14), Industrial and Domestic Vegetation Control Non-food Sites (USC 16), Ornamentals Outdoors (USC 27) and Turf (USC 30).

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

The toxicology database for glyphosate acid (hereafter called glyphosate) was extensive, consisting of all guideline toxicity studies required to characterize toxicity of a pesticide. For each study type currently required, several studies were available to satisfy the data requirements. Considered individually, some of these studies do not meet the current standards for testing, although they were considered acceptable at the time of their initial evaluation. Overall, the database was considered adequate to define the majority of the toxic effects that may result from exposure to glyphosate. Relevant acceptable scientific studies published in the peer-reviewed literature were also incorporated into the hazard assessment, including those studies that were considered by the World Health Organization's (WHO) International Agency for Research on Cancer (IARC) in their recent hazard classification for glyphosate. Hazard identification, including carcinogenic potential, is an important component in the determination of the potential human health risk of a pesticide. The determination of such risk, however, is not solely driven by the hazard profile but is also a function of the potential exposure to the pesticide. For this reason, both the hazard and exposure potential must be considered together when performing a human health risk assessment for a pesticide, since an identified hazard may be offset by the fact that the potential for human exposure is considered to be sufficiently low so as not to pose a risk of concern to human health.

Metabolism studies in rats indicated that glyphosate was incompletely but rapidly absorbed following administration of single low, single high and repeated oral doses. At low doses, the peak plasma concentration was reached within an hour of dosing. Following single high doses, the peak plasma concentration was reached five hours after dosing. The bioavailable fraction was about 20-23%. The parent compound was the primary form detected in tissues and excreta, indicating glyphosate was not metabolized extensively. Approximately 1-5% of the administered dose (AD) was distributed in the gastrointestinal (GI) tract, liver, kidneys, bone, lungs, spleen, salivary glands and brain. The distribution phase was rapid with a distribution half-life of 20-30 minutes. About 1-9% of the AD was metabolized to aminomethylphosphonic acid (AMPA). Higher quantities (6-9% of AD) of AMPA were detected in feces than in urine

(≤1% of AD). In single low- or high-dose oral studies, the excretion of glyphosate was rapid and nearly complete after 72 hours. The primary route of excretion was the feces (80-90% of AD) followed by urine (10-20% of AD) following single low, single high, and repeated oral doses. The elimination half-life of glyphosate was around 14 hours while the elimination half-life of AMPA was approximately 15 hours following oral doses of glyphosate.

Glyphosate was of low acute oral and inhalation toxicity in the rat, and of low dermal toxicity in the rabbit. Glyphosate was neither a dermal irritant nor a dermal sensitizer. It was severely irritating to rabbit eyes.

In oral repeat-dose toxicity studies, effects on salivary glands in rodents, decreased body weight, body-weight gain, and clinical signs of toxicity were consistently observed in all test species. Additional target organs of toxicity were liver and kidney in rats and dogs, and stomach in mice in most of these studies at higher dose levels. Changes in several clinical chemistry parameters were consistent with a mild dehydration. The high doses in most studies reached or exceeded the limit dose of testing (in other words, 1000 mg/kg bw/day) due to the low toxicity of glyphosate.

In guideline and non-guideline (National Toxicology Program-NTP) 90-day oral studies in rodents, the primary effect in rats was an increased incidence and severity of cytoplasmic alterations of the parotid and submandibular glands. Although this effect was also noted in mice, it occurred at a dose that exceeded the limit dose. The effects in the parotid gland in Sprague Dawley rats was considered to be at the threshold of toxicological adversity at the lowest dose tested (30 mg/kg bw/day) due to the mild nature of this effect, and given that these effects in the rat salivary glands were commonly observed starting at 100 mg/kg bw/day in other toxicity studies. In a 28-day oral study, salivary gland effects were noted in three rat strains at the limit dose, but with varying degrees of severity and reversibility. A 14-day mechanistic oral study in rats designed to test the hypothesis that the salivary gland effects of glyphosate were mediated through an adrenergic pathway did not provide conclusive evidence to substantiate this mechanism.

Other effects noted in the short-term studies included increased kidney and lungs weights in male mice, and decreased thymus weights, body weight, body-weight gain, and increased plasma bile acids in rats. In addition, decreased sperm counts were also noted in rats at dose groups where sperm analysis was conducted (three highest doses), with increased testis weights observed at higher dose levels. However, no effects were observed in the other examined sperm parameters (epididymal weights, epididymal sperm motility, total spermatid heads, and total spermatid heads/gram caudal tissue). The estrus cycle length was also slightly longer (5.4 days compared to 4.9 days) in the high-dose females.

In the 21-day dermal toxicity studies in rats and rabbits, no treatment-related systemic or dermal effects were noted in Wistar rats at doses up to 1000 mg/kg bw/day, while SD rats had increased incidences of erythema and desquamation of the skin and increased incidences of unilateral papillary necrosis, urothelial hyperplasia and pelvic dilation in the kidneys at this dose. Slight dermal irritation, but no systemic toxicity was observed in New Zealand White (NZW) rabbits. In a 90-day dog study, the only adverse effects noted were decreases in several clinical chemistry parameters at a very high dose, which were consistent with decreased food consumption.

Decreased ovary weights and increased serum ALP were also observed in females at the high dose. Three 12-month dog studies reported more systemic toxicity (body weight and epididymal effects) at lower dose levels in males compared to females. However, males were not more sensitive than females in other test species. One 12-month study had increased incidences of clinical signs of toxicity and increased liver and kidney weights in males. A second study reported a dose-related increased incidence of lymphoid nodules in the epididymis and decreased pituitary weight in males, with kidney tubular regeneration accompanied by epithelial cells and urinary protein in females at this same dose. Increased absolute and relative testis and ovary weights were found in the high-dose group.

A third study reported decreased levels of plasma phosphorus, decreased epididymides weights and increased transitional epithelial hyperplasia in the kidneys in males, with decreased plasma phosphorus levels and thyroid weights in the high-dose females only.

Glyphosate was not genotoxic in the standard battery of in vitro and in vivo tests assessing gene mutation, chromosome aberration, and mouse micronucleus anomalies. There was no evidence of carcinogenicity in four long-term rat studies. In mice, treatment with glyphosate was associated with a marginal increase in the incidence of unilateral tubulostromal adenomas in the ovaries, but only at the limit dose of testing. Although historical control data were unavailable, based on the marginal increase in the incidence of the ovarian tumours coupled with its occurrence at the limit dose and the negative findings in a battery of genotoxicity assays, these tumours were considered to be of low concern for human health risk assessment.

Chronic effects were assessed in four long-term rat toxicity studies. One study did not elicit any overt toxicity as the dose range was insufficiently high, whereas the high-dose group in the other three studies either exceeded or was at the limit dose of testing. Effects included increased incidences and severity of cellular alteration in the submandibular and parotid glands, and inflammation and hyperplasia of the squamous mucosa in the stomach in both sexes; decreased and/or absence of epididymal sperm, degeneration of seminiferous tubules, increased testis weight and testicular effects, and myeloid hyperplasia of the bone marrow in males; and increased kidney papillary necrosis in females. At or above the limit dose, males had a marginally increased incidence of necrosis in the glandular stomach and an increase in kidney papillary necrosis and prostatitis, while females had increased incidences of mammary gland hyperplasia and cataracts/lens fiber degeneration.

In three gavage rat developmental-toxicity studies, the high doses reached or exceeded the limit dose and no evidence for sensitivity of the young was observed. Maternal toxicity occurred at the limit dose in rats and included clinical signs of toxicity (salivation, and noisy respiration), hydronephrosis and one total litter resorption. In addition, mortality, and decreased body weight and body-weight gain were observed at doses above the limit dose. Developmental toxicity was also observed only at or above the limit dose. Effects comprised an increased incidence of skeletal variants, wavy ribs/rib distortions and hydroureter. Decreased fetal weight, reduced ossification, decreased numbers of viable fetuses/dam, and an increased incidence of absent kidneys and ureters were also observed at a dose that exceeded the limit dose by over three-fold. In three gavage developmental toxicity studies in rabbits, maternal toxicity comprised mainly of GI disturbances at similar dose levels, with excessive maternal mortality occurring at higher

doses in one study. Post-implantation loss and intra-uterine deaths were commonly noted at the highest dose tested. Developmental toxicity included decreased fetal body weight, reduced ossification, and increased incidences of 27th presacral vertebrae, and 13th rudimentary and full ribs. In one study an increased incidence of fetal cardiovascular variations accompanied with an increased incidence of fetal cardiovascular malformations (mainly interventricular septal defects) was noted at the highest dose tested. The observation of cardiovascular malformations was considered a serious effect in this study, although maternal toxicity was present at the same dose level. No evidence of sensitivity of the young was noted.

The reproductive toxicity of glyphosate was investigated in three, two-generation toxicity studies in rats. In two of these studies, the high dose reached or exceeded the limit dose. Parental toxicity included an increased incidence of hypertrophy of acinar cells with granular cytoplasm in the parotid and submandibular glands in both parental generations. At doses at or above the limit dose, there was decreased body weight and an increased incidence of soft stools or diarrhea in both parental generations, decreased body weight during gestation in F_1 females, increased liver and kidney weights in the P generation with increased incidences of transitional epithelial hyperplasia in the kidney, and glandular and luminal dilatation of the uterus in the F_1 generation. Reproduction toxicity was noted only at a dose that exceeded the limit dose and included decreased litter size with no increase in the number of dead pups per litter. There were no effects on mating, pregnancy and fertility indices, sperm parameters, or reproductive performance. However, an increased mean number of estrual cycles (P generation) and decreased mean estrual cycle length (P and F_1 generations) in females was noted at the limit dose. Offspring toxicity consisted primarily of decreased body weight in pups. At doses at or exceeding the limit dose, there were decreases in litter size, a marginal increase in tubular dilatation/cysts in the kidneys, decreased pup spleen and thymus weights and an increased incidence of unilateral and bilateral pelvic dilatation of the kidneys. Although decreased body weight in pups was observed at non-maternally toxic dose in two of the three studies, this reduction in body weight was considered marginal and evidence from other studies in rats indicated that effects on the salivary glands (not assessed in these two reproduction toxicity studies) would be expected to occur at this dose level in the adult animals. Thus, no evidence of sensitivity of the young was observed in these reproduction toxicity studies.

The neurotoxic potential of glyphosate was investigated in acute and 90-day oral neurotoxicity studies in rats. In the acute oral (gavage) neurotoxicity study, decreased motor activity was observed in females on the first day of dosing. An increased incidence of reduced splay reflex and decreased motor activity in males was observed along with other findings (decreased activity, subdued behaviour, hunched posture, pinched in sides, tip-toe gait, hypothermia, abnormal respiratory noise, diarrhea, and a single mortality in females) at a dose level that was two-fold greater than the limit dose. In the 90-day dietary neurotoxicity study, decreased body-weight gain and food efficiency were noted in males. In the high-dose group, decreased body weight and an increased incidence of decreased pupillary response to light were observed in males. Decreased body-weight gain and motor activity on week 5 were observed in females of the high-dose group. Overall, findings in both acute and short-term neurotoxicity studies were considered to reflect systemic/general toxicity rather than evidence of selective neurotoxicity.

In a 28-day immunotoxicity study, dose-related increased T-cell dependent antibody response and total spleen activity were observed in the test animals. In addition, a non-dose related increase in spleen cellularity was noted. Although this test was designed to examine immunosuppression, an altered function of the immune system could not be ruled out.

Epidemiology

A number of published epidemiology studies were reviewed for incorporation into the hazard assessment of glyphosate, which included the subset of epidemiological information considered by the WHO (IARC) in their summary report for glyphosate. However, the majority lacked adequate characterization of glyphosate exposure, rendering them of limited use for supplementing the hazard assessment. A prospective cohort study of licensed pesticide applicators in Iowa and North Carolina, known as the Agricultural Health Study, examined the relationship between glyphosate exposure and cancer incidence. The most relevant finding in this study was the suggested association between multiple myeloma and glyphosate exposure. However, a number of confounding factors (for example, the lack of consideration of exposure to UV radiation from sunlight) rendered these findings inconclusive and chance occurrence could not be ruled out. The study investigators also indicated that this association required additional follow-up.

Cancer Assessment

In consideration of the strength and limitations of the large body of information on glyphosate, which included multiple short and long term (lifetime) animal toxicity studies, numerous in vivo and in vitro genotoxicity assays, as well as the large body of epidemiological information, the overall weight of evidence indicates that glyphosate is unlikely to pose a human cancer risk. This is consistent with all other pesticide regulatory authorities world-wide, including the most recent, ongoing comprehensive re-evaluation by Germany (Rapporteur Member State for the European Union) that was published for public consultation in 2014 (http://dar.efsa.europa.eu/dar-web/provision).

Toxicity Studies on the Metabolite Aminomethylphosphonic Acid

In a single dose metabolism study with radiolabelled metabolite aminomethylphosphonic acid (AMPA), absorption was incomplete. Small quantities of AMPA were recovered in most tissues, with the highest percent detected in the muscle and the GI tract. Over 90% of the AD was excreted as unchanged AMPA, indicating that AMPA was not further metabolized. Most of the excretion occurred via feces compared to urine. Overall, this study showed that AMPA possessed metabolic patterns that were similar to those of its parent compound, glyphosate.

AMPA was of low acute oral and dermal toxicity in the rat. AMPA was neither a dermal irritant in rabbits nor a dermal sensitizer in guinea pigs. It was minimally irritating to rabbit eyes.

In a 90-day oral study in rats, decreased liver weights were observed in males. An increased incidence and severity of mucosal hyperplasia of the bladder was also observed at a dose level greater the limit dose. Decreased body weight, and body-weight gain were observed in males.

An increased incidence of renal pelvic epithelial hyperplasia was observed at a dose that was about five-fold greater than the limit dose. In a supplemental oral 90-day study in rats, a slight reduction in body-weight gain in females and a slight increase in kidney weights in males were observed at the limit dose.

In a 30-day oral study in dogs, decreased red blood cell counts, hemoglobin concentration, and hematocrit levels were noted in females in all dose groups and in the high-dose group in males. Increased reticulocyte counts also accompanied these effects. However, in a 90-day oral study in dogs, no toxicity was observed at similar dose levels.

AMPA tested negative for gene mutation tests in bacteria and mammalian lymphoma cell lines and also tested negative in mouse micronucleus and unscheduled DNA synthesis assays.

In a gavage developmental toxicity study in rats, increased incidences of hair loss and soft and mucoid feces were noted in dams. Decreased body weight, body-weight gain and food consumption was observed at the limit dose of testing. Developmental toxicity included decreased body weight at the limit dose. No evidence of the sensitivity of the young was observed in this study. In a supplemental developmental toxicity study, no maternal toxicity was noted. Developmental toxicity included increased incidences of reduced ossification and skeletal variations.

Overall, based on the available toxicity studies, AMPA was considered of no greater toxicological concern than glyphosate. Although no repeated dose toxicity studies were available for glyphosate metabolites resulting from genetically modified organism (GMO) crops (in other words, N-acetylglyphosate and N-acetyl AMPA), these metabolites were not considered to be of a greater toxicological concern than the parent compound, glyphosate, based on a European Food Safety Authority assessment. In summary, glyphosate toxicology endpoints were considered adequate for the risk assessment of AMPA and the acetylated metabolites of glyphosate.

Results of the toxicology studies conducted on laboratory animals with glyphosate and AMPA are summarized in Table 1A and Table 1B of Appendix III, respectively. The toxicology endpoints for use in the human health risk assessment are summarized in Table 2 of Appendix III.

Pest Control Products Act Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account the completeness of the data with respect to the exposure of and toxicity to infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to completeness of the toxicity database as it pertains to the toxicity to infants and children, the database contains several studies for each type of required guideline study including developmental toxicity studies in rats and rabbits, and two-generation reproduction toxicity studies in rats. In addition, applicable studies from the published scientific literature were considered, including reviews of studies that were submitted to the European Union Glyphosate Task Force.

With respect to identified concerns relevant to the assessment of risk to infants and children, the two-generation reproduction toxicity studies in rats provided no indication of increased sensitivity of the young. In these studies, offspring toxicity commonly consisted of decreased body weight observed at dose levels that produced toxicity to the adult animals. In addition, the prenatal developmental toxicity studies in rats did not demonstrate increased sensitivity of the fetuses to in utero exposure of glyphosate. In these studies, decreased fetal weights and number of viable fetus/dam, in addition to developmental abnormalities (absent kidneys and ureters, skeletal variants, wavy ribs, a single incidence of hydroureter) were observed at dose levels that reached or exceeded the limit dose and produced moderate to severe toxicity in maternal animals.

In developmental toxicity studies in the rabbits, there was no observed increase in susceptibility of the fetuses to in utero exposure of glyphosate. In these studies, an increased incidence of reduced ossification at various sites was commonly noted at dose levels that produced maternal toxicity. In one of these studies, an increased incidence of fetal cardiovascular malformations, comprised mainly of interventricular septal defects, was noted in the presence of maternal toxicity at the highest dose tested.

Overall, the endpoints in the young were well characterized. The increased incidence of fetal cardiovascular malformations noted in a rabbit developmental toxicity study was considered a serious endpoint. However, the concern regarding the serious nature of this effect was tempered by the presence of maternal toxicity at the same and lower dose levels in this study. Therefore, the *Pest Control Products Act* factor was reduced to three-fold when this endpoint was used to establish the point of departure. For all other scenarios, the *Pest Control Products Act* factor was reduced to one-fold since there were no residual uncertainties with respect to the completeness of the data, or with respect to potential toxicity to infants and children.

3.2 Dietary Exposure and Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to glyphosate from potentially treated imported foods is also included in the assessment. These dietary assessments are age specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when risk exceeds 100% of the reference dose. The PMRA Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute, chronic and cancer-risk assessment procedures.

Residue estimates used in the dietary risk assessment may be based conservatively (in other words, use upperbound estimates) on the maximum residue limits (MRLs) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency (CFIA) National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program (USDA PDP). Specific and empirical processing factors as well as specific information regarding percent of crops treated may also be incorporated to the greatest extent possible.

In situations where the need to mitigate dietary exposure has been identified, the following options are considered. Dietary exposure from Canadian agricultural uses can be mitigated through changes in the use pattern. Revisions of the use pattern may include such actions as reducing the application rate or the number of seasonal applications, establishing longer pre-harvest intervals (PHIs), and/or removing uses from the label. In order to quantify the impact of such measures, new residue chemistry studies that reflect the revised use pattern would be required. These data would also be required in order to amend MRLs to the appropriate level. Imported commodities that have been treated also contribute to the dietary exposure and are routinely considered in the risk assessment. The mitigation of dietary exposure that may arise from treated imports is generally achieved through the amendment or specification of MRLs.

Acute and chronic exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model – Food Commodity Intake Database™ (DEEM-FCID™, Version 2.14), which incorporates consumption data from the United States Department of Agriculture (USDA) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994 to 1996 and 1998. For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendices IV, V and VI.

3.2.1 Determination of Acute Reference Dose

General Population (Excluding Females 13-49 Years of Age)

To estimate acute dietary risk (one day), a rabbit developmental toxicity study with a no observed adverse effect level (NOAEL) of 100 mg/kg bw/day was selected for risk assessment. An increased incidence of soft stools and diarrhea was observed immediately following the start of dosing at 175 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. The *Pest Control Products Act* factor was reduced to one-fold for the reasons outlined in the *Pest Control Products Act* Hazard Characterization section. Therefore, the composite assessment factor (CAF) is 100.

The ARfD is calculated according to the following formula:

$$\textbf{ARfD} = \frac{\textbf{NOAEL}}{\textbf{CAF}} = \frac{\textbf{100 mg/kg bw/day}}{\textbf{100}} = \textbf{1.0 mg/kg bw of glyphosate}$$

Females 13-49 years of age

To estimate acute dietary risk (one day) for females 13-49 years of age, a rabbit developmental toxicity study with a NOAEL of 150 mg/kg bw/day was selected for risk assessment. An increased incidence of cardiovascular malformations was observed at 450 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. The *Pest Control Products Act* factor was reduced to three-fold for the reasons outlined in the *Pest Control Products Act* Hazard Characterization section. Therefore, the composite assessment factor (CAF) is 300.

The ARfD is calculated according to the following formula:

$$\textbf{ARfD} = \frac{\textbf{NOAEL}}{\textbf{CAF}} = \frac{\textbf{150 mg/kg bw/day}}{\textbf{300}} = \textbf{0.5 mg/kg bw of glyphosate}$$

3.2.2 Acute Dietary Exposure and Risk Assessment

The acute dietary risk was calculated considering the highest ingestion of glyphosate that would be likely on any one day, and using food consumption and food residue values. The expected intake of residues is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is not of concern.

The acute dietary exposure assessments were conducted for the acid form of glyphosate (including all the metabolites comprised in the residue definition), which is considered to be the common moiety for all currently registered forms of glyphosate.

Following the PMRA's tiered approach, basic (in other words, upperbound) exposure assessments were performed for females 13-49 years old and all other population subgroups by using MRL/tolerance-level residues for all commodities, default processing factors and assuming that all crops were 100% treated. Canadian MRLs, United States tolerances or Codex MRLs, whichever was greater, were used for all crops, including imports. Drinking water contribution to the exposure was accounted for by direct incorporation of the appropriately estimated environmental concentration (EEC), obtained from water modelling (see Section 3.3.1), into the dietary exposure evaluation model.

The acute exposure estimate at the 95th percentile for females 13-49 years old is 31% of the ARfD and therefore is not of concern. Acute exposure estimates at the 95th percentile for population subgroups other than females 13-49 years old range from 12% to 45% of the ARfD and therefore are also not of concern.

3.2.3 Determination of Acceptable Daily Intake

To estimate dietary risk of long-term exposure, the 26-month chronic toxicity and carcinogenicity study in rats with a NOAEL of 32/34 mg/kg bw/day was selected for risk assessment. No treatment-related effects were noted in this study. This was the highest (combined) NOAEL for the long-term toxicity studies in rats. The lowest (combined) LOAEL was 100 mg/kg bw/day, based on reduction in body weight in male rats in the interim sacrifice and increased incidences and severity of cellular alterations in the parotid and submandibular glands in a 24-month chronic toxicity and carcinogenicity study in rats. These NOAELs/LOAELs were further supported by the NOAEL of 30 and the lowest observed adverse effect level (LOAEL) of 100 mg/kg bw/day in one-year studies in dogs. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intra-species variability were applied. The *Pest Control Products Act* was reduced to one-fold for the reasons outlined in the *Pest Control Products Act* Hazard Characterization section. Therefore, the CAF is 100.

The ADI is calculated according to following formula:

$$\textbf{ADI} = \frac{\textbf{NOAEL}}{\textbf{CAF}} = \frac{\textbf{32 mg/kg bw/day}}{\textbf{100}} = \textbf{0.3 mg/kg bw/day of glyphosate}$$

This ADI provides a margin of 500 to the NOAEL of 150 mg/kg bw/day for the fetal cardiovascular malformations in the rabbit developmental toxicity study.

3.2.4 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated by using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is not of concern.

The chronic dietary exposure assessments were conducted for the acid form of glyphosate (including all the metabolites comprised in the residue definition), which is considered to be the common moiety for all currently registered forms of glyphosate.

Following the PMRA's tiered approach, basic (in other words, upperbound) exposure assessments were performed for the general population and all population subgroups by using MRL/tolerance-level residues for all commodities, default processing factors and assuming that all crops were 100% treated. Canadian MRLs, US tolerances or Codex MRLs, whichever was greater, were used for all crops, including imports. Drinking water contribution to the exposure was accounted for by direct incorporation of the appropriate EEC, obtained from water modelling (see Section 3.3.1), into the dietary exposure evaluation model.

The chronic exposure estimate for the general population is 30% of the ADI and, therefore, is not of concern. Exposure estimates for population subgroups range from 20% to 70% of the ADI and, therefore, are not of concern.

3.3 Exposure from Drinking Water

Residues of glyphosate and its metabolite aminomethylphosphonic acid (AMPA) in potential drinking water sources were estimated from modelling.

3.3.1 Concentrations in Drinking Water

Drinking water EECs of combined residues of glyphosate and its transformation product AMPA in potential sources of drinking water were calculated using PRZM/EXAMS models for a small reservoir. EECs in groundwater were not calculated as leaching to groundwater was not detected. Most scenarios were run using 50-year weather data. Level 2 (refined) surface water modelling was carried out with nine scenarios across Canada to reflect typical crop uses, application rates and timing and application methods. The highest surface water reservoir daily peak EEC value of 0.267 ppm and yearly average EEC value of 0.197 ppm for combined residues of glyphosate and AMPA (please refer to Appendix XI, Table XI.7) were used in the acute and the chronic dietary exposure assessments, respectively.

3.3.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure estimates were combined with food exposure estimates, with EEC point estimates incorporated directly in the dietary (food + drinking water) assessments. Please refer to Sections 3.2.2 and 3.2.4 for details.

3.4 Occupational and Non-Occupational Exposure and Risk Assessment

For the purpose of this assessment, information was summarized for glyphosate and each of the five salt forms. This integration of information was based on the fact that the majority of use patterns among the salt forms are similar and that although variations exist in terms of the range of use sites and rates of applications, these differences are limited.

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

3.4.1 Toxicology Endpoint Selection for Occupational and Non-Occupational Risk Assessment

Incidental Oral, Short-term Dermal and Inhalation Routes

For **incidental oral and occupational/bystander risk assessments for short-term dermal and inhalation routes**, a 90-day oral study in rats was selected. A NOAEL was not established in this study. The LOAEL was 30 mg/kg bw/day based on an increased incidence and severity of cellular alteration in the parotid gland. This LOAEL was considered to be at the threshold of toxicological adversity due to the mild nature of the cellular alteration in the parotid glands at this dose level. As a result, an uncertainty factor (UF_L) for extrapolating from a LOAEL to a NOAEL was not deemed necessary. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. Therefore, the target **Margin of Exposure (MOE) is 100**.

Intermediate- and Long-term Dermal and Inhalation Routes

For **occupational/bystander risk assessments for intermediate- and long-term and dermal and inhalation routes**, the 26-month chronic toxicity and carcinogenicity study in rats with a NOAEL of 32/34 mg/kg bw/day was selected for risk assessment. No treatment-related effects were noted in this study. This was the highest (combined) NOAEL for the long-term toxicity studies in rats. The lowest (combined) LOAEL was 100 mg/kg bw/day based on reduction in body weight in male rats in the interim sacrifice and increased incidences and severity of cellular alterations in the parotid and submandibular glands in a 24-month chronic toxicity and carcinogenicity study in rats. These NOAELS/LOAELS were further supported by the NOAEL of 30 and LOAEL of 100 mg/kg bw/day in one-year studies in dogs. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. Therefore, the target **Margin of Exposure (MOE) is 100**.

Dermal Absorption

Based on a chemical-specific in vivo dermal absorption study, a dermal absorption factor of 4% was determined for the exposure assessment of glyphosate.

3.4.2 Occupational Exposure and Risk Assessment

Workers can be exposed to glyphosate through mixing, loading, or applying the pesticide, and when entering a treated site to conduct activities such as scouting.

Mixer, Loader, and Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders and applicators. The following scenarios were assessed:

- Mixing/loading liquids.
- Liquid groundboom, aerial, airblast, mechanically pressurized handgun, backpack, roller, wick and other wiper implements, cut stump, right-of-way (ROW) sprayer, and injection application to trees.
- Injection application of pastes (pre-loaded cartridges) to trees.

Based on the number of applications and the timing of application, workers applying glyphosate would generally have a short (< 30 days) duration of exposure. Custom applicators may also have intermediate-term (in other words, up to several months) exposure for those crops with multiple applications. Injection applications to trees can occur year-round (except when the barks of trees are frozen), so exposure in these scenarios can be long-term.

Handler exposure was estimated based on the following personal protection:

Baseline PPE: Long sleeved shirt, long pants and chemical-resistant gloves (unless otherwise specified). For groundboom application, this scenario does not include gloves as the data quality was better for non-gloved scenarios than gloved scenarios.

Dermal and inhalation exposures were estimated using data from the *Pesticide Handlers Exposure Database* (PHED), *Version 1.1*. The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment (PPE).

Glyphosate is registered for cut stump applications for which no PHED scenario exists. It was assumed that exposure from mixing/loading and applying glyphosate by a manually pressurized handwand would be comparable to the squirt bottle method used for cut stump applications.

Glyphosate is registered for tree injection applications for which no PHED scenario exists. For this scenario, the mixing and loading (liquid) scenario was used to estimate exposure of preparing the solution and loading the cartridges. Applicator exposure is expected to be minimal as activities are conducted in a closed system. It was assumed that this scenario would be protective of the preloaded paste cartridges scenario, as exposure during mixing and loading the liquid solution would be higher.

Glyphosate is not applied by hose-end spray or low-pressure nozzle gun sprayer connected to a truck. Therefore, these application equipment types were not assessed in the applicator risk assessment.

Mixer/loader/applicator exposure estimates are based on the best available data at this time. Route-specific MOEs for mixer/loader and applicators for agricultural crops, commercial and recreational areas are outlined in Appendix VII, Tables 1 and 2. Calculated dermal, inhalation, and combined (total exposure from dermal and inhalation routes) MOEs for mixer/loaders and applicators of glyphosate exceeded target MOEs for all uses and are not of concern.

Postapplication Worker Exposure and Risk Assessment

The postapplication occupational risk assessment considered exposures to workers who enter treated sites to conduct agronomic activities involving foliar contact (for example, scouting). Based on the glyphosate use pattern, there is potential for short-term (< 30 days) postapplication exposure to glyphosate residues for workers.

Activity-specific transfer coefficients (TCs) from the Agricultural Re-entry Task Force (ARTF) were used to estimate postapplication exposure resulting from contact with treated turf and foliage at various times after application. A TC is a factor that relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination (for example, hand harvesting apples, scouting late season corn) and reflect standard clothing worn by adult workers. Postapplication exposure activities include (but are not limited to): scouting, weeding, and transplanting.

As glyphosate is a non-selective herbicide, applications are usually made in the dormant season or prior to planting. If application is required when the crop is developing, sprays are directed between rows, and shields, wipers and rollers are used to prevent crop damage. In this case, it is unlikely that there will be significant residues on the foliage of these crops to which workers could come into contact when performing various postapplication activities. However, some activities, such as scouting and irrigation, may result in contact with treated foliage. Therefore, these postapplication activities were assessed.

Dislodgeable foliar residue (DFR) and turf transferrable residues (TTR) refer to the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant or turf. There were no chemical-specific DFR or TTR studies submitted to the PMRA for the re-evaluation of glyphosate; therefore the following defaults were used:

- A default peak value of 25% of the application rate with a dissipation rate of 10% per day was used for DFR.
- A default peak value of 1% of the application rate with a dissipation rate of 10% per day was used for TTR.

For workers entering a treated site, restricted entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely enter after application. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE.

The PMRA is primarily concerned with the potential for dermal exposure for workers performing postapplication activities in crops treated with a foliar spray. Based on the vapour pressure of glyphosate, inhalation exposure is not likely to be of concern provided that the minimum 12-hour REI is followed.

Calculated dermal MOEs for worker postapplication exposure to glyphosate in commercial crops exceeded target MOEs and are not of concern. REIs were set at the standard minimum value of 12 hours for all postapplication activities. The postapplication exposure assessment is outlined in Appendix VII, Table 3.

3.4.3 Non-Occupational Exposure and Risk Assessment

Non-occupational risk assessment involves estimating risks to the general population, including youth and children, during or after pesticide application.

The United States Environmental Protection Agency (USEPA) has generated standard default assumptions for developing residential exposure assessments for both applicator and postapplication exposures when chemical- and/or site-specific field data are limited. These assumptions may be used in the absence of, or as a supplement to, chemical- and/or site-specific data and generally result in high-end estimates of exposure. These assumptions are outlined in the Standard Operating Procedures (SOPs) for Residential Pesticide Exposure Assessments (2012). The following sections from the Residential SOPs were used to assess residential exposure to glyphosate:

- Section 3: Lawns and Turf
- Section 4: Gardens and Trees

Residential Handler Exposure and Risk Assessment

A residential applicator would be an adult who purchased a domestic-class glyphosate product for outdoor residential use.

Residential applicators are assumed to be wearing shorts, short-sleeved shirts, shoes and socks. Based on label directions, domestic-class glyphosate products are assumed to be applied two times per year (with a seven-day interval); therefore they would have potential for short-term (1-30 days) exposure during application to lawns or turf.

Domestic-class glyphosate products are available in both liquid and tablet (water soluble) formulations. For tablet formulations, the label instructs the handler to open the tablet packages and, without touching the tablets, drop them directly into water to dissolve. This would result in minimal handler exposure to the tablet itself. Thus, the tablet formulation was not assessed separately, as it was assumed that the risk assessment for the liquid formulation, which has a higher level of exposure, would be protective of exposure from the tablet formulation.

Based on the typical use pattern, the major scenarios identified were:

- mixing and loading liquids
- mixing and loading of water soluble tablets
- manually pressurized handwand, backpack and sprinkler (liquid) application to lawns and turf and gardens and trees
- ready-to-use sprayer application to lawns and turf, and gardens and trees

Calculated dermal, inhalation, and combined (total exposure from dermal and inhalation routes) MOEs for residential handler exposure to glyphosate exceeded target MOEs and are not of concern. The residential handler risk assessment is outlined in Appendix VIII, Table 1.

Residential Postapplication Exposure and Risk Assessment

Residential postapplication exposure refers to an exposure scenario in which an individual is exposed through dermal, inhalation, and/or incidental oral (non-dietary ingestion) routes as a result of being in a residential environment that has been previously treated with a pesticide. The area could have been treated by a residential applicator using a domestic-class product or a commercial applicator hired to treat the residential area.

There is potential for short-term exposure to adults, youth (11 to < 16 years old), and children (6 to < 11 years old and 1 to < 2 years old) through contact with transferable residues following commercial applications of glyphosate to turf, as well as following domestic applications of glyphosate to lawns and turf. Adults, youth and children have the potential for postapplication dermal exposure; children (1 to < 2 years old) also have the potential for incidental oral exposure. As the use rate of domestic class products is greater than the commercial use rate for residential settings, the postapplication assessment for products applied by a residential applicator is protective of the postapplication exposure to homeowners, youth and children after a commercial application of glyphosate to turf.

The following scenarios were assessed for the postapplication exposure to glyphosate:

- Lawns and Turf
    - Adults, youth, and children (1 to < 2 years old) dermal exposure resulting from activities on turf
    - Adult and youth dermal exposure resulting from mowing
    - Adult, youth and children (6 to < 11 years old) dermal exposure resulting from golfing
    - Children (1 to < 2 years old) incidental oral exposure

As per label directions, glyphosate can be applied twice per year (with a seven-day interval). This assumption was taken into consideration when determining postapplication risk.

The PMRA is primarily concerned with the potential for dermal exposure for homeowners performing postapplication activities in treated residential areas. Non-dietary ingestion of soil was not assessed as glyphosate becomes inactive once in the soil.

Postapplication dermal exposure using activity-specific TCs was calculated using estimates for foliar residue, leaf-to-skin residue transfer for individuals contacting treated foliage during certain activities, and exposure time. A TC is a factor that relates exposure to dislodgeable residues. It is the amount of treated surface that a person contacts while performing activities in a given period (usually expressed in units of cm^2 per hour) and is specific to a particular population.

For the residential postapplication assessment of glyphosate, transfer coefficients were derived in the Residential SOPs for activities conducted on turf, such as mowing and golfing.

Calculated dermal MOEs for residential postapplication exposure, golf and incidental oral exposure to glyphosate exceeded target MOEs and are not of concern. The residential postapplication risk assessment is outlined in Appendix VIII, Tables 2-5.

Exposure to homeowners who apply glyphosate and conduct postapplication activities in treated areas, along with potential dietary exposure, are considered in Section 3.5 – Aggregate Exposure and Risk Assessment.

Dermal Bystander Exposure and Risk Assessment

There is potential for short-term exposure to glyphosate for adults, youth (11 to < 16 years old) and children (6 to < 11 years old) by entry into treated non-cropland areas (in other words, hiking through forests or parks that have recently been treated with glyphosate).

Calculated dermal MOEs for bystander exposure to glyphosate exceeded target MOEs and are not of concern. Bystander exposure is outlined in Appendix VIII, Table 6.

3.5 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

3.5.1 Toxicology Endpoint Selection for Aggregate Risk Assessment

For **aggregate risk assessment (all durations)**, the selected toxicological endpoint was the effect on salivary glands. Salivary glands were not examined in the dermal toxicity studies and a short-term inhalation study was not available. Effects on salivary glands could potentially result from exposure to glyphosate via inhalation or dermal routes, similar to the effects observed following oral exposure to glyphosate. Therefore, the most relevant study was the 26-month chronic toxicity and carcinogenicity study in rats with a NOAEL of 32/34 mg/kg bw/day. This was the highest (combined) NOAEL for the long-term toxicity studies in rats.

The lowest (combined) LOAEL was 100 mg/kg bw/day based on reduction in body weight in male rats in the interim sacrifice and increased incidences and severity of cellular alterations in the parotid and submandibular glands in a 24-month chronic toxicity and carcinogenicity study in rats. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. Therefore, the target **Margin of Exposure (MOE) is 100.**

3.5.2 Residential and Non-Occupational Aggregate Exposure and Risk Assessment

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurences of exposure.

For glyphosate, the following scenarios that were expected to co-occur are:

- Inhalation and dermal exposure to homeowners (adults) applying glyphosate to lawns/turf + postapplication dermal exposure (adults) performing activities in treated areas + chronic dietary (food and drinking water).
- Postapplication dermal exposure (youth and children [6 to < 11 years old]) from performing postapplication activities in treated lawns/turf + chronic dietary (food and drinking water).
- Postapplication dermal exposure (children 1 to < 2 years old) + incidental oral exposure (hand-to-mouth) from performing postapplication activities in treated lawns/turf + chronic dietary (food and drinking water).

When conducting the aggregate exposure assessment, two applications (with a seven-day interval) at the highest rate were assumed. All calculated MOEs reached the target MOE except for the children (1 to < 2 years old) for the postapplication + incidental oral exposure + chronic dietary scenario. Therefore, dietary and non-dietary exposure refinements were required.

The dietary exposure assessment used United States Tolerances or Codex MRLs whenever they happened to be greater than Canadian MRLs. However, domestic production and import statistics indicated that barley, oats and wheat consumed in Canada are almost totally produced in Canada (> 99%), with < 1% imported. Thus it was considered reasonable to use Canadian MRLs for these crops as a refinement in the calculation of the chronic dietary exposure estimates for the purpose of aggregation with residential exposure only, rather than the United States and Codex group tolerance of 30 ppm. The current Canadian MRLs in these cereal crops are as follows: barley (and barley flour) – 10 ppm, barley milling fractions (except flour) – 15 ppm, oat (and oat flour) – 15 ppm, oat milling fractions (except flour) – 35 ppm, wheat (and wheat flour) – 5 ppm, and wheat milling fraction (except flour) – 15 ppm.

In addition, assuming two applications (with a seven-day interval) at the maximum application rate is a highly conservative exposure assumption, as it is unlikely that children would be exposed to turf residues of the highest rate, at the lowest interval of application immediately after application. Therefore, a refinement using one application of glyphosate along with a seven-day time-weighted TTR average was used (the average resides of glyphosate were calculated over a seven-day span) for the entire aggregate assessment for all populations.

Using these refinements, all calculated MOEs exceeded the target MOE and are not of concern. The aggregate exposure estimates from residential scenarios are presented in Appendix IX, Table 1.

3.6 Polyethoxylated Tallow Amines

Polyethoxylated tallow amines (POEA) is a family of several compounds that are used as surfactants in many glyphosate products registered in Canada. In 2010, the USEPA completed a human health risk assessment for phosphate ester, tallowamine, ethoxylated (ATAE), which is a subfamily of POEA (PMRA #2439855). The USEPA currently uses this assessment as the basis for the approval of POEA. The USEPA assessment is considered to be applicable to the Canadian exposure profile and can be relied upon by PMRA to evaluate POEA risks. This assessment was considered acceptable by the PMRA.

The USEPA ATAE assessment was based on very conservative assumptions (for example, all crops treated at 100%, highest application rates and default values). Since exposures from all pesticidal sources of POEA need to be considered, the potential occupational, non-occupational and aggregate exposures from 57 highly used herbicides, fungicides and insecticides were evaluated. Given this approach, the POEA risk assessment and conclusions apply broadly to all pesticide products.

No risks of concern were identified, provided end-use products contained no more than 20% POEA by weight. All of the currently registered glyphosate end-use products in Canada meet this limit.

In addition, no new toxicity data relevant to the hazard assessment of POEA were found following a search of the published scientific literature beyond that identified in the USEPA ATAE health risk assessment. As such, an updated risk assessment was not required.

3.7 Incident Reports Related to Human Health

Since 26 April 2007, registrants have been legally required to report incidents to the PMRA that include adverse effects to the health of Canadians and to the environment. Information about the reporting of pesticide incidents can be found on the PMRA website. Incident reports were searched and reviewed for the active ingredient glyphosate. As of January 2014, the PMRA had received 71 human and 167 domestic animal incident reports involving glyphosate.

A total of 75 individuals were affected in the human incidents. In almost half of these incidents, the described effects were considered to be associated with the reported pesticide exposure. Major incident reports involving glyphosate occurred mainly in the United States as a result of accidental ingestion. Other highly acutely toxic active ingredients (such as diquat and paraquat) were also noted in these incidents. Therefore, any adverse effects could not be attributed specifically to glyphosate. Non-serious incidents, which included a prevalence of eye and skin irritation effects, occurred as a result of activities associated with application. Commercial class products were frequently identified in these incidents.

The domestic animal incidents involving glyphosate were mostly animal deaths that occurred in the United States. Overall, the reported symptoms in animals were clinical signs of toxicity such as vomiting. Contact with a treated area and ingestion of vegetation treated with a product containing glyphosate were commonly noted as activities leading to exposure in animal incidents.

No label changes resulting from these incident reports are considered necessary at this time.

4.0 Impact on the Environment

The environmental assessment was conducted based on data and information from registrants as well as from other regulatory agencies. Additional relevant data from published and unpublished scientific literature and monitoring data from federal and provincial governments were also considered.

4.1 Fate and Behaviour in the Environment

The fate and behaviour data for glyphosate and its transformation products in terrestrial and aquatic environments are presented in Appendix X, Tables X.1 and X.2.

Glyphosate enters the terrestrial environment when it is used as a herbicide in agriculture, forestry (site preparation) and non-cropland (right of ways and industrial sites). In the terrestrial environment, glyphosate is expected to be non-persistent to moderately persistent in aerobic soil (DT_{50} 1.9-151 d), producing the major soil biotransformation product AMPA. Under anaerobic conditions (flooded soil), glyphosate is more readily bound to soil and less readily transformed. Phototransformation is not expected to be an important route of dissipation.

Glyphosate has a low vapour pressure (1.3×10^{-7} Pa at 25°C) and a low Henry's law constant (2.1×10^{-9} Pa m^3) and is not expected to volatilize under field conditions from water or moist soil. Glyphosate is very soluble in water (12 000 mg a.e./L). Under Canadian field conditions (agriculture and forestry), glyphosate generally remains in the upper soil horizons and is considered to be non-persistent to moderately persistent (DT_{50} ranging from 6 to 82 days). Adsorption/desorption studies, soil column leaching studies, soil thin layer chromatography (TLC) studies, ground water modelling, as well the criteria of Cohen et al. (1984) and the groundwater ubiquity score (GUS) all indicate that glyphosate has low mobility in soil, remains in the upper soil horizon and has a low potential to leach to groundwater. Detection of glyphosate in lower structured soil horizons (loams and clay loams) by several researchers is believed to be the result of preferential flow through macropores. Glyphosate is rarely detected in known drinking water sources and groundwater in Canada, further supporting the conclusion that glyphosate is unlikely to contaminate groundwater. In terrestrial environments, AMPA is produced mainly through soil biotransformation and is non-persistent to moderately persistent (DT_{50} 2.1 to 107 days).

Glyphosate can enter aquatic environments through spray drift and runoff from the application site. Aerobic aquatic studies indicate that glyphosate dissipates rapidly from the water phase and partitions to sediment where transformation occurs more slowly (whole system DT_{50} 7.1 to 135 days). AMPA is the major transformation product produced. Hydrolysis (DT_{50} at 25°C and pH 7 was estimated to be >162 days) and aquatic phototransformation (DT_{50} 69 to 413 days at pH 7) of glyphosate are not important routes of dissipation. Under anaerobic conditions, glyphosate was non-persistent to persistent (DT_{50} 7 to 208 days).

In aerobic aquatic environments, AMPA is found in both water and sediment and is non-persistent to moderately persistent (total system DT_{50} 10 to 83.4 days). In the water column, AMPA partitions to the sediment where it is further transformed to CO_2.

The surfactant POEA is expected to be non-volatile, non-persistent in soil and water and immobile in soil and sediment. It is not likely to leach to groundwater due to rapid microbial transformation and strong adsorption to soil particles.

Glyphosate and AMPA are not expected to bioaccumulate in aquatic and terrestrial organisms due to their low octanol-water partition coefficients. Certain surfactants found in glyphosate formulations, that are derived from POEA compounds (mixture of 100 discrete tertiary amine molecules) may have the potential for bioaccumulation. However, given that the components of these compounds are easily broken down and that they are not persistent in soil and water, significant bioaccumulation under field conditions is unlikely.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. EECs are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. EECs are presented in Appendix X, Tables X.3 to X.7. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level). Summaries of toxicity data for both terrestrial and aquatic non-target organisms to glyphosate are presented in Appendix X, Tables X.8 to X.16.

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk

quotient is then compared to the level of concern (LOC). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data (Appendix XI), results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible. Data derived from monitoring studies may also be used in refining a risk assessment.

Where possible the analysis of toxicity data also includes the determination of the hazardous concentration to five percent of species (HC_5) from species sensitivity distributions (SSDs) or determination of the most sensitive endpoint in each taxonomic group and category. The HC_5 is calculated for acute and chronic data sets using the LC_{50}/EC_{50} values and no observed effect concentration (NOEC) values as appropriate (EC_{25} was also used for terrestrial plants when no other data was available). The HC_5 is the concentration that is assumed to be protective for ninety-five percent of species of the assessed taxonomic group or assemblage as related to the assessment endpoint and ecological protection goal. At an EEC equal to the HC_5, ninety-five percent of all species (within each taxonomic group) are not expected to be exposed to concentrations exceeding their threshold toxicity value (for example, LC_{50}, NOEC).

The software program ETX 2.0 was used with a log-logistic model to generate SSDs where sufficient toxicity endpoints were available for different taxa, using all available relevant information on toxicity. This reduces the uncertainty in risk estimates and provides endpoints that are scientifically robust as compared to single species toxicity test endpoints, as well as returning endpoints that are more ecologically relevant as compared to relying on the most sensitive species available. Median HC_5 values are reported for SSDs and where possible are used to determine risk and mitigation measures. The variability in the data sets is indicated by the upper and lower bound HC_5 estimates and the confidence limit of the fraction of species affected, which indicates the minimum and maximum percent of species that could be affected when exposed to the HC_5 concentration.

Where an HC_5 value could not be determined due to insufficient species numbers or lack of model fit, etc., the most sensitive species endpoint was reported with the use of appropriate uncertainty factors. Where multiple data points are available for one species, a geometric mean was used to represent the sensitivity of the species. SSDs were determined for different glyphosate formulations, the transformation product AMPA and the formulant POEA for the following taxonomic groups (results are reported in Appendix X, Table X.17).

- Terrestrial plants
- Freshwater invertebrates, fish, algae, amphibians and aquatic plants
- Marine fish, invertebrates and algae

4.2.1 Risks to Terrestrial Organisms

Certain glyphosate formulations include the surfactant POEA, which has been shown to be toxic to aquatic organisms under laboratory conditions. For the environmental risk assessment, the technical grade active ingredient, transformation product AMPA, POEA and formulated end-use products were evaluated. Results for formulated end-use products were categorized into those products that contain POEA, those that do not and those for which information was not available to determine if they included POEA or not.

Summaries of the toxicity data considered in this review are presented in Appendix X, Tables X.8 to X.16. For the assessment of risk, toxicity endpoints chosen from the most sensitive species or obtained from the SSD were used as surrogates for the wide range of species that can be potentially exposed following treatment with glyphosate. The terrestrial assessment took into account the range of agricultural application rates that are registered for glyphosate, taking into consideration that there may be multiple applications of glyphosate in a single-use season.

All data sets were grouped by test material type including technical grade active ingredient (technical grade active ingredient, includes all forms of glyphosate actives), end-use products containing the surfactant POEA (EUP + POEA), end-use products that do not contain POEA (EUP NO POEA), POEA alone and the glyphosate transformation product AMPA. All toxicity values were normalized to acid equivalent (a.e.).

Terrestrial Invertebrates

Earthworms, Soil Beneficial Insects, Bees, Predators and Parasitic Arthropods

Acute and chronic studies indicate that glyphosate is not toxic to earthworms and the resulting risk quotients based on the maximum application rate indicate that glyphosate is not expected to pose a risk to earthworms (Appendix X, Table X.18). A risk to the soil beneficial arthropod *Folsomia candida* was observed at the screening level (from in-field treatment), but refinement of the risk assessment based on drift including a soil deposition factor and also on field studies from scientific publications (not reported in tables) indicated arthropod populations would recover from exposure to glyphosate applied at the maximum rate in apple orchards and canola fields (Appendix X, Table X.18).

Glyphosate is not acutely toxic (contact and oral) to adult bees and risk quotients indicate that glyphosate is not expected to pose a risk to adult bees (Appendix X, Table X.19). Chronic bee toxicity studies were not available for review; however, chronic effects are not expected based on the mode of action and the lack of effects in acute toxicity studies with adult bees (no sublethal effects or mortality at the highest test concentrations). Data on larval and brood toxicity were not available for review, however risks are not expected based on limited exposure (due to the mode of action of glyphosate), a lack of effects observed on adult bees and the lack of significant effects on other immature insects (chironomids and beneficial arthropods). This evidence, in combination with the absence of bee incident reports associated with the long history of use in Canada and foreign countries, indicates that glyphosate is unlikely to pose significant risks to honeybees for the proposed use pattern.

Under laboratory conditions, acute and chronic risks to predatory and parasitic arthropods were observed at the screening level (considering results from glass plate studies with both *Typhlodromus pyri* and *Aphidius rhopalosiphi*). Risk quotients also slightly exceeded the level of concern for *T. pyri* when considering results of extended laboratory conditions (leaf substrate) for apple, canola and potato uses (*T. pyri*, RQs = 1.9, 1.8 and 1.1 for apple, canola and potato uses, respectively). Refinement of the risk assessment and comparison with results obtained for other beneficial arthropods in recent scientific publications indicated that predator and parasitic arthropod populations would recover from exposure to glyphosate at the maximum rate of application in apple orchard and canola fields, respectively (7285 g a.e./ha and 6990 g a.e./ha) (Appendix X, Table X.19).

Risk to Birds

A tiered assessment of the risks to birds progressing from a conservative screening assessment to a more refined assessment was conducted. In the vast majority of studies, no toxic effects were reported. Consequently, a very conservative assessment was conducted using risk quotients generated using the highest concentration tested even though in all but one case, no toxic effects were observed. This assessment found only very small exceedences of the LOC and concluded that the risk to birds from acute oral, dietary and reproduction exposure to glyphosate and its formulations is expected to be low.

The screening level risk quotients based on acute oral exposure of birds to glyphosate technical may slightly exceed the level of concern for small- and medium-sized birds (RQ < 1.9 and < 1.5 for small- and medium-sized birds, respectively). However, this is based on the maximum concentration tested and no adverse effects were observed. The screening level risk quotients for reproduction also slightly exceed the level of concern for all sizes of birds (RQs range from 1.0 to 2.0) (Appendix X, Table X.20). Risks were further characterized by expanding the scope of the assessment to include other guilds, dietary exposure, mean residue levels and off-field exposure. Note that the acute oral LD_{50} and dietary LD_{50} values are greater than the highest doses tested, and the reproduction NOELs are the highest doses tested. Thus, the risk quotients are very conservative and may not reflect a true concern.

Based on the crop and the type of equipment used, spray drift factors were applied to the in-field exposure values to obtain off-field exposure values. The product label specifies that the spray droplets must be at least coarse, based on the American Society of Agricultural Engineers (ASAE) classification. Consistent with the use pattern for apples considered in this assessment, for a coarse droplet size, the maximum spray drift deposition at one metre downwind from the point of application is 3% of the rate for field sprayer application to agricultural crops. In the refined assessment, risk quotients slightly exceed the level of concern for on-field exposure of small and medium insectivorous birds on an acute, dietary and reproduction basis (maximum and mean residues), and large herbivores on a dietary and reproduction basis (maximum residues only) (Appendix X, Table X.21).

For these groups, the risk quotients exceed the level of concern by only a small margin and most are "less than" values, which means that the level of concern may not actually be exceeded. The risk quotients for off-field exposure do not exceed the level of concern. It should be noted that none of the toxicity studies conducted with technical glyphosate resulted in measured toxic effects in birds.

Screening-level estimated dietary exposure (EDE) values and RQ calculations for birds exposed to single applications of glyphosate formulations are presented in Appendix X, Table X.22. Based on acute oral exposure to glyphosate formulations, the screening level risk quotients exceed the level of concern for all sizes of birds (RQ = 1.6 to 3.1). The risk to birds from exposure to glyphosate formulations was further characterized by expanding the scope of the assessment to include other guilds, dietary exposure, mean residue levels as well as off-field exposure. In the refined risk assessment, for acute oral exposure of birds to glyphosate formulations, risk quotients exceed only the level of concern for small and medium insectivores (maximum residues RQ = 2.4 to 3.1, mean residue RQ = 1.7 to 2.2), and large herbivores (maximum residue RQ = 1.5 to 1.6) (Appendix X, Table 23). None of the dietary toxicity studies conducted with glyphosate formulations resulted in measured toxic effects in birds (the dietary LD_{50} values are greater than the highest doses tested), resulting in risk quotients for dietary exposure of birds to glyphosate formulations all having less than values (maximum residues RQ < 18.8 to < 0.7 and mean residues RQ < 13 to < 0.6) (Appendix X, Table X.23). The toxicity endpoints and associated risk quotients for dietary exposure are very conservative as they are based on an absence of effects.

Bird toxicity studies indicate that acute oral exposure (gavage) to glyphosate formulations can result in effects (and some risk quotients exceeding the level of concern). However, dietary studies, which are more representative of the potential route of exposure in the environment (in other words, through contaminated food items) reported that no toxic effects were observed with exposure to dried residues of the formulation in the diet. The predominant route of exposure will be from ingestion of dried residues on food items. It should be noted, however, that exposure to the sprayed formulation, which could occur via preening if birds are sprayed directly or through spray drift, was not considered in this assessment. Thus, more weight is given to conclusions of the dietary assessment than to the acute oral assessment. Therefore, the risk to birds from acute oral, dietary and reproduction exposure to glyphosate and its formulations is expected to be low. The absence of incident reports for birds related to the use of glyphosate supports this conclusion. Bird hazard statements are not required on glyphosate product labels.

Risk to Mammals

Toxic effects were reported in only a few of the available studies conducted with mammals and these effects were observed only at very high doses. A tiered assessment of the risks to mammals progressing from a conservative screening assessment to a more refined assessment was conducted. This assessment found only very small exceedences of the LOC and concluded that the risk to mammals from acute oral and reproduction exposure to glyphosate and its formulations is expected to be low.

Screening level risk quotients exceed the level of concern for all sizes of mammals for acute oral exposure to glyphosate technical (RQ = 2.2 to 4.2) but did not exceed the level of concern for reproduction (RQ ≤ 0.9) (Appendix X, Table X.20). The risk to mammals from exposure to glyphosate technical was further characterized by expanding the scope of the assessment to include other guilds, dietary exposure, mean residue levels, off-field exposure as well as other endpoints. Eighteen acute oral glyphosate technical toxicity studies were available for mammals. Whereas a few studies measured effects at high doses, the majority indicated LD_{50} values greater than the highest dose tested. Based on the most sensitive endpoint for acute oral exposure, the risk quotients exceed the level of concern for on-field exposure of small insectivorous mammals when considering maximum (RQ = 2.2) and mean (RQ = 1.5) residues, medium-sized insectivorous and herbivorous mammals when considering maximum and mean residues (maximum residue RQ = 1.9 to 4.2 and mean residue RQ = 1.3 to 1.5) and large-sized insectivorous and herbivorous mammals when considering maximum residues only (RQ = 1.0 to 2.3) (Appendix I, Table). No risk quotients exceed the level of concern for off-field exposure. Given the range of toxicity values available, risk quotients were also calculated using the least sensitive acute oral endpoint for mammals. Based on an acute oral LD_{50} of 5600 mg/kg bw, risk quotients very slightly exceed the level of concern for on-field exposure of medium-sized herbivorous mammals exposed to maximum residues of glyphosate (RQ = 1.2) (Appendix X, Table X.24).

Screening level acute oral exposure RQ values for glyphosate formulations exceed the level of concern for all sizes mammals (RQ = 5.7 to 11) (Appendix X, Table X.22). The risk to mammals from exposure to glyphosate formulations was further characterized by expanding the scope of the assessment to include other guilds, mean residue levels, off-field exposure as well as other endpoints. Fifty acute oral toxicity studies (based only on three distinct species) with glyphosate formulations were available for mammals. Eight of these studies measured effects at high doses, but the majority indicated LD_{50} values greater than the highest dose tested. Based on the most sensitive endpoint for acute oral exposure, the risk quotients exceed the level of concern for on field exposure of insectivorous and herbivorous mammals of all sizes (maximum residue RQ = 2.6 to 11, mean residue RQ = 1.2 to 3.9), and small and medium-sized frugivores (maximum residue RQ = 1.5 to 1.8) (Appendix I). Risk quotients for off-field exposure did not exceed the level of concern. Risk quotients were also calculated using the least sensitive acute oral endpoint. Based on an acute oral LD_{50} of > 4000 mg/kg bw, risk quotients do not exceed the level of concern for mammals of any size (RQs ≤ 0.5) (Appendix X, Table X.25).

Overall, available data indicate that risks to mammals following acute oral exposure to glyphosate and its formulations are low. If any, acute risks to mammals would be restricted to on-field exposure of only a few guilds (herbivores and perhaps insectivores). No reproductive risks to mammals are expected from the use of glyphosate. This conclusion is supported by the absence of incident reports for mammals related to the use of glyphosate. Mammalian hazard statements are not required on glyphosate product labels.

Risk to Non-target Terrestrial Plants

Glyphosate is a broad spectrum herbicide and as such toxicity to susceptible non-target plants is expected if exposed to sufficiently high concentration. The risk assessment for non-target terrestrial plants identified some areas of potential risk and consequently measures to minimize exposure to non-target plants are required.

Based on EECs equal to the maximum cumulative application rates for the uses on apples, canola, corn and potatoes and the toxicity endpoints selected for seedling emergence (the most sensitive EC_{50}) and vegetative vigour (the EC_{50} for formulation without POEA and HC_5 of SSDs for formulations with POEA), all screening level risk quotients exceed the level of concern (Appendix X, Table X.26). The most sensitive terrestrial plant endpoint is the EC_{50} value of 0.014 kg a.e./ha for the end-use product without POEA based on vegetative vigour. Cumulative application rates were calculated using a soil DT_{50} of 32.6 days for seedling emergence and a foliar DT_{50} of 14.4 days for vegetative vigour, to account for dissipation between applications. The risk to terrestrial vascular plants was further characterized by looking at off-field exposure from drift.

For an ASAE coarse droplet size, the maximum spray drift deposition at one metre downwind from the point of application is 3% of the application rate for field sprayer application to agricultural crops and 17% for aerial application. Aerial application is registered for use on canola (pre-harvest), but not on apples, corn or potatoes. Based on the risk quotients using the off-field EECs from drift, the level of concern for terrestrial vascular plants is not exceeded for seedling emergence, but is exceeded for vegetative vigour in all cases, except for the use of formulations without POEA on potatoes (Appendix X, Table X.26).

To protect non-target terrestrial vascular plants, spray buffer zones are required on glyphosate product labels, both those with and without the surfactant POEA (Appendix XII).

Transformation Product (AMPA)

Earthworms and birds were the only terrestrial organisms tested with the transformation product AMPA. The screening level risk quotients for acute and chronic exposure did not exceed the level of concern. Since AMPA is mainly formed in soils through biological processes, has a low log K_{ow} (-2.36 to -1.63) and binds tightly to soil particles, exposure and risk to mammals and foliage dwelling arthropods is expected to be negligible. To date, no ecotoxicological incidents have been reported concerning AMPA. As such no additional studies are required at this time.

Endocrine Disruption

The USEPA Endocrine Disruptor Screening Program (EDSP) is a scientific program to screen pesticides, other chemicals, and environmental contaminants for substances having the potential to affect the estrogen, androgen or thyroid hormone systems. Glyphosate was included in the second EDSP List. The PMRA will consider the results of these screening tests as they become available.

4.2.2 Risks to Aquatic Organisms

Glyphosate can enter water bodies and expose non-target aquatic organisms through runoff or via spray drift. The aquatic risk assessment was conducted following a tiered approach with a very conservative screening assessment followed by refinements if concerns were identified at the screening level. Overall there are few risks of concerns for aquatic organisms with the exception of aquatic plants and some marine invertebrates and these areas of concern were mainly identified with formulations containing the surfactant POEA.

Summaries of the aquatic toxicity data considered in this review are presented in Appendix X, Table 27. The most sensitive aquatic taxonomic group is freshwater plants and the acute HC_5 value is 0.003 mg a.e./L for the EUP + POEA formulation. The order of species sensitivity was determined to be: freshwater plants (0.003 mg a.e./L) > marine fish and invertebrates (0.1 mg a.e./L) > freshwater algae (0.12 mg a.e./L) > freshwater invertebrates (0.19 mg a.e./L) > marine algae (0.33 mg a.e./L) > freshwater fish (0.36 mg a.e./L), and amphibians (0.86 mg a.e./L) (Appendix X, Table X.17).

Screening level risk quotients for all freshwater organisms that were tested with end-use products containing POEA following acute and/or chronic exposures were all above the level of concern. All tested glyphosate formulations that do not contain POEA had risk quotients below the level of concern, except for freshwater algae. Saltwater invertebrates (acute exposure) and algae (chronic exposure) exposed to glyphosate formulation containing POEA had risk quotients above the level of concern. The surfactant POEA tested alone had risk quotients above the level of concern for freshwater and marine/estuarine invertebrates and freshwater fish, confirming the international scientific consensus that POEA added to glyphosate increases the environmental risk to these organisms.

The transformation product AMPA is not toxic to aquatic organisms.

Refined Risk Assessment for Aquatic Organisms and Potential Risk from Drift

The risk to aquatic organisms was further characterized by taking into consideration the concentrations of glyphosate that could be deposited in off-field aquatic habitats that are downwind and directly adjacent to the treated field through drift of spray. The spray drift data of Wolf and Caldwell (2001) was used to determine the maximum spray deposit into an aquatic habitat located one metre downwind from a treated field. Review of the labels for glyphosate containing end-use products indicate that the end-use products are applied by ground and aerial application methods. The maximum percentage of the applied spray that is expected to drift 1m downwind from the application site during spraying using field sprayer and aerial application methods is determined based on a coarse spray droplet size: field sprayer – 3%, aerial – 17%, respectively. Given the variation in percent drift off site for each of the application methods, the assessment of potential risk from drift was done using the maximum single application for potato (groundboom application: 4320 g a.e./ha) and the maximum cumulative application rate for canola (aerial application: 4320 + 4320 + 902 at 10-day intervals g a.e./ha). The EECs resulting from drift for these two crops cover the full range of EECs from drift anticipated from all application rates and application methods.

For freshwater snails, freshwater and saltwater fish and saltwater algae, the risk quotients, after refinement, were below the level of concern.

For freshwater invertebrates, the risk quotients derived for acute exposure to spray drift from the surfactant POEA alone exceeded the level of concern (RQ = 1.8 – 16.1). Based on acute toxicity endpoints (HC_5) derived for POEA containing glyphosate formulations, the level of concern is slightly exceeded at the highest cummulative aerial application rate (RQ = 1.1).

For freshwater plants and marine/estuarine invertebrates, the level of concern is exceeded for acute effects at all application rates and for all application methods (freshwater plants RQ = 6.7 to 67 and marine/estuarine invertebrate RQ = 2 to 20), with the risk quotients being based on the toxicity to glyphosate formulations that contain POEA. Based on glyphosate formulations that do not contain POEA, the level of concern for acute effects is exceeded for freshwater algae at the highest application rate (RQ = 3.3).

Based on amphibian laboratory toxicity data, the level of concern is slightly exceeded for amphibians exposed to spray drift from glyphosate formulations containing POEA at the highest cumulative aerial application rate on an acute and chronic basis (acute RQ = 1.1, chronic RQ = 1.2), however the level of concern for acute and chronic effects is not exceeded when amphibian toxicity data derived from field and mesocosm level studies are considered (Appendix X, Table X.28).

To protect aquatic species, spray buffer zones are required on glyphosate product labels, both those with and without the surfactant POEA.

Assessment of Potential Risk from Runoff

Aquatic organisms can also be exposed to glyphosate applied to foliage as a result of runoff into a body of water. The linked models Pesticide Root Zone Model (PRZM) and Exposure Analysis Modeling System (EXAMS) were used to predict EECs resulting from runoff of glyphosate following application. Considering the crop uses and geographic crop distribution, as well as the available scenarios, nine standard regional scenarios were modelled to represent different regions of Canada. The Level 1 glyphosate EECs in a 1-ha receiving water body (15 and 80 cm deep) predicted by PRZM-EXAMS for these crops applications are presented in Tables XI.3-5, Appendix XI. The values reported by PRZM/EXAMS are 90th percentile concentrations of the concentrations determined at a number of time-frames including the yearly peak, 96-hr, 21-d, 60-d, 90-d and yearly average.

Acute and chronic risk quotient values were calculated using an EEC for the time frame that most closely matched the exposure time used to generate the endpoint. For example, a 96-hour LC_{50} would use the 96-hour value generated by the model; a 21-day NOEC would use the 21-day EEC value. At the screening level, RQ values for organisms (acute and/or chronic exposure) exceeded the level of concern. The EECs used for calculation of the RQs were the highest values for the appropriate depth and appropriate time frame (in other words, potato-use scenario in Prince Edward Island); when the RQ based on the highest EEC exceeded the level of concern, an

RQ based on the lowest EEC values (apple-use scenario in British Columbia) was also calculated. Screening level acute and chronic RQ values for freshwater and marine organisms are reported in Appendix X, Table X.27.

Refinement was done for runoff, with all endpoints being based on exposure to glyphosate formulations containing POEA, unless otherwise indicated.

The risk quotients for runoff derived for acute exposure exceed the level of concern for freshwater algae and marine invertebrates (freshwater algae RQ = 1.6, marine invertebrates RQ = 9.6) at the highest EECs (potato-use scenario in Prince Edward Island), but not at the lowest EECs (apple-use scenario in British Columbia). The risk quotients derived for chronic exposure indicate that the level of concern is exceeded for freshwater aquatic plants (RQ = 26) at the highest EECs (potato-use scenario in Prince Edward Island), but not at the lowest EECs (apple-use scenario in British Columbia) (Appendix X, Table X.29).

Refinement with Monitoring Data

The risk assessment was refined by considering all available Canadian monitoring data. A summary of water monitoring data is presented in Appendix XI. An EEC of 40.8 ug/L (the highest detection of glyphosate in surface water) was used for the refined risk assessment. Risk quotients were calculated for organisms (acute and/or chronic exposure) that showed exceedence of the level of concern at the screening level. The refined RQ values (Appendix X, Table X.30) indicate that the level of concern not exceeded for aquatic organisms with the exception of freshwater plants (RQ = 14).

Label statements are specified to help reduce runoff to aquatic habitats.

4.2.3 Incident Reports Related to the Environment

Since 26 April 2007, registrants have been required by law to report incidents to the PMRA that include adverse effects to Canadian health or the environment. Information about the reporting of pesticide incidents can be found on the PMRA website. Incident reports involving all forms of the active ingredient glyphosate were reviewed. As of 10 May 2013, there were 37 environmental incident reports in the PMRA database involving a form of the active ingredient glyphosate (PMRA# 2304789 and 2310009).

There were three major environmental incidents in which fish were killed when water used to douse a chemical warehouse fire was released into a stream. It was unclear which chemical may have been responsible for the fish mortality.

The remaining incidents were minor in nature and mostly involved grass damage following the direct application of a glyphosate product. There were six minor non-grass incidents that occurred following the drift of a glyphosate product onto non-target plants. Overall, there was a high degree of association between the reported environmental exposure to glyphosate and the effects observed.

Table 4.1 Minor Incidents Listed by Type of Organism Affected and Causality Level

Organism	Highly Probable	Probable	Possible	Unlikely	Total
Grass/Lawn	19	6	—	—	25
Herbaceous Plants	3	2	—	2	7
Trees or shrubs	1	2	1	—	4
Total	**23**	**10**	**1**	**2**	**36**[1]

[1] One incident reported damage to onions (herbaceous plant) and two different types of trees. The total count of incidents by organism type (36) is therefore higher than the number of minor incident reports received.

The USEPA Ecological Incident Information System (EIIS) was also queried for glyphosate incidents that were available in the database as of 29 November 2012. There were 633 incident reports available in the EIIS database that involved glyphosate (116 incidents), glyphosate isopropylamine salt (516 cases) or glyphosate potassium salt (1 case). The most frequently reported site/crop affected was agricultural area (139 incidents), cotton (51 incidents), corn (36 incidents), soybean (27 incidents), and home/lawn (26 incidents). Plant damage (449 cases) and mortality (171 cases) were the most frequently reported symptoms. Of the 633 reports, nearly half were considered to be related to the misuse of a product (48%) and 95% were considered to have a certainty of at least possible (180 possible, 352 probable and 42 highly probable). 54% of all reports were the result of drift, while 23% were treated directly.

All the information stated above was considered in this evaluation and did not affect the risk assessment.

5.0 Value

5.1 Value of Glyphosate

Glyphosate plays an important role in Canadian weed management in both agricultural production and non-agricultural land management and is the most widely used herbicide in Canada.

Value to Canadian Agriculture

Glyphosate is an important herbicide for Canadian agriculture:

- Due to its broad and flexible use pattern and its wide weed control spectrum, it is the most widely used herbicide in several major crops grown in Canada such as canola, soybean, field corn and wheat. It is also one of only a few herbicides regularly used in fruit orchards such as apple.
- It is the essential herbicide for use on the glyphosate tolerant crops (GTCs) including canola, soybean, corn, sweet corn and sugar beet. The combination of GTCs and glyphosate has been adopted as an important and common agricultural production practice in Canada.

- It is identified by growers (in the Canadian Grower Priority Database [version 22, August 2011]) as a priority for 17 new uses relating to 17 commodities: almond, bluegrass, kentucky bluegrass, bromegrass, canary seed, creeping red fescue, fescue, bermuda grass, pearl millet (grain), orchard grass, peanut, pecan, ryegrass, soybean, sunflower, timothy and wheatgrass.
- Among all herbicides registered, glyphosate has the broadest range of use sites because it can be used on all crops when applied prior to planting. In addition, it has the widest weed control spectrum including annual and perennial weeds, weedy trees and brush.
- Compared to other non-selective herbicides, it controls weeds of various sizes as well as the roots of these weeds since glyphosate is translocated throughout the plant.
- Glyphosate can be tank-mixed with many residual herbicides to broaden the weed spectrum and extend the duration of weed control thus decreasing the number of herbicide applications while maximizing yield and lowering fuel and energy consumption.
- Glyphosate has a wide application window including pre-seeding, after seeding (prior to crop emergence), in-crop, pre-harvest and post-harvest, allowing a flexible and effective weed management program:
    - When applied prior to seeding, application of it does not delay the seeding step due to its non-residual activity, therefore increasing flexibility for farming practices while providing a clean start for the new crop.
    - Glyphosate can also be applied in-crop as a postemergence treatment in conventional crops either as spot treatment or with wiper and wick application to control weeds taller than crops, which otherwise are impossible to control with other herbicides.
    - The pre-harvest application of glyphosate provides additional benefits to growers as it functions both as a harvest management and a desiccation treatment: equalizing the ripening or advancing the ripening process in uneven crops to achieve an earlier and more uniform harvest, lowering harvested grain seed moisture content, and increasing combine harvester efficiency. As compared to alternative crop desiccators such as diquat, glufosinate and carfentrazone, glyphosate also controls perennial weeds and can be used in a wider range of crops.
    - Post-harvest stubble treatment with glyphosate allows reduced or zero tillage, which has facilitated the adoption of conservation agriculture, where appropriate, thus reducing soil erosion, improving soil structure and retaining soil moisture as well as providing other benefits such as reduced tractor and fuel use.

Value to Non-agricultural Land Management

Glyphosate is also an important weed control tool in non-agricultural land management for these reasons:

- Due to its flexible use pattern and broad weed control spectrum, it is the most widely used herbicide in forestry. It can be applied at various stages in the forest regeneration cycle including site preparation, conifer release and stand thinning stages. Compared to alternative herbicides such as phenoxy, sulfonylnurea and triclopyr, glyphosate controls a wider range of weeds. Special application methods such as cut stump or injection treatment allow for year round application.
- It is also one of the widely used herbicides for pasture renovation, around structures on farms, amenity and industrial areas, and along rights-of-way.
- It is an effective tool for the control of many invasive weed species and for the control of toxic plants such as poison ivy.

For some speciality or minor use crops, glyphosate provides specific selective weed control techniques (weed wipers, shrouded sprayers and stem injection) where in many cases selective use of glyphosate is the only method of weed control possible or remaining in pasture and rangeland, vegetables, fruit crops and for the control of invasive weeds among desirable plants/trees.

Glyphosate has a unique mode of action and is the only molecule that is highly effective at inhibiting the enzyme EPSP of the shikimate pathway. It plays a role in delaying herbicide resistance development in weeds when used in rotation or combination with active ingredients from other herbicide site of action groups. However, the current Canadian agricultural production system relies heavily on glyphosate, resulting in more and more occurrences of glyphosate-resistant weeds. Kochia, Canada fleabane, giant ragweed and common ragweed are examples of such resistant weeds reported in Canada. These glyphosate-resistant weeds affect the efficacy and broader value of glyphosate. In order to prevent or delay the development of glyphosate-resistant weeds, it is crucial to maintain diversity in weed management practices.

5.2 Commercial Class Products

A total of 97 Commercial Class end-use products containing glyphosate were registered as of 3 May 2012. All Commercial Class glyphosate uses are supported by the registrant. As risk concerns identified can be mitigated, alternatives to the uses of glyphosate are not presented in this document.

5.3 Domestic Class Products

A total of 34 Domestic Class products containing glyphosate were currently registered as of 3 May 2012. All Domestic Class glyphosate uses are supported by the registrant. As risk concerns identified can be mitigated, alternatives to the uses of glyphosate are not presented in this document.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, those that meet all four criteria outlined in the policy: in other words, persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*.

During the review process, glyphosate was assessed in accordance with the PMRA Regulatory Directive DIR99-03[3] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Glyphosate does not meet all Track 1 criteria and is not considered a Track 1 substance (see Table 6.1).
- Glyphosate does not form any transformation products that meet the Track 1 criteria.

The use of glyphosate is not expected to result in the entry of TSMP Track 1 substances into the environment.

[3] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy.*

Table 6.1 Toxic Substances Management Policy Considerations – Comparisons to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion Value		Glyphosate Are Criteria Met?
Toxic or toxic equivalent as defined by the *Canadian Environmental Protection Act*	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]	Soil	Half-life ≥ 182 days	No for aerobic soils: 15.3-142 days. Some potential for anaerobic soils: 3-1699 days.
	Water	Half-life ≥ 182 days	No: 1-5.4 days (water phase in aerobic system).
	Sediment	Half-life ≥ 365 days	No: 26-58.1 days (sediment phase in aerobic system).
	Air	Half-life ≥ 2 days or evidence of long range transport	Glyphosate has a low vapour pressure of 6.0×10^{-7} Pa at 20°C (4.5×10^{-9} mm Hg) and according to the classification of Kennedy and Talbert (1977) is expected to be relatively non-volatile under field conditions. However, the Henry's law constant of 0.168 Pa m^3/mole (equivalent to 1.66×10^{-6} atm m^3/mole and a calculated $1/H = 3.38 \times 10^4$) indicates that glyphosate is slightly volatile from water surface or moist soil. The EFSA (2009) reported that glyphosate volatilization from water, soil and plant surfaces is expected to be low.
Bioaccumulation[4]	Log $K_{ow} \geq 5$		Log $K_{ow} = 4.1$
	BCF ≥ 5000		BCF = 248-430
	BAF ≥ 5000		NA
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.

[1]All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (in other words, all other TSMP criteria are met).

[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

[4]Field data (for example, bioaccumulation factors [BAFs]) are preferred over laboratory data (for example, bioconcentration factors [BCFs]) which, in turn, are preferred over chemical properties (for example, log K_{ow}).

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical product are compared against the list in the *Canada Gazette*.[4] The list is used as described in the PMRA Notice of Intent NOI2005-01[5] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[6], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Based on the manufacturing process used, impurities of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the glyphosate products.
- Technical grade Glyphosate and its end-use products do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02 (PMRA Formulants Policy).

7.0 Organisation for Economic Co-operation and Development Status of Glyphosate

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups member countries and provides a forum in which governments can work together to share experiences and seek solutions to common problems.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member country to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Glyphosate is currently acceptable for use in other OECD countries, including the United States, Australia and the European Union. As of 17 March 2015, no decision by an OECD member country to prohibit all uses of glyphosate for health or environmental reasons has been identified.

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4 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

5 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

6 DIR2006-02, *PMRA Formulants Policy.*

8.0 Summary

8.1 Human Health and Safety

The toxicology database submitted for glyphosate is adequate to define the majority of toxic effects that may result from exposure. Observations of slight systemic toxicity consisting of decreased body weight and body-weight gain, altered hepatic and renal functions, and diarrhea were common in the toxicity studies with glyphosate. Cellular changes in the salivary glands were also observed in the rodent studies. Glyphosate was not genotoxic or neurotoxic. A marginally increased incidence of ovarian adenomas was observed in mice, but at the limit dose only. These tumours were considered to be of low degree of concern for human health risk assessment. Glyphosate produced an altered response of the immune system. No evidence of increased sensitivity of the young was observed in the reproduction or prenatal developmental toxicity studies.

However, the finding of fetal cardiovascular malformations in the presence of maternal toxicity in a rabbit developmental toxicity was considered a serious effect. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in the animal tests.

8.1.1 Dietary Risk

There were no dietary risk concerns from the acute and chronic dietary risk assessments (food and drinking water) for the general population and all population subgroups, including infants, children, teenagers, adults and seniors.

8.1.2 Non-Occupational Risk

Risks to residential applicators for all residential label uses are not of concern. Residential postapplication risk is not of concern, including from golfing and incidental oral exposure. There is no risk of concern for bystanders entering treated sites.

8.1.3 Occupational Risk

Risk estimates associated with mixing, loading and applying activities for all commercial label uses are not of concern.

Postapplication risks for workers were not of concern. An REI of 12 hours is required for all agricultural postapplication activities.

8.1.4 Aggregate Risk

There were no risks of concern from aggregate exposure to glyphosate from food, drinking water and residential uses.

8.1.5 Polyethoxylated Tallow Amines

No risks of concern were identified, provided end-use products contain no more than 20% POEA by weight.

8.2 Environmental Risk

Available studies indicate that in the natural environment, glyphosate is non-persistent to moderately persistent in soil and water and produces one major transformation product in soil and water, aminomethyl phosphonic acid (AMPA), which is non-persistent to persistent in the environment. Carryover of glyphosate and AMPA into the next growing season is not expected to be significant. Glyphosate and AMPA are expected to be immobile in soil and are unlikely to leach to groundwater. Glyphosate is very soluble in water and non-volatile and is expected to partition to sediment in aquatic environments. Glyphosate and AMPA are unlikely to bioaccumulate.

Certain glyphosate formulations include the surfactant POEA, which is non-persistent to slightly persistent in the environment and is toxic to aquatic organisms. In general, glyphosate formulations that contain POEA are more toxic to freshwater and marine/estuarine organisms than formulations that do not contain POEA. POEA compounds have the potential to bioaccumulate but given that the components are easily broken down and that it is not persistent in soil and water, significant bioaccumulation under field conditions is unlikely.

In the terrestrial environment the only area of risk concern identified from the available data was for terrestrial plants and therefore spray buffer zones are required to reduce exposure to sensitive terrestrial plants. Glyphosate formulations containing POEA may pose a risk to freshwater invertebrates, freshwater plants and marine/estuarine invertebrates. Glyphosate formulations that do not contain POEA may pose a risk to freshwater algae only. Glyphoste technical grade active ingredient is toxic to estuarine/marine fish. Hazard statements and mitigation measures (spray buffer zones) are required on product labels to protect aquatic organisms.

Due to its rapid dissipation and low toxicity, the transformation product AMPA is not expected to pose a risk to terrestrial and aquatic organisms based on proposed application rate of glyphosate.

8.3 Value

Glyphosate is an important herbicide for Canadian agriculture as well as for weed control in non-agricultural land management.

9.0 Proposed Re-evaluation Decision

9.1 Proposed Regulatory Actions

After a re-evaluation of glyphosate, Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing continued registration of glyphosate and associated end-use products for certain uses of glyphosate in Canada, provided that the mitigation measures for the health and the environment described in this document are implemented.

9.1.1 Proposed Regulatory Action Related to Human Health

9.1.1.1 Proposed Label Amendments

1) Label amendments for the glyphosate technical product labels are proposed and summarized in Appendix XII.
2) The restricted entry interval of 12 hours is proposed for all agricultural uses (Appendix XII).
3) There may be potential for exposure to bystanders from drift following pesticide application to agricultural areas. In the interest of promoting best management practices and to minimize human exposure from spray drift or from spray residues resulting from drift, label statement is proposed under Use Precautions (Appendix XII).

9.1.1.2 Residue Definition for Risk Assessment and Enforcement

Glyphosate is registered for use on a wide range of conventional crops (in other words, glyphosate non-tolerant crops) as well as on transgenic crops (in other words, glyphosate tolerant crops). Currently registered transgenic crops include crops containing the 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) gene and/or the glyphosate oxidoreductase (GOX) gene and crops containing the glyphosate *N*-acetyl transferase (GAT) gene (in other words, soybeans, corn and canola). The residue definition (RD) in all conventional crops and in transgenic EPSPS/GOX crops is comprised of glyphosate and the metabolite AMPA. The RD in transgenic GAT crops is the sum of glyphosate and the metabolites *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA. The RD in animal commodities is the sum of glyphosate and the metabolites *N*-acetylglyphosate and AMPA. These RDs are used for both enforcement and dietary risk assessment purposes. No modification to the current RDs is proposed as the result of this re-evaluation. The metabolites included in the RDs are expressed as stoichiometric equivalents of glyphosate. The RD in drinking water for dietary risk assessment is defined as the sum of glyphosate and the metabolite AMPA. The acetylated metabolites are not included in the RD for drinking water because they are not formed in soil. In other words, *N*-acetylglyphosate is not applied to plants; it is rather a metabolite produced in GAT crops as a result of the application of glyphosate.

9.1.1.3 Maximum Residue Limits for Glyphosate in Food

Maximum residue limits (MRLs) have been specified for residues of glyphosate (including all the metabolites comprised in the RDs) and the trimethylsulfonium (TMS) cation, the major metabolite of the discontinued glyphosate-TMS salt, in/on registered crops. Information on Canadian MRLs is presented in Appendix VI.

MRLs for pesticides in/on food are established by Health Canada's PMRA under the authority of the *Pest Control Products Act*. After the revocation of an MRL or where no specific MRL is specified for a pesticide under the *Pest Control Products Act*, Subsection B.15.002(1) of the Food and Drug Regulations applies. This requires that residues do not exceed 0.1 ppm, which is considered as a general MRL for enforcement purposes. Therefore, residues in/on all other crops appearing on the registered glyphosate labels are regulated under the general MRL not to exceed 0.1 ppm for glyphosate (including relevant metabolites) and 0.1 ppm for the TMS cation.

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to remove Canadian MRLs that are no longer supported. Given that all glyphosate-TMS-containing products have been discontinued, it is proposed that all MRLs for the TMS cation be revoked.

A complete list of MRLs established in Canada can be found in the PMRA MRL database on the Pesticides and Pest Management section of the Health Canada website. The database is an online query application that allows users to search for established MRLs regulated under the *Pest Control Products Act*. For supplemental MRL information regarding the international situation and trade implications, refer to Appendix VI.

9.1.1.4 Proposed Mitigation Measures Related to Products Containing Polyethoxylated Tallow Amines

The determination of acceptable risk for the POEA health evaluation is applicable to end-use products that contain no more than 20% POEA by weight. As such, registrants will be required to ensure that end-use products comply with the maximum of 20% POEA by weight.

9.1.2 Proposed Regulatory Action Related to the Environment

To reduce the effects of glyphosate in the environment, mitigation in the form of precautionary label statements and spray buffer zones are required. Environmental mitigation statements are listed in Appendix XII.

9.1.3 Other Label Amendments

Information on cumulative rate per year, maximum number of applications per year and minimum interval between applications is not currently specified on labels for use on agricultural cropland and non-cropland, as it is for fruit tree, berry and vine crops. In order for use directions for glyphosate products to be consistent with the assumptions used in the PMRA health risk assessment, it is recommended that labels be updated to include this information for all sites, as described in Appendix II.

9.2 Additional Data Requirements

No additional data are required under section 12 of the *Pest Control Products Act.*

Note that in addition to data supplied by registrants and published information, certain studies from non-glyphosate task forces were used in the risk assessments. These are included in the reference list of this document:

- Activity specific transfer coefficients from the Agricultural Reentry Task Force (ARTF, 2008) were used in the assessment of postapplication agriculture exposure.

- The USEPA Residential SOPs (2012) were also used in the risk assessment for glyphosate. Data from several exposure task forces were used to develop the Residential SOPs. Specifically ARTF, Agricultural Handlers Exposure Task Force (AHETF), and Outdoor Residential Exposure Task Force (ORETF) data are included in the scenarios used from the SOPs.

Furthermore, the PMRA is in the process of revising its approach to buffer zones for all chemicals. Information (data, research) that would facilitate buffer zone refinement may be submitted during the consultation period of this Proposed Re-evaluation Decision. Buffer zones for glyphosate may be revised based on new information as a result of this process.

List of Abbreviations

Abs.	Absolute
AD	administered dose
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism and excretion
AFC	antibody forming cell
a.e.	acid equivalent
AHETF	Agricultural Handlers Exposure Task Force
AHS	agricultural health study
a.i.	active ingredient
ALT	alanine aminotransferase
AMPA	aminomethylphosphonic acid
ALP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
AST	Aspartate transaminase
ATPD	area treated per day
atm	atmosphere
BAF	bioaccumulation factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
BWG	body-weight gain
$[Ca^{++}]$	concentration of calcium
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CFIA	Canadian Food Inspection Agency
cm	centimetres
cm^2	entimetres squared
CSFII	Continuing Surveys of Food Intakes by Individuals
DA	dermal absorption
DBH	diameter at breast height
DFOP	double first order in parallel
DFR	dislodgeable foliar residue
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the time required to observe a 90% decline in concentration)
EbR_{50}	effective biomass rate on 50% of the population
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EEC	estimated environmental concentration
EFSA	European Food Safety Authority

EIIS	Ecological Incident Information System from USEPA
EPA	Environmental Protection Agency
EPSPS	5-enolpyruvylshikimate-3-phosphate synthase
ER_{50}	effective rate on 50% of the population
ERS	exposure re-evaluation section
et al.	and others
EXAMS	Exposure Analysis Modeling System
F_1	first generation
F_2	second generation
F_{2b}	pertaining to offspring produced from the second mating of the second generation
FC	food consumption
FE	food efficiency
FIR	food ingestion rate
FOB	functional observational battery
g	gram(s)
GAT	glyphosate *N*-acetyl transferase
GD	gestation day
GMO	genetically modified organism
GOX	glyphosate oxidoreductase
GUS	groundwater ubiquity score
ha	hectare
HC	historical control
HC_5	hazardous concentration to 5% of the species
HED	Health Evaluation Directorate
hr(s)	hour(s)
HPLC	high performance liquid chromatography
IARC	International Agency for Research on Cancer
IgM	Immunoglobulin M
IUPAC	International Union of Pure and Applied Chemistry
IV	intravenous(ly)
$[K^+]$	concentration of potassium ion
kg	kilogram(s)
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
K_{oc}	organic-carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50%
LD	lactation day
LD_{50}	lethal dose to 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOEC	lowest observed effect concentration
LOD	limit of detection
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
m	metres
m^2	metres squared

max	maximum
mg	milligram
min	minutes
MIS	maximal irritation score
mL	millilitre
M/L/A	mixer/loader/applicator
mmHg	millimetres of mercury
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
MTD	maximum tolerated dose
n/a	not available
N/A	not applicable
ND	not determined
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NR	not reported
NTP	National Toxicology Program
NZW	New Zealand White
OC	organic carbon content
OECD	Organisation for Economic Co-Operation and Development
OM	organic matter content
ORETF	Outdoor Residential Exposure Task Force
P	parental generation
pChE	plasma cholinesterase
PDP	Pesticide Data Program (United States data)
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	postnatal day
POEA	polyethoxylated tallow amine
PPE	personal protective equipment
PRZM	Pesticide Root Zone Model
ppm	parts per million
RBC	red blood cell
RD	residue definition
REI	restricted entry interval
Rel.	relative
RfD	reference dose
ROW	right-of-way
RSD	Relative Standard Deviation
RQ	risk quotient
S9	supernatant fraction from liver homogenate obtained by centrifuging at 9000 g
SD	Sprague-Dawley
SFO	single first order
SOP	standard operating procedure

$t_{1/2}$	half-life
$t_{rep\ ½}$	representative half-life of kinetic models
TC	transfer co-efficient
TLC	thin layer shromatography
TMS	trimethylsulfonium
TSMP	Toxic Substances Management Policy
TTR	turf transferable residue
UF	uncertainty factor
µg	microgram
µL	microlitres
USC	use site category
USDA	United States Department of Agriculture
USEPA	United States Environmental Protection Agency
UV	ultraviolet
V_{ss}	volume of distribution at steady state
v/v	volume per volume dilution
WHO	World Health Organization
Wk	week
Wt.	weight

Appendix I Products Containing Glyphosate that are Registered in Canada Excluding Discontinued Products or Products with a Submission for Discontinuation as of 3 May 2012, Based Upon the PMRA's Electronic Pesticide Regulatory System (e-PRS) Database[1]

Registration Number	Marketing Type[2]	Registrant Name	Product Name	Formulation Type	Guarantee[3] (Salt Form – g a.e./L)
29995	C	Agwest Inc.	Crush'r Plus	Solution	GPI-360
28322	C	Albaugh Inc.	Clearout 41 Plus Herbicide Solution	Solution	GPI-360
30093	C	Alligare, LLC.	Alligare Glyphosate 4+	Solution	GPI-360
29677	C	Chanoix Trading Inc.	Lajj Plus	Solution	GPI-360
26828	C	Cheminova Canada, Inc.	Cheminova Glyphosate Soluble Concentrate Herbicide	Solution	GPI-356
27287	C		Glyfos Au Soluble Concentrate Herbicide	Solution	GPI-360
28925	C		Cheminova Glyphosate (TM) II	Solution	GPI-356
29363	C		Glyfos Bio Herbicide	Solution	GPI-360
29364	C		Glyfos Bio 450 Herbicide	Solution	GPI-450
30234	C		Forza Bio Silvicultural Herbicide	Solution	GPI-360
30235	C		Forza Bio 450 Silvicultural Herbicide	Solution	GPI-450
27394	C	Dow Agrosciences Canada Inc.	Prepass B Herbicide Solution (A Component Of Prepass Htm)	Solution	GPI-360;
27615	C		Vantage Plus Max Herbicide Solution	Solution	GPI-480
28245	C		Maverick II Herbicide Solution	Solution	GPI-480
28540	C		Eclipse II B Herbicide Solution	Solution	GPI-480
28977	C		Maverick III Herbicide Solution	Solution	GPX-480
29033	C		Eclipse III B Herbicide	Solution	GPX-480
29652	C		Prepass XC B Herbicide	Solution	GPX-480
29994	C		Vantage XRT Herbicide	Solution	GPX-480
21262	C	Ezject, Inc.	Diamondback Herbicide Shells	Paste	GPI-0.15
29731	C	Global Ag Brands Inc.	Glyking	Solution	GPI-360
29732	C		Clean-Up	Solution	GPI-360
26846	C	Interprovincial Cooperative Limited	Glyphosate Herbicide – Agricultural and Industrial	Solution	GPI-360
29216	C		Glyphosate Water Soluble Herbicide	Solution	GPI-309(+51)
29266	C	Libertas Now Inc.	Knockout Extra	Solution	GPI-360
29517	C		Burndown	Solution	GPI-360
29524	C		Clearcrop	Solution	GPI-360
29525	C		Cleanfield	Solution	GPI-360
29733	C		GP Advantage	Solution	GPI-360
28623	C	Loveland Products Canada Inc.	Sharpshooter Plus Herbicide	Solution	GPI-360
28631	C		Sharpshooter Herbicide	Solution	GPI-356
29126	C	Mey Canada Corporation	Wise Up Herbicide Solution	Solution	GPI-356
19536	C	Monsanto Canada Inc.	Rustler Summerfallow Herbicide	Solution	GPI-108 DXB-182
20423	C		Mocan 943 Water Soluble Herbicide	Solution	GPI-120 DIC-86

Registration Number	Marketing Type[2]	Registrant Name	Product Name	Formulation Type	Guarantee[3] (Salt Form – g a.e./L)
21572	C		Rustler Fallow Liquid Herbicide	Solution	GPI-132 DIC-60
25604	C		Roundup Fast Forward Preharvest Herbicide	Solution	GPI-300 GLG-16
25795	C		Roundup Fastforward Preseed Agricultural	Solution	GPI-300 GLG-10
25898	C		Focus Herbicide	Solution	GPI-132 DXB-82
25918	C		Mon 77759 Water Soluble Herbicide	Solution	GPI-300 GLG-36
26625	C		Mon 78027 Water Soluble Herbicide	Solution	GPI-180 GLG-131
26920	C		Roundup Transorb Max Liquid Herbicide	Solution	GPI-480
27200	C		Rustler Liquid Herbicide	Solution	GPI-194 DIC-46
29841	C		Mon 76431 Liquid Herbicide	Solution	GPP-540
29868	C		Mon 76429 Liquid Herbicide	Solution	GPP-540
29290	C	Newagco Inc.	Mpower Glyphosate	Solution	GPI-356
25866	C	Nufarm Agriculture Inc.	Nufarm Credit Liquid Herbicide	Solution	GPI-356
27950	C		Credit Plus Liquid Herbicide	Solution	GPI-360
29124	C		Credit 45 Herbicide	Solution	GPI-450
29125	C		Nufarm Credit 360 Liquid Herbicide	Solution	GPI-360
29470	C		Nuglo Herbicide	Solution	GPI-450
29471	C		Nufarm Glypbosate 450 Herbicide	Solution	GPI-450
29479	C		Polaris	Solution	GPI-360
29480	C		Racketeer	Solution	GPI-360
29888	C		Credit Xtreme Herbicide	Solution	GPO-540
30442	C	Rack Petroleum Ltd.	The Rack Glyphosate	Solution	GPI-360
28802	C	Syngenta Canada Inc.	Cycle Herbicide	Solution	GPP-500
29308	C		Touchdown Pro Herbicide	Solution	GPM-360
29341	C		Halex GT Herbicide	Solution	GPP-250 AME-250 MER-25
29552	C		Takkle Herbicide	Solution	GPI-140 DIC-70
29644	C		Flexstar Herbicide	Solution	GPM-315 FOF-79
30412	C		Flexstar GT Herbicide	Solution	GPM-271 FOF-67
29022	C	Teragro Inc	Weed-Master Glyphosate 41 Herbicide	Solution	GPS-356
29629	C	Viterra Inc.	Viterra Glyphosate	Solution	GPI-360
24359	C+R	Cheminova Canada, Inc.	Glyfos Soluble Concentrate Herbicide	Solution	GPI-360
26401	C+R		Forza Silvicultural Herbicide	Solution	GPI-360
28924	C+R		Glyfos Soluble Concentrate Herbicide II	Solution	GPI-360
26171	C+R	Dow Agrosciences Canada Inc.	Vantage Plus Herbicide Solution	Solution	GPI-360
26172	C+R		Vantage Herbicide Solution	Solution	GPI-356
26884	C+R		Vantage Forestry Herbicide Solution	Solution	GPI-356
28840	C+R		Vantage Plus Max II Herbicide Solution	Solution	GPX-480
29588	C+R		GF-772 Herbicide	Solution	GPI-360
29773	C+R		Depose Herbicide Solution	Solution	GPI-356
29774	C+R		Durango Herbicide Solution	Solution	GPX-480

Registration Number	Marketing Type[2]	Registrant Name	Product Name	Formulation Type	Guarantee[3] (Salt Form - g a.e./L)
30423	C+R		Prepass 480 Herbicide Solution	Solution	GPX-480
30516	C+R		Vantage Max Herbicide Solution	Solution	GPS-480
27988	C+R	Interprovincial Cooperative Limited	Ipco Factor 540 Liquid Herbicide	Solution	GPP-540
29775	C+R		Matrix Herbicide Solution	Solution	GPX-480
30319	C+R		Vector Herbicide Solution	Solution	GPX-480
30076	C+R	Loveland Products Canada Inc.	Mad Dog Plus	Solution	GPI-360
29219	C+R	Makhteshim Agan Of North America Inc.	Glyphogan Plus Liquid Herbicide	Solution	GPI-356
19899	C+R	Monsanto Canada Inc.	Vision Silviculture Herbicide	Solution	GPI-356
25344	C+R		Roundup Transorb Liquid Herbicide	Solution	GPI-360
27487	C+R		Roundup Weathermax With Transorb 2 Technology Liquid Herbicide	Solution	GPP-540
28486	C+R		Roundup Ultra 2 Liquid Herbicide	Solution	GPP-540
28487	C+R		R/T 540 Liquid Herbicide	Solution	GPP-540
28608	C+R		Mon 79828 Liquid Herbicide	Solution	GPP-540
28609	C+R		Mon 79791 Liquid Herbicide	Solution	GPP-540
29498	C+R		Start Up Herbicide	Solution	GPP-540
30104	C+R		Mon 76669	Solution	GPP-540
27736	C+R		Vision Max Silviculture Herbicide	Solution	GPP-540
27764	C+R		Roundup Ultra Liquid Herbicide	Solution	GPP-540
27946	C+R		Renegade HC Liquid Herbicide	Solution	GPP-540
28198	C+R		Roundup Transorb HC Liquid Herbicide	Solution	GPP-540
27192	C+R	Syngenta Canada Inc.	Touchdown IQ Liquid Herbicide	Solution	GPM-360
28072	C+R		Touchdown Total Herbicide	Solution	GPP-500
29201	C+R		Traxion Herbicide	Solution	GPP-500
29009	C+R	Teragro Inc	Weed-Master Glyphosate Forestry Herbicide	Solution	GPI-356
26609	D	Cheminova Canada, Inc.	Glyfos Herbicide 143 Concentrate	Solution	GPI-143
26610	D		Glyfos Herbicide 7 Ready-To-Use	Solution	GPI-7
26827	D		Glyfos Concentrate 356 Herbicide	Solution	GPI-356
27351	D	Dow Agrosciences Canada Inc.	Glyphosate 18% Herbicide Solution Concentrate	Solution	GPI-143
27352	D		Glyphosate 0.96% Herbicide Ready-To-Use	Solution	GPI-7
22627	D	Monsanto Canada Inc.	Roundup Concentrate Non-Selective Herbicide	Solution	GPI-143
22759	D		Roundup Super Concentrate Grass & Weed Control	Solution	GPI-356
22807	D		Roundup Ready To Use Non-Selective Herbicide With Fastact Foam	Solution	GPI-7
23786	D		Roundup Quik Stik Non-Selective Herbicide Tablets	Tablet	GPS-60
24299	D		Roundup Ready-To-Use Grass & Weed Control With Fastact Foam	Solution	GPI-7
26263	D		Roundup Ready-To-Use With Fastact Foam Pull'n Spray Non-Selective Herbicide	Solution	GPI-7
27460	D		Roundup Ready-To-Use Non-Selective Herbicide	Solution	GPI-7.2
27506	D		Roundup Ready-To-Use Pull'n Spray Non-Selective Herbicide	Solution	GPI-14.0
27507	D		Roundup Ready-To-Use Pull'n Spray Poison Ivy & Brush Control Non-Selective Herbicide	Solution	GPI-14.0
28974	D		Roundup Pump'N Go	Solution	GPI-7

Registration Number	Marketing Type[1]	Registrant Name	Product Name	Formulation Type	Guarantee[2] (Salt Form – g a.e./L)
29003	D		Roundup Ready-To-Use Poison Ivy & Brush Control Non-Selective Herbicide	Solution	GPI-14
29034	D		Roundup Ready-To-Use Poison Ivy & Brush Control With Quick Connect Sprayer	Solution	GPI-14
27013	D	Sure-Gro IP Inc.	Later's Grass & Weed Killer Ready To Use	Solution	GPI-7
27014	D		Later's Grass & Weed Killer Concentrate	Solution	GPI-143
27015	D		Later's Grass & Weed Killer Super Concentrate	Solution	GPI-356
29580	D		Later's Grass & Weed Killer Ready To Use EZ Spray	Solution	GPI-7
29307	D	Syngenta Canada Inc.	Touchdown Ready-To-Use Herbicide	Solution	GPM-8.4
29309	D		Touchdown Super Concentrate Herbicide	Solution	GPM-360
29310	D		Touchdown Diquat Quick-Kill Ready-To-Use Herbicide	Solution	GPM-8.3 DIQ-0.28
28464	D	Teragro Inc	Totalex Concentrate Brush, Grass & Weed Killer Home Gardener	Solution	GPI-143
28467	D		Totalex Concentrate Brush, Grass & Weed Killer Virterra	Solution	GPI-143
28469	D		Totalex Ready-To-Use Brush, Grass & Weed Killer Virterra	Solution	GPI-7
28470	D		Totalex Ready-To-Use Brush, Grass & Weed Killer Home Gardener	Solution	GPI-7
28471	D		Totalex Super Concentrate Brush, Grass & Weed Killer Home Gardener	Solution	GPI-356
28472	D		Totalex Super Concentrate Brush, Grass & Weed Killer Virterra	Solution	GPI-356
28574	D		Totalex Rtu Brush, Grass & Weed Killer With 1 Touch Power Sprayer Home	Solution	GPI-7.0
28575	D		Totalex Rtu Brush, Grass & Weed Killer With 1 Touch Power Sprayer	Solution	GPI-7.0
28576	D		Totalex Extra Strength Rtu Brush, Grass & Weed Killer With 1 Touch Power Sprayer Home Gardener	Solution	GPI-14
28577	D		Totalex Extra Strength Rtu Brush, Grass & Weed Killer With 1 Touch Power Sprayer Virterra	Solution	GPI-14
25600	M	Cheminova Canada, Inc.	Glyphosate Concentrate Herbicide	Solution	GPI-46.3
27497	M		Glyfos 356 MUC	Solution	GPI-356
26449	M	Dow Agrosciences Canada Inc.	Glyphosate 62% Solution Manufacturing Concentrate	Solution	GPI-46
27074	M		Vantage Herbicide Solution Manufacturing Concentrate	Solution	GPI-356
27075	M		Vantage Plus Herbicide Solution Manufacturing Concentrate	Solution	GPI-360
28783	M		Gf-1667 Herbicide Manufacturing Concentrate	Solution	GPX-49
28963	M		Glyphosate 85% Manufacturing Concentrate	Solution	GPS-85
29267	M	Libertas Now Inc.	Knockout 62	Solution	GPI-46.0
21061	M	Monsanto Canada Inc.	Mon 0139 Solution Herbicide Manufacturing Concentrate	Solution	GPI-46.0
26919	M		Mon 77945 Herbicide Manufacturing Concentrate Solution	Solution	GPI-46
27183	M		Mon 77973 Herbicide Manufacturing Concentrate	Solution	GPS-85
27485	M		Mon 78623 Herbicide Manufacturing Concentrate	Solution	GPP-47.3
28603	M		Mon 79380 Herbicide Manufacturing Concentrate	Solution	GPP-540
28604	M		Mon 79582 Herbicide Manufacturing Concentrate	Solution	GPP-540
28605	M		Mon 79544 Herbicide Manufacturing	Solution	GPP-540

Registration Number	Marketing Type[2]	Registrant Name	Product Name	Formulation Type	Guarantee[3] (Salt Form - g a.e./L)
			Concentrate		
28625	M		Mon 78087 Herbicide Manufacturing Concentrate	Solution	GPI-356
29123	M	Nufarm Agriculture Inc.	Nufarm Glyphosate IPA Manufacturing Concentrate	Solution	GPI-46
27871	M	Syngenta Canada Inc.	Glyphosate 600 SL Manufacturing Concentrate	Solution	GPS-600
29719	M	Teragro Inc	Teragro Glyphosate Manufacturing Concentrate	Solution	GPI-46
29645	T	Agromarketing Co. Inc.	Nasa Glyphosate Technical	Solid	GPS-96.37
28321	T	Albaugh Inc.	Clearout Glyphosate Technical	Solid	GPS-96.7
24337	T	Cheminova Canada, Inc.	Glyphosate Technical	Solid	GPS-85.8
29143	T		Glyfos Soluble Concentrate Herbicide 2	Solid	GPS-97.9
29326	T		Cheminova Glyphosate Technical II	Solid	GPS-95.7
29530	T		Cheminova Glyphosate Technical III	Solid	GPS-98.2
26450	T	Dow Agrosciences Canada Inc.	Glyphosate Technical Herbicide	Solid	GPS-96.3
28967	T		Technical Glyphosate Herbicide	Solid	GPS-96.2
29265	T	Libertas Now Inc.	Knockout Tech	Solid	GPS-98.1
29799	T	Mey Corporation	Mey Corp Glyphosate Technical	Solid	GPS-98.5
30099	T		Mgt Glyphosate Technical	Solid	GPS-96.4
19535	T	Monsanto Canada Inc.	Glyphosate Technical Grade	Solid	GPS-96.3
29381	T	Newagco Inc.	Newagco Glyphosate Technical	Solid	GPS-96.0
28857	T	Nufarm Agriculture Inc.	Nufarm Glyphosate Technical Acid	Solid	GPS-96.5
29980	T	Sharda Worldwide Exports Pvt. Ltd./Sharda International Fze	Sharda Glyphosate Technical Herbicide	Solid	GPS-96.2
24344	T	Syngenta Canada Inc.	Glyphosate Acid Wet Paste Herbicide	Paste	GPS-88.8
28983	T		Technical Touchdown Herbicide	Solid	GPS-97.1
29540	T		Touchdown Technical Herbicide	Solid	GPS-99
28882	T	Teragro Inc	Glyphosate Technical Herbicide	Solid	GPS-97.5

[1] GPS = glyphosate acid, GPI = glyphosate isopropylamine or ethnolamine salt, GPM = glyphosate mono-ammonium or diammonium salt, GPP = glyphosate potassium salt, GPX = glyphosate dimethylsulfonium salt, and GPO = GPI + GPP. Note that GPT (gltphosate trimethylsulfonium salt) has been voluntarily discontinued by the registrant Syngenta Canada Inc.

[2] C = Commercial Class, C+R = Commercial and Restricted Class, D = Domestic Class, M = Manufacturing Concentrate, T = Technical grade active ingredient.

[3] AME = s-metolachlor, DIC = dicamba, DIQ = diquat, DXB = 2,4-D (isomer specific), FOF = fomesafen, GLG = glufosinate ammonium and MER = mesotrione.

Appendix IIa Registered Commercial Class Uses of Glyphosate in Canada as of 3 May 2012. Uses From Discontinued Products or Products With a Submission for Discontinuation are Excluded[1]

USCs[2]	Sites[3]	Weeds and/or Harvest Management	Application Methods and Equipment[4]	Maximum Application Rate (kg a.e./ha)		Maximum Number of Applications Per Year[5]	Minimum Interval Between Applications (Days)[6]
				Single	Cumulative Per Year[5]		
13 14	Wheat Barley Oats	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use** Knapsack or high-volume equipment (hose and handguns, hand sprayer or other suitable nozzle arrangement)	4.320	9.542	4	[7]
13 14	Rye	Annual weeds and foxtail barley	Field sprayer **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	0.902	0.902	1	Not applicable
7 13 14	Soybeans	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use** Knapsack or high-volume equipment (hose and handguns, hand sprayer or other suitable nozzle arrangement) Boom or boomless Roller applicators Wick or other wiper applicators	4.320	9.542	6	[7]
7 13 14	Soybeans (Glyphosate tolerant or Roundup Ready soybean varieties or Roundup Ready 2 Yield soybean varieties)	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	12.062	5	[7] For in crop treatment, 14 for sequential application and the second application must be no later than flowering stage of soybean.

USCs[2]	Sites[3]	Weeds and/or Harvest Management	Application Methods and Equipment[4]	Maximum Application Rate (kg a.e./ha)		Maximum Number of Applications Per Year[5]	Minimum Interval Between Applications (Days)[5]
				Single	Cumulative Per Year[5]		
7 13 14	Corn	Annual and perennial weeds	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use** Knapsack or high-volume equipment (hose and handguns, hand sprayer or other suitable nozzle arrangement)	4.320	8.640	3	[7]
7 13 14	Corn (glyphosate tolerant)	Annual and perennial weeds	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	10.445	4	[7]
14	Corn – Sweet (Roundup Ready 2 Technology)	Annual and perennial weeds	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	10.438	4	[7]
7 13 14	Canola	Weed Control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	9.542	3	[7]
7 13 14	Canola (glypbosate tolerant)	Weed Control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	10.890	5	[7]
7	Canola – Roundup Ready Hybrid canola seed production	When pollination is complete or near completion	Boom sprayer	0.902	1.804	2 (sequential application)	At least 5 days
13 14	Peas	Weed Control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	9.542	3	[7]
14	Dry beans	Weed Control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use** Knapsack or high-volume equipment (hose and handguns, hand sprayer or other suitable nozzle arrangement) Roller applicators Wick or other wiper applicators	4.320	9.542	6	[7]

USCs[1]	Sites[1]	Weeds and/or Harvest Management	Application Methods and Equipment[4]	Maximum Application Rate (kg a.e./ha)		Maximum Number of Applications Per Year[5]	Minimum Interval Between Applications (Days)[5]
				Single	Cumulative Per Year[5]		
7 13 14	Flax (including low linoleic acid varieties)	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	9.542	3	[7]
14	Lentils	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	9.542	3	[7]
13 14	Chickpeas Lupin (dried) Fava bean (dried)	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	9.542	3	[7]
7 13 14	Mustard (yellow/white, brown, oriental)	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	9.542	3	[7]
13	Pearl millet (pearl millet grain is to be harvested for use as animal feed only. Do not graze treated pearl millet forage or cut for hay.)	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	9.542	3	[7]
14	Sorghum (grain) (not for use as a forage crop)	Weed control: Annual and perennial weeds Harvest management	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	9.542	3	[7]
7 13 14	Sugar beets	Annual and perennial weeds	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use** Knapsack sprayers, hand held and high-volume equipment handguns or other suitable nozzle arrangement	4.320	12.600	3	[7]
7 13 14	Sugar beets (Roundup Ready only)	Emerged annual and perennial weeds	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	0.902	3.607	4	10

USC[2]	Sites[3]	Weeds and/or Harvest Management	Application Methods and Equipment[4]	Maximum Application Rate (kg a.e./ha)		Maximum Number of Applications Per Year[4]	Minimum Interval Between Applications (Days)[5]
				Single	Cumulative Per Year[5]		
14	Asparagus	Annual and perennial weeds	Boom or boomless	4.320	12.600	3	[7]
14	Ginseng (North American) – new garden (BC only)	Volunteer grain	Boom sprayer, shielded sprayer, hand-held guns	0.902	0.902	1	Not applicable
	Ginseng (North American) – Existing/established gardens			0.902	1.804	2	[7]
13	Forage grasses and legume including seed production	Weed control: Annual and perennial weeds Harvest management	Boom or boomless Knapsack or high-volume equipment (hose and handguns, hand sprayer or other suitable nozzle arrangement)	4.320	10.440	4	[7]
13	Pasture	Annual and perennial vegetation Most herbaceous weeds, woody brush and trees	Boom or boomless Mist blower Hand-held high volume equipment **Ground Restricted use** **Aerial Restricted use**	4.320	8.640	2	[7]
14	Strawberry	Annual and perennial weeds	Boom or boomless Knapsack or high-volume equipment (hose and handguns, hand sprayer or other suitable nozzle arrangement) Wiper	4.320	12.600	4	[7]
14	Blueberry (highbush)	Annual and perennial weeds	Boom or boomless Shielded sprayer, hand held and high-volume orchards guns Knapsack or high-volume equipment (hose and handguns, hand sprayer or other suitable nozzle arrangement)	4.320	12.600	3	[7]
14	Blueberry (lowbush)	Annual and perennial weeds Woody brush	Boom or boomless Shielded sprayer, hand held and high-volume orchards guns Knapsack or high-volume equipment (hose and handguns, hand sprayer or other suitable nozzle arrangement)	4.320	12.600	3	[7]
14	Cranberry	Annual and perennial weeds	Boom or boomless Wipers and wicks	4.320	12.600	2	[7]
13 (apples only)	Apples Apricot Cherry – (Sweet/Sour) Peaches	Annual and perennial weeds	Boom sprayer, shielded sprayer, hand held and high-volume orchards guns Rollers	4.320	12.600	3	[7]

USCs[1]	Sites[2]	Weeds and/or Harvest Management	Application Methods and Equipment[3]	Maximum Application Rate (kg a.e./ha)		Maximum Number of Applications Per Year[4]	Minimum Interval Between Applications (Days)[5]
				Single	Cumulative Per Year[6]		
14	Pears Plums		Wick or other wiper applicators				
14	Grapes	Annual and perennial weeds	Boom sprayer, shielded sprayer, hand held and high-volume orchards guns Rollers Wick or other wiper applicators	4.320	12.600	3	[7]
14	Filberts or Hazelnut	Annual weeds	Boom or boomless Shielded sprayer, hand held and high-volume orchards guns	4.320	12.600	[3]	[7]
14	Walnut, Chestnut, Japanese heartnut	Annual and perennial weeds	Boom sprayer, shielded sprayer, hand held and high-volume orchards guns Wipers	4.320	12.600	2 Apply as a directed spray or as a wiper solution	[7]
4 27	Shelterbelts Nursery stock Woody ornamentals Including forest tree nursery and Christmas tree plantations – Deciduous	Annual and perennial weeds	Boom or boomless Rollers Wick or other wiper applicators	4.320	8.640	4	[7]
4 27	Short rotation intensive culture (SRIC) poplar	Annual and perennial weeds	Boom or boomless Shielded sprayers for post-directed spray solution	4.320	4.320	3	42
7 13 14	All other crops – Pre-seeding	Annual and perennial weeds	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia – Restricted use**	4.320	4.320	1	Not applicable
7 13 14	Summer fallow	Annual and perennial weeds	Boom or boomless **Aerial – Prairie provinces only (including Peace River region of British Columbia) – Restricted use**	4.320	4.320	1	Not applicable
4	Forest and Woodlands	Herbaceous weeds, woody brush and trees, Ericaceous species (for example, *Kalmia* spp.- sheep laurel, lamb kill)	Boom or Boomless Mist blower **Aerial – Restricted use** Hand held and high-volume equipment Roller application Wick or other wiper applicators	4.320	9.000 This is derived from the label of PCP# 29308 (glyphosate at 360 g/L) in which the annual maximum rate is 25	[2]	[7]

USCs[2]	Sites[3]	Weeds and/or Harvest Management	Application Methods and Equipment[4]	Maximum Application Rate (kg a.e./ha)		Maximum Number of Applications Per Year[5]	Minimum Interval Between Applications (Days)[5]
				Single	Cumulative Per Year[5]		
			Injection application Diamondback Herbicide injection system (EZJECT) and equipment Cut stump application		L/ha. The calculated cumulative rate per year is 8.640 kg a.e./ha.		
16	Non-crop land and industrial uses	Annual and perennial weeds Woody brush and trees	Boom or boomless Hand held and high-volume application **Aerial application: Restricted use** Mist blower Rollers Wick or other wiper applicators Injection applications Diamondback Herbicide injection system (EZJECT)and equipment Low pressure equipment (for example, squirt bottle or similar device)	4.320	12.960	[3]	[7]
30	Turf grass (Prior to establishment or renovation)	Annual and perennial weeds	Boom or boomless Mist blower Hand-held high-volume application	4.320	9.000	2.	[7]

1. All uses are supported by the registrants. Information in [ ] is provided by the registrants.
2. USCs 1 to 14 belong to the use sector AGRICULTURE AND FORESTRY, USCs 15-23 belong to the use sector INDUSTRY and USCs 24-33 belong to the use sector SOCIETY.
3. Sites are either as stated on the product label or as interpreted by the PMRA so as to achieve consistency in naming. For agricultural cropland use, the labels state that all crops can be treated with glyphosate prior to planting. This "prior to planting use on all crops" is captured in two parts. (1) It is captured in the Site column corresponding to the crop which appears on the labels for other use claim(s). For example, wheat appears on the label for in-crop spot treatment as well as pre-harvest application; the "prior to planting use" is added under the Wheat site; (2) It is captured in the "All other crops" section of the site column corresponding to the crop which does not appear on the label (for example, vegetables). Post-harvest stubble use is dealt with similarly. Thus, all claimed uses for a specific site are presented together.
4. The Equipment column covers application equipment appearing on all product labels listing all possible application equipment for the specific site. All aerial applications are restricted uses and in bold text.
5. Cumulative rate per year, maximum number of applications per year and minimum interval between applications: This information is currently specified for use on fruit tree, berry and vine crops but is not clearly specified for other uses such as agricultural cropland and non-cropland. For agricultural cropland use, crops can, in theory, be treated with glyphosate at each of four windows: pre-planting, in-crop spot, pre-harvest and/or post-harvest. Typically, only one application at most is made at each application window. However, the product labels also state that a repeat treatment is required if heavy rainfall occurs immediately after application. In a growing season, it is possible to do sequential applications at some or all application windows, in other words: prior to planting + in-crop spot + pre-harvest + post-harvest stubble. For forestry and non-cropland use, the product labels state that repeat applications may be necessary to control late germinating weeds, regeneration from underground parts or seeds, and new growth or second flush of weeds germinating from the canopy closure. In addition, for wiper applications, the product labels state that best results may be obtained if two applications are made in opposite directions. The cumulative product rate per year is expressed to reflect the possible repeat application required if heavy rainfall occurs immediately after application. The cumulative a.i. rate per year, maximum number of applications per year and minimum interval between applications for a specific site are expressed to reflect all possible applications across the growing season, representing the worst case scenario.

Appendix IIb Registered Domestic Class Uses of Glyphosate in Canada as of 23 October 2012. Uses from Discontinued Products or Products with a Submission for Discontinuation are Excluded.[1]

USCs[2]	Sites[3]	Weeds	Application Equipment	Maximum Application Rate (g a.e./m²)		Maximum Number of Applications Per Year	Minimum Interval Between Applications (Days)[4]
				Single	Cumulative Per Year		
16	Hard to mow areas, around buildings, foundations and fence posts, lawn trimming/ edging, patio, vacant lots, storage and recreational areas, driveways and along fence lines	Most annual and perennial grasses and weeds such as quackgrass, chickweed, ragweed, knotweed, poison ivy, Canada thistle, milkweed and bindweed	Ground Do not use hose-end sprayers For Ready to Use products – Pull'N Spray or 1 Touch Power Sprayer or with on/off nozzle or with child resistant closure lock or EZ SPRAY™ or Pump'N Go	0.700	1.400	[2] Heavy rainfall immediately after application may wash the chemical off the foliage and repeat treatment may be required. Use a repeat application on any seedlings that regrow from seeds or as new seedlings and vegetation emerge.	[7]
				0.386	0.771		
27	Around trees/shrub/ ornamentals	Most annual and perennial grasses and weeds such as quackgrass, chickweed, ragweed, knotweed, poison ivy, Canada thistle, milkweed and bindweed		0.700	1.400		
				0.386	0.771		
14 27	Garden renovation	Most annual and perennial grasses and weeds such as quackgrass, chickweed, ragweed, knotweed, poison ivy, Canada thistle, milkweed and bindweed		0.700	1.400		
				0.386	0.771		
30	Lawn renovation			0.700	1.400		
				0.386	0.771		
16	Brush control (for domestic use)	Most brush such as poplar, alder, maple and raspberry		0.700	1.400		
				0.386	0.771		
14 27	In flower beds and vegetable gardens In large areas for garden plot preparation	Poison ivy and brush Most types of weeds and grasses	Ready to Use – Pull'N Spray	0.355	0.710		
30	In large areas for lawn replacement						

1. All uses are supported by the registrants and the Glyphosate Task Force.
2. USCs 1 to 14 belong to the use sector AGRICULTURE AND FORESTRY, USCs 15-23 belong to the use sector INDUSTRY and USCs 24-33 belong to the use sector SOCIETY.
3. Sites are either as stated on the product label or as interpreted by the PMRA so as to achieve consistency in naming.
4. Information in [ ] is provided by the registrants.

Appendix III Toxicity Profile and Endpoints for Health Risk Assessment

Table III.1A Summary of Toxicology Studies for Glyphosate Acid

Note: Effects noted below are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Effects on organ weights are known or assumed to reflect changes in absolute weight and relative (to body weight) weight unless otherwise noted.

Study Type/ Animal/ PMRA #	Study Results
	Toxicokinetic Studies
Single Dose (Gavage or IV) F344 Rat PMRA#: 2391579	**Absorption**: Peak blood radioactivity levels were reached within 1st and 2nd hours of oral administration for the low and high-dose groups, respectively. The peak blood radioactivity level was about 0.20% of the administered dose (AD) for the low oral dose and about 0.70% of the AD for the high oral dose. The 10-fold increase in the oral dose resulted in a 35-fold increase in the peak blood concentrations. The blood radioactivity versus time plot fit a two-compartment model with a rapid distribution phase of 30 minutes and slower elimination phase of 13 hours. Blood radioactivity levels declined rapidly following an intravenous dose of 5.6 mg/kg such that within 6 hours of dosing, over 90% of radioactivity was recovered in the urine. Comparison of the pattern of elimination following i.v. and oral administration of ^{14}C glyphosate suggested that the compound was incompletely absorbed. **Distribution**: Most of the radioactivity levels in the tissues were recovered in the gastrointestinal (GI) tract (mostly in the small intestine) up to the 12-hour time point following single oral administration of the low and high doses. Radioactivity was also detected in the liver, kidneys, skin and blood, but in comparably small amounts to the small and large intestines (0.1-0.7% of AD in these tissues and at different time-points). The tissue radioactive residues decreased from 12% of total radioactivity to less than 1% within 24 hours. **Excretion**: Following oral administration of ^{14}C-glyphosate, elimination was similar in the low and high-dose groups although a higher percentage (58-74%) of radioactivity excreted through the feces and a lower portion (~ 35%) excreted through the urine. The fecal excretion peaked towards the end of the measurement (72-hour time point) for both dose groups. The urinary excretion of the radioactivity plateaued at 12 hours in the low-dose group and at 72 hours in the high-dose groups. Following the intravenous administration of a low dose (5.6 mg/kg) of ^{14}C-glyphosate, the elimination was rapid (90% excreted within 6 hours) and occurred primarily through the urine.
Single Dose (IP) Sprague-Dawley Rat PMRA#: 2391580	**Metabolism**: The major radioactive excreted component was unchanged glyphosate. **Excretion**: feces (6-14%), urine (74-78%) after 5 days, negligible excretion via air. Tissue retention at 120 hrs was 1%.
Single Dose (Gavage) Wistar Rat PMRA#: 1184961	**Absorption**: Rapidly absorbed **Metabolism**: The major radioactive excreted component was unchanged glyphosate. 6.9 to 8.6% of AD in feces extracts corresponded to Aminomethylphosphonic acid (AMPA) **Excretion**: in urine (14% in ♂, 35-40% in ♀) and feces (81% in ♂) after 48hrs, negligible excretion via air.

Study Type/ Animal/ PMRA #	Study Results
Single Dose (Gavage) Wistar Rat PMRA#: 1212026	**Absorption**: Incomplete (based on increased rapid fecal excretion) **Distribution**: Autoradiograms showed greater intensity of the radioactivity in bones and kidneys (reducing to negligible amounts by 48 hrs in kidneys.) **Excretion**: In urine (17.9% in ♂, 12.8% in ♀) and feces (59.3% in ♂, 80.3% in ♀) after 24 hours. In urine (34% in ♂, 12.5% in ♀) and feces (60.5% in ♂, 91.2% in ♀) after 48 hours. Radioactivity recovered in the expired air was negligible.
Single Dose (Gavage) Wistar Rat PMRA#: 1212027	**Absorption**: Incomplete (based on increased rapid fecal excretion) **Distribution**: Less than 0.19/0.17% in ♂/♀ of AD present in the GI tract after 72 hrs. Tissue concentrations accounted for 0.5% of AD. Highest concentrations were in bone, liver, kidneys and lungs. **Excretion**: About 90% excreted within 24 hrs of dosing. In urine (13% in ♂, 11% in ♀) and feces (88.5% in ♂, 89% in ♀) after 72 hours
Single Dose (Gavage) Wistar Rat PMRA#: 1212028	**Absorption**: Incomplete (based on increased rapid fecal excretion) **Distribution**: Less than 0.12% of AD present in the GI tract after 72 hrs. Tissue concentrations accounted for 0.5% of AD. Highest concentrations were in bone, liver, and kidneys. **Excretion**: About 90% excreted within 24hrs of dosing. In urine (11% in ♂, 11% in ♀) and feces (87% in ♂, 91% in ♀) after 72 hours
Single Dose (Gavage) Wistar Rat PMRA#: 1212029	**Absorption**: Based on excretion and tissue distribution, the extent of absorption of an oral dose of glyphosate did not exceed 21%. **Distribution**: Tissue concentrations were not examined in this study. **Metabolism**: Poor metabolism since the parent (unchanged) compound excreted in the urine. **Excretion**: Unchanged glyphosate acid with < 1% AMPA in urine. Unchanged glyphosate acid in feces 1000 mg/kg bw bile duct cannula dose: in urine (20.8% in ♂, 16.3% in ♀) and feces (39.1% in ♂, 30.5% in ♀), bile (0.06% in ♂ and ♀) after 48 hrs. 1000 mg/kg bw: in urine (16.0% in ♂, 16.7% in ♀) and feces (79.3% in ♂, 63.9% in ♀) 10 mg/kg bw after 14 unlabelled doses: in urine (10.5% in ♂, 10.5% in ♀) and feces (52.9% in ♂, 72.1% in ♀) 10 mg/kg bw: in urine (12.7% in ♂, 10.5% in ♀) and feces (74.8% in ♂, 55.2% in ♀)
Single Dose (Gavage) Wistar Rat PMRA#: 1212031	**Absorption**: higher in fasted vs. non-fasted animals based on urinary and fecal radioactivity levels **Distribution**: The residues in carcass accounted for 2% of the dose in fasted and 0.5% in nou-fasted animals. The residues in GI tract were 0.23% in fasted and 0.13% in non-fasted animals. **Excretion**: in urine (fasted: 51%, non-fasted: 15%) and feces (fasted: 47%, non-fasted: 85%)
Single Dose (IV) Wistar Rat PMRA#: 1212032	**Distribution**: Around 3% of radioactivity was recovered in all tissues that included in decreased order of concentration: bone, spleen, kidneys, lungs, liver, GI tract and salivary glands. **Excretion**: in urine (88.3% in ♂, 74.6% in ♀) and feces (5.1% in ♂, 14.2% in ♀) after 72 hours
Single Dose (Gavage)	**Absorption**: Incomplete (based on increased rapid fecal excretion) **Distribution**: Tissue concentration of radioactivity was low (accounted for less than 0.6% of

Study Type/ Animal/ PMRA #	Study Results
Wistar Rat PMRA#: 1212033	the AD). Highest concentration in bone > kidneys > liver > lungs > spleen > salivary glands > brain. **Excretion:** Over 87% excreted within 24 hrs. Excretion in urine (17% in ♂, 17.5% in ♀) and feces (90% in ♂, 84.5% in ♀) after 72 hours.
Single Dose (Gavage or IV) Non-guideline Wistar Rat PMRA#: 2391577	**Absorption**: Glyphosate was slowly and poorly absorbed orally. The absorption half-life was 2.29 hours while the maximal plasma concentration was 4.64 µg/ml and time to maximal plasma concentration was 5.16 hrs after the oral administration of glyphosate. The oral bioavailability of glyphosate was 23.21%. **Metabolism**: Not extensively metabolized in rats. AMPA was the main metabolite which represented 6.49% of the parent plasma concentrations. **Distribution**: After IV administration of 100 mg/kg bw, the distribution phase of glyphosate was fast ($T_{1/2\alpha}$ = 0.345 hr) and with a high volume of distribution at steady state (V_{ss} = 2.99 L/kg) suggesting extensive distribution in extravascular tissues. The two compartment model was the best fit for both groups to establish the toxicokinetic characteristics. The values of apparent volume of distribution in the second compartment were 2.39 and 2.32 L/kg after IV and oral administration, respectively. **Elimination**: The rate of elimination of AMPA ($T_{1/2\beta}$ = 15.08 hr) after oral glyphosate administration was similar to that of glyphosate ($T_{1/2\alpha}$ = 14.38). The elimination half-life calculated after IV administration was 9.99 hours. The elimination half-life of glyphosate increased by 44% (to 14.38 hr) after oral administration compared to the IV administration.
14-Day Toxicokinetic (Diet) Wistar Rat PMRA#: 1182530 or 1184946	**Absorption**: Poor (based on increased rapid fecal excretion) **Distribution**: The body load (= cumulative intake – cumulative excretion) < 5% of the AD for low and high-dose groups (mid-dose group calculation resulted in a negative value). Maximum concentration levels reached in tissues by 10th day of exposure. Tissue concentration: kidney, spleen > fat > liver > ovaries > heart > muscle > brain > testes (the trend in all dose groups). **Excretion**: Rate of excretion in urine and feces equalled the rate of intake by day 6-8 (indicating a plateau/steady state level had been reached). Mean urinary excretion was 8.3%, 10.5% and 8.5% of the AD for low, mid- and high-dose groups by the end of the treatment. Fecal excretion was over 90% of the AD for each dose group. The urinary excretion had decreased by 96% two days after cessation of the treatment. The fecal excretion was negligible four days after treatment was stopped.
Single Dose (Gavage) NZW Rabbits PMRA#: 1184958, 1184959	**Metabolism**: The major radioactive excreted component was unchanged glyphosate **Distribution**: Highest in gut (2.5%) followed by liver, kidney, spleen, heart, muscles, and gonads. **Excretion**: Feces (80 %), urine (7-10%) after 5 days, negligible excretion via air.
Acute Toxicity Studies	
Acute Oral Toxicity (Gavage) SPF Mice PMRA#: 1161775	LD_{50} > 2000 mg/kg bw **@ 2000 mg/kg bw**: ↑ piloerection and sedation shortly noted after treatment but returned to normal after 24 hours. **Low acute toxicity**
Acute Oral Toxicity (Gavage)	LD_{50} = 5600 mg/kg bw

Study Type/ Animal/ PMRA #	Study Results
Wistar Rat PMRA#: 1184851	**≥ 2500 mg/kg bw:** ↑ piloerection, ↑ lethargy (persisted up to 7 days after dosing), ↑ pale liver and kidneys (animals which died), ↑ ataxia, ↑ convulsions, ↑ muscle tremors, ↑ red nasal discharge, ↑ clear oral discharge, ↑ urinary staining of the abdomen, ↑ soft stool, ↑ fecal staining of the abdomen **Low acute toxicity**
Acute Oral Toxicity (Gavage) Wistar Rat PMRA#: 1161752	LD_{50} > 5000 mg/kg bw **@ 5000 mg/kg bw:** ↑ diarrhea noted on day 2 **Low acute toxicity**
Acute Oral Toxicity (Gavage) Wistar Rats PMRA#: 1211998	LD_{50} > 5000 mg/kg bw **Low acute toxicity**
Acute Oral Toxicity (Gavage) Wistar Rats PMRA#: 1874174	LD_{50} > 5000 mg/kg bw **@ 5000 mg/kg bw:** 1♀ exhibited laboured breathing on day 4 and 6 after treatment **Low acute toxicity**
Acute Oral Toxicity (Gavage) Rabbits PMRA #: 1184695	LD_{50} = 3800 mg/kg bw **≥ 2000 mg/kg bw:** ↑ hypoactivity **≥ 3000 mg/kg bw:** ↑ mortality, ↑ hemorrhage and ulceration of the stomach **Low acute toxicity**
Acute Dermal Toxicity Sprague-Dawley Rats PMRA#: 1161756	**Supplemental** LD_{50} > 2000 mg/kg bw **@ 2000 mg/kg bw:** Piloerection and reduced activity. Scab formation @ the test site 2-14 days after dosing. **Low acute toxicity**
Acute Dermal Toxicity Wistar Rats PMRA#: 1211999	LD_{50} > 2000 mg/kg bw **@ 2000 mg/kg bw:** One male showed slight erythema on days 2 and 3 and one female had scabs from days 3 to 8. **Low acute toxicity**
Acute Dermal Toxicity Wistar Rats PMRA#: 1874176	LD_{50} > 2000 mg/kg bw **Low acute toxicity**
Primary Dermal Irritation	**Supplemental**

Study Type/ Animal/ PMRA #	Study Results
NZW Rabbit PMRA#: 1161763	**Non irritating**
Primary Dermal Irritation NZW Rabbit PMRA#: 1212002	**Non irritating**
Primary Dermal Irritation NZW Rabbit PMRA#: 1874186	**Non irritating**
Dermal Sensitization Hartley Guinea Pig PMRA#: 2391580	**Negative**
Dermal Sensitization ♀ Guinea Pigs PMRA#: 1161765	**Negative**
Dermal Sensitization ♀ Guinea Pigs PMRA#: 1212003	**@ 75% w/v prep:** animals showed scattered mild redness (considered skin irritation) **Negative**
Dermal Sensitization Guinea Pigs PMRA#: 1874187	**Negative**
Primary Eye Irritation Study Rabbit PMRA#: 1184853	Unwashed eyes: 5 showed conjunctival redness, one showed chemosis, one eye showed conjunctival necrosis, one eye showed corneal opacity and ulceration. Washed eyes: 2/3 show corneal opacity and ulceration, conjunctival redness and chemosis. The effects cleared by Day 7. **Mildly irritating**

Study Type/ Animal/ PMRA #	Study Results
Eye Irritation NZW Rabbit PMRA#: 1161760	**Supplemental** One rabbit was tested first and observed 1 hour after instillation. As severe irritation characterized by conjunctival redness and chemosis, corneal opacity, discharge were noted, other animals were not tested. **Severely irritating**
Eye Irritation NZW Rabbit PMRA#: 1161761	**Supplemental** Iritis and moderate conjunctival redness and chemosis **Moderately irritating**
Eye Irritation NZW Rabbit PMRA#: 1212001	Corneal effects included slight to mild opacity affecting up to the entire cornea (seen in all animals during first two days). Conjunctival effects included slight to moderate redness, slight to moderate chemosis and slight to severe discharge noted in all animals up to day 4. Additional observations included mucoid discharge, eye closed, irregular corneal surface, convoluted eyelids, and erythema of the upper and/or lower eyelids, raised corneal opacity, Harderian gland discharge and nictitating membrane partially hemorrhagic. **Moderately irritating**
Eye Irritation NZW Rabbit PMRA#: 1874178	Slight conjunctival redness (MIS = 1.67) and chemosis (MIS = 0.67 to 1.33) were observed. **Minimally irritating**
Acute Inhalation Toxicity (Head only) Sprague-Dawley Rat PMRA#: 1161758	**Supplemental** LC_{50} > 4.98 mg/L **Low acute toxicity**
Acute Inhalation Toxicity (Nose-only) Wistar Rat PMRA#: 1212000	LC_{50} > 4.27 mg/L ≥ 2.43 mg/L: ↑ hunched posture, ↑ piloerection, ↑ wet fur, ↑ breathing irregularities, ↑ reduced righting reflex, ↑ shaking, ↑ splayed gait @ 4.27 mg/L: ↑ mortality (2/5 ♂ and 2/5 ♀) **Low acute toxicity**
Acute Inhalation Toxicity (Head only) Wistar Rat PMRA#: 1874177	LC_{50} > 2.15 mg/L **Low acute toxicity**

Study Type/ Animal/ PMRA #	Study Results
	Short-Term Toxicity Studies
90-Day Oral Toxicity (Diet) CD-1 Mouse PMRA#: 1161787	**Supplemental** **≥ 935/939 mg/kg bw/day:** ↑ incidence of cortical tubular epithelial hypertrophy (*adaptive and not clearly dose-responsive*) Parotid and sublingual salivary glands were not examined. Collection of small plasma volumes affected hematology and clinical chemistry analysis.
90-Day Oral Toxicity (Diet) B6C3F$_1$ Mouse PMRA#: 2391579	NOAEL = 507 mg/kg bw/day (♂) NOAEL = 753 mg/kg bw/day (♀) No treatment-related effect on food consumption, sperm counts, morphology and motility, or estrual cycle length. **≥ 507/753 mg/kg bw/day:** ↑ right kidney wt, ↑ lungs wt (♂) **≥ 1065/1411 mg/kg bw/day:** ↑ incidence and severity of cytoplasmic alterations of the parotid salivary gland; ↑ heart wt (♂)
28-Day Oral Toxicity (Diet) Sprague-Dawley Rat Range-finding PMRA#: 1161768	**≥ 255/277 mg/kg bw/day:** ↑ ALT; ↑ ALP, ↑ phosphate (♂); ↑ mineral deposits at the corticomedullary junction in the kidneys (2/5 [1 very mild, 1 mild], 2/5 [1 very mild, 1 mild], 4/5 [2 very mild, 2 mild] @ top three doses respectively) (♀) **≥ 1034/1047 mg/kg bw/day:** ↓ BWG; ↑ WBC, ↑ lymphocytes (♂); ↓ BW, ↑ ALP, ↓ adrenals wt (♀) **@ 2592/2614 mg/kg bw/day:** ↑ incidence of soft feces , ↓ BW, ↓ adrenals wt (♂); ↓ pChE (♀) Salivary glands were not examined.
28-Day Oral Toxicity (Diet) Wistar Rat Range-finding PMRA#: 1212041	**≥ 100 mg/kg bw/day:** ↓ BW (♂) **≥ 250 mg/kg bw/day:** ↑ ALP; ↑ ALT (♂); ↓ urinary pH, ↓ FE (♀) **@ 1000 mg/kg bw/day:** ↑ RBC, ↑ platelet, ↑ incidence of hydronephrosis (1/6, 1/6 vs. 0/6); ↓ FC, ↓ FE, ↑ glucose, ↓ abs. brain wt, ↑ rel. testes wt (♂); ↓ BW, ↓ BUN, ↓ kidney wt (♀)
90-Day Oral Toxicity (Diet) F344 Rats PMRA#: 2391579	NOAEL = ND LOAEL = 205 mg/kg bw/day (♂) LOAEL = 213 mg/kg bw/day (♀) **≥ 205/213 mg/kg bw/day:** ↑ ALP, ↓ thymus wt, ↑ incidence and severity of cytoplasmic alterations of the parotid and submandibular salivary glands **≥ 410/421 mg/kg bw/day:** ↑ ALT (♂) **≥ 811/844 mg/kg bw/day:** ↑ Hct, ↑ RBC, ↓ sperm counts (10-20%) (♂) **≥ 1678/1690 mg/kg bw/day:** ↓ BW, ↓ BWG, ↑ bile acids; ↑ rel. liver wt, ↑ rel. right kidney wt, ↑ rel. right testicle wt, ↑ Hgb (♂) **@ 3393/3939 mg/kg bw/day:** ↑ incidence of diarrhea, ↓ FC; ↑ platelet, ↓ abs. heart wt (♂); ↑ lymphocytes, ↑ WBC, ↑ MCH, ↑ MCV, ↑ rel. right kidney wts, ↑ estrous cycle length (5.4 days vs. 4.9 days) (♀)

Study Type/ Animal/ PMRA #	Study Results
90-Day Oral Toxicity (Diet) Sprague-Dawley Rat PMRA#: 1161777	NOAEL = ND LOAEL = 30 mg/kg bw/day (♂) LOAEL = 31 mg/kg bw/day (♀) **≥ 30/31 mg/kg bw/day:** ↑ incidence and severity of cellular alterations of the parotid salivary gland
90-Day Oral Toxicity (Diet) Wistar Rat PMRA#: 1212004 and 1410983	NOAEL = 414 mg/kg bw/day (♂) NOAEL = 1821 mg/kg bw/day (♀) **≥ 81/90 mg/kg bw/day:** ↑ ALT, ↑ ALP; ↑ prothrombin time, ↓ platelet count (♂) (*non-adverse*) **≥ 414/447 mg/kg bw/day:** ↓ platelet count (♀) (*non-adverse*) **@ 1693/1821 mg/kg bw/day:** ↓ BUN; ↓ BW, ↓ BWG, ↓ FE, ↓ triglycerides, ↓ plasma total protein, ↓ heart wt, ↓ liver wt (♂); ↑ AST (♀) Salivary glands were not examined.
21-Day Dermal Toxicity Sprague-Dawley Rat PMRA#: 1161790	LOAEL (irritation) = 1000 mg/kg bw/day LOAEL (systemic) = 1000 mg/kg bw/day **@ 1000 mg/kg bw/day:** ↑ very slight erythema (♂: 2/5, ♀: 3/5 during wk 2, only 1/5 ♀ showed this effect during wk 3), ↑ desquamation (♂: 3/5 moderate to severe, ♀: 5/5 mild to severe during wk 2, 1/5 in each of ♂ and ♀ during wk 3 with mild severity grading; 1/5 ♀ thickening and severe desquamation during wk 3); ↑ unilateral dilatation of the kidneys (2/5 vs. 0/5), ↑ unilateral papillary necrosis (1/5 vs. 0/5), ↑ urothelial hyperplasia (2/5 vs. 0/5), ↑ pelvic dilation (3/5 [severity grade: +, ++, +++] vs. 0/5) (♂)
21-Day Dermal Toxicity Wistar Rat PMRA#: 1212007	NOAEL (irritation) ≥ 1000 mg/kg bw/day NOAEL (systemic) ≥ 1000 mg/kg bw/day Not systemic or dermal irritation effect
21-Day Dermal Toxicity NZW Rabbit PMRA#: 2443653	NOAEL (irritation) = 1000 mg/kg bw/day NOAEL (systemic) ≥ 5000 mg/kg bw/day No systemic toxicity (no treatment-related effect on BW, hematology, clinical chemistry, organ weights, or histopathology) **@ 5000 mg/kg bw/day:** ↑ slight dermal irritation (erythema and edema on intact and abraded skin of both sexes); ↓ FC (♀)
90-Day Oral Toxicity (Diet) Beagle Dog PMRA#: 1184795	**Supplemental** No treatment-related effect on BW, hematology, clinical organ weights, or histopathology
90-Day Oral Toxicity (Diet) Beagle Dog PMRA: 1212005	NOAEL = 323 mg/kg bw/day (♂) NOAEL = 334 mg/kg bw/day (♀) **≥ 68/68 mg/kg bw/day:** ↑ abs. adrenals wt, ↑ liver wt (♂) (*non-adverse*) **≥ 323/334 mg/kg bw/day:** ↑ creatine kinase, ↑ kidneys wt (♂) (*non-adverse*) **@ 1680/1750 mg/kg bw/day:** ↓ BWG; ↓ RBC, ↓ albumin, ↓ total protein, ↓ [Ca^{++}], ↓ [K^{+}] (♂);

Study Type/ Animal/ PMRA #	Study Results
	↑ ALP, ↓ ovaries wt (♀)
12-Month Oral Toxicity (Capsule) Beagle Dog PMRA#: 1161788	NOAEL = 30 mg/kg bw/day (♂) NOAEL = 300 mg/kg bw/day (♀) **≥ 30 mg/kg bw/day**: ↓ BW, ↓ BWG, ↑ liver wt (♂) **≥ 300 mg/kg bw/day**: ↑ incidence of soft/loose/liquid stool **@ 1000 mg/kg bw/day:** ↓ urinary pH; ↑ kidneys wt (♂); ↓ BW, ↓ BWG (♀)
12-Month Oral Toxicity (Capsule) Beagle Dog PMRA #: 1202148	NOAEL = 20 mg/kg bw/day **≥ 100 mg/kg bw/day**: ↓ pituitary wt, ↑ lymphoid nodules in epididymis (1/6, 2/6 @ mid and high dose) (♂); ↑ tubular regeneration of the kidneys (accompanied with presence of epithelial cells and protein in urine of 1/5 in mid- and high-dose group) (♀) **@ 500 mg/kg bw/day:** ↑ testes wt (abs.: 14%, rel.: 13%), ↑ ovaries wt (9%)
12-Month Oral Toxicity (Diet) Beagle Dog PMRA#: 1212006	NOAEL = 90.9 mg/kg bw/day (♂) NOAEL = 448 mg/kg bw/day (♀) **≥ 90.9/92.1 mg/kg bw/day**: ↓ plasma phosphorus, ↑ creatine kinase, ↓ epididymides wt, ↑ transitional epithelial hyperplasia in the kidneys (♂) **@ 906/926 mg/kg bw/day:** ↓ BW; ↓ brain wt, ↑ kidneys wt, ↑ thyroid wt (♂); ↓ plasma phosphorus, ↓ thyroid wt (♀)
Chronic Toxicity/Oncogenicity Studies	
24-month Oncogenicity (Diet) CD-1 mouse PMRA #: 1161786, 1161795	NOAEL = 98 mg/kg bw/day (♂) NOAEL = 102 mg/kg bw/day (♀) **≥ 98/102 mg/kg bw/day**: ↓ adrenals wt (♂); ↑ ovaries wt, ↑ thymus wt (♀)(*non-adverse*) **≥ 297/298 mg/kg bw/day**: ↑ incidence of mineral deposits in the brain; ↑ thymus wt, ↑ abs. lungs wt, ↑ liver wt (♂); ↑ incidence of unilateral foci of tubulostromal hyperplasia in the ovaries **Equivocal evidence of oncogenicity**
26-month Oral Toxicity and Oncogenicity (Diet) Sprague-Dawley Rat PMRA#: 1184837 1184838 1184839	NOAEL ≥ 32 mg/kg bw/day (♂) NOAEL ≥ 34 mg/kg bw/day (♀) No treatment-related effect on mortality, clinical signs of toxicity, hematology, clinical chemistry, urinalysis, organ weights, or histopathology. MTD was not reached. **No evidence of carcinogenicity** Submandibular gland was examined histologically
24-month Oral Toxicity and Oncogenicity (Diet) Sprague-Dawley Rat	NOAEL = 89 mg/kg bw/day (♂) NOAEL = 113 mg/kg bw/day (♀) No treatment-related effects on clinical signs of toxicity, mortality. **≥ 362/457 mg/kg bw/day**: ↑ inflammation and hyperplasia of squamous mucosa in the stomach; ↓ and/or absence of sperm in the epididymides, ↑ cell detritus in the duct lumen of the

Study Type/ Animal/ PMRA #	Study Results
PMRA #: 1235214, 1235215	epididymides (♂) **@ 940/1183 mg/kg bw/day**: ↓ urinary pH, ↑ abs. and rel. liver wt (interim and terminal sacs), ↑ testes wt (rel. to brain wt), ↑ necrosis in glandular stomach, ↑ myeloid hyperplasia of the bone marrow (7/50, vs. 3/50), ↑ testicular effects (♂),↑ cataract/lens fiber degeneration; ↓ BW, ↓ BWG, ↑ ALP, ↑ mammary gland hyperplasia (39% vs. 20% [16/58, 19/54, 13/59, 22/57]) (♀) **No evidence of carcinogenicity** Submandibular salivary gland was examined histologically
24-month Oral Toxicity and Oncogenicity (Diet) Sprague-Dawley Rat PMRA #s: 1161796, 1161797, 1161798	NOAEL = 10 mg/kg bw/day (♂) NOAEL = 10 mg/kg bw/day (♀) **≥ 10 mg/kg bw/day**: ↓ BW (@ 52 wk), ↓ abs. kidneys wt (@ 52 wk), ↓ abs. liver wt (@ 52 wk), ↑ parotid gland wt (@ wk 52) (♂); ↓ rel. liver wt (@ wk 52) (♀) **≥ 101/103 mg/kg bw/day**: ↑ incidence and severity of cellular alteration in the submandibular and parotid salivary glands @ interim and terminal sacs, ↓ BWG (interim sac animals only); ↑ ALP (3, 6, 12, 18, and 24-month) (♀) **No evidence of carcinogenicity**
24-month Oral Toxicity and Oncogenicity (Diet) Wistar Rat PMRA #: 1212011, 1212012, 1212013	NOAEL = 361 mg/kg bw/day (♂) NOAEL = 437 mg/kg bw/day (♀) **≥ 121/145 mg/kg bw/day**: ↑ incidence of red-brown staining of tray paper **≥ 361/437 mg/kg bw/day:** ↑ ALP, ↑ ALT, ↑ AST (various time-points @ this dose, throughout all time points at the high dose); ↓ plasma creatinine (wk 27 @ this dose and wk 14 @ high dose), ↑ incidence of papillary necrosis in the kidneys (♀) **@ 1214/1498 mg/kg bw/day**: ↑ incidence of red-brown coloured urine, ↓ BW, ↓ FC, ↓ FE; ↑ total bilirubin, ↓ triglycerides, ↓ cholesterol, ↓ urinary pH, ↑ incidence of transitional cell hyperplasia in the kidneys, ↑ incidence of papillary necrosis in the kidneys, ↑ incidence of prostatitis (♂) **No evidence of carcinogenicity**
Developmental/Reproductive Toxicity Studies	
Two-generation reproduction toxicity (Diet) Sprague-Dawley Rat PMRA#: 1235339	**Parental Toxicity** NOAEL = 685 mg/kg bw/day (♂) NOAEL = 779 mg/kg bw/day (♀) No treatment-related effect on gross necropsy, and histopathology findings. **≥ 685/779 mg/kg bw/day**: ↓ BW (*non-adverse*) **@ 1768/2322 mg/kg bw/day**: ↑ soft stools (P & F_1), ↓ BW (P♂&♀), ↓ BWG (P & F_1); ↓ BW (all GD periods, and on LD 0, 7, & 14, respectively) **Offspring toxicity** NOAEL = 115/160 mg/kg bw/day (♂/♀) **≥ 685/779mg/kg bw/day:** ↓ BW (F_{2a} on LD 21)

Study Type/ Animal/ PMRA #	Study Results
	@ 1768/2322mg/kg bw/day: ↓ BW (F_{1a} on LD 21, respectively), ↓ litter size (F_{1a}, F_{2a}, F_{2b}, this effect was not accompanied with an increase in the dead pups/litter), ↑ tubular dilatation/cysts in the kidneys (F_{2b}) **Reproductive toxicity** NOAEL = 685 mg/kg bw/day (♂) NOAEL = 779 mg/kg bw/day (♀) **@ 1768/2322mg/kg bw/day**: ↓ litter size (F_{1a}, F_{2a}, F_{2b}, this effect was not accompanied with an increase in the dead pups/litter) No treatment-related effects on mating, pregnancy, and fertility indices. Sperm parameters (motility and morphology), estrous cycle length and periodicity, and ovarian follicle were not examined. **No sensitivity of the young**
Two-generation reproduction toxicity (Diet) Sprague-Dawley Rat PMRA#: 1161793	**Parental Toxicity** NOAEL = 48 mg/kg bw/day (♂) NOAEL = 59 mg/kg bw/day (♀) **≥ 143/179 mg/kg bw/day**: ↑ (minimal) hypertrophy of acinar cells with (prominent) granular cytoplasm in the parotid and submandibular salivary glands **Offspring toxicity** NOAEL ≥ 488/595 mg/kg bw/day (♂/♀) No treatment-related effects on mean litter wt, mean pup wt, preputial separation and vaginal opening. **Reproduction toxicity** NOAEL ≥ 488/595 mg/kg bw/day (♂/♀) No treatment-related effects on mating, pregnancy, and fertility indices Sperm parameters (motility and morphology), estrous cycle length and periodicity, and ovarian follicle were not examined **No sensitivity of the young**
Two-generation reproduction toxicity (Diet) Wistar Rat PMRA#: 1212014, 1212015	**Parental Toxicity** NOAEL = 293 mg/kg bw/day (♂) NOAEL = 323 mg/kg bw/day (♀) No treatment-related effect on gross necropsy, organ weights, and histopathology findings. **≥ 293/323 mg/kg bw/day**: ↑ scaly tails (P♂ and F_1♀); ↑ incidence and severity of luminal dilatation of the uterus **@ 985/1054 mg/kg bw/day**: ↑ rel. liver wt (P), ↑ rel. kidney wt (P) ↑ incidence of transitional epithelial hyperplasia (F_1); ↓ BW (F_1♂), ↓ FC (F_1♂); ↑ glandular dilatation of uterus (F_1), **Offspring toxicity** NOAEL = 99.4 mg/kg bw/day (♂) NOAEL = 104 mg/kg bw/day (♀)

Study Type/ Animal/ PMRA #	Study Results
	≥ 293/323 mg/kg bw/day: ↓ BW (F_{1a}♂ on LD 22 at this dose and throughout all LDs @ high dose, respectively) **@ 985/1054 mg/kg bw/day:** ↓ spleen wt (F_{1a}♀, F_{2a}♀), ↓ abs. thymus weight (F_{1a}♂: 11% and F_{1a}♀: 13%), ↑ incidence of unilateral and bilateral pelvic dilatation of the kidneys (F_{2a}) Microscopic pathology was not conducted in the offspring. **Reproduction toxicity** NOAEL = 985 mg/kg bw/day (♂) NOAEL = 323 mg/kg bw/day (♀) **@ 985/1054 mg/kg bw/day**: ↑ mean # of estrual cycles (P), ↓ mean estrual cycle length (P, F_1) No treatment-related findings on number of sperm, sperm motility parameters, sperm morphology, number of oocytes or reproductive performance. **No sensitivity of the young**
Prenatal Developmental (Gavage) Sprague-Dawley Rat PMRA#: 1184726	**Maternal Toxicity** NOAEL = 300 mg/kg bw/day **≥ 1000 mg/kg bw/day**: ↑ incidence of hydronephrosis (one in each of mid- and high-dose groups) **Developmental Toxicity** NOAEL = 1000 mg/kg bw/day **@ 3500 mg/kg bw/day**: ↓ BW, ↓ number of viable fetuses/dam, ↑ absent kidneys and ureters (3 fetuses, 2 litters), ↑ skeletal variants, ↑ incidence of reduced ossification of the sternebrae **No evidence of malformation or sensitivity of the young**
Prenatal Developmental (Gavage) Sprague-Dawley Rat PMRA#: 1161778	**Maternal Toxicity** NOAEL = 300 mg/kg bw/day **≥ 1000 mg/kg bw/day:** ↑ noisy respiration, ↓ BWG (started during the 1st two days of treatment and continued throughout to GD 20) **Developmental Toxicity** NOAEL = 300 mg/kg bw/day **≥ 1000 mg/kg bw/day**: ↑ skeletal anomalies, ↑ incidence of wavy ribs/rib distortions **No evidence of malformation or sensitivity of the young**
Prenatal Developmental (Gavage) Wistar Rat PMRA#: 1212016	**Maternal Toxicity** NOAEL = 500 mg/kg bw/day **@ 1000 mg/kg bw/day:** 1/24 total litter resorption (0/24 in other groups) **Developmental Toxicity** NOAEL = 500 mg/kg bw/day **@ 1000 mg/kg bw/day:** ↑ not ossified odontoid (unossified skeletal effect), , ↑ hydroureter **No sensitivity of the young**

Study Type/ Animal/ PMRA #	Study Results
Prenatal Developmental (Gavage) NZW Rabbit PMRA#: 1212017, 1411000	**Maternal Toxicity** NOAEL = 100 mg/kg bw/day **≥ 100 mg/kg bw/day:** ↑ diarrhea: few and no feces, and staining in genital area, ↓ FC, ↓ gravid uterus weight (*non-dose-responsive*) **@ 300 mg/kg bw/day:** ↓ BW, ↑ post-implantation loss, ↑ early intra uterine deaths **Developmental Toxicity** NOAEL = 175 mg/kg bw/day **@ 300 mg/kg bw/day:** ↓ fetal BW, ↑ incidence of partially ossified transverse process 7th cervical vertebrae, ↑ incidence of unossified transverse process 7th thoracic vertebrae, ↑ incidence of 27th pre-sacral vertebrae, ↑ incidence of partially ossified 6th sternebrae, ↑ manus score, ↑ pes score **No evidence of malformation or sensitivity of the young**
Prenatal Developmental (Gavage) Dutch belted Rabbit PMRA#: 1184727	**Maternal Toxicity** NOAEL = 75 mg/kg bw/day **≥ 175 mg/kg bw/day**: ↑ mortality, ↑ soft stools and diarrhea, one abortion (GD 27) **Developmental Toxicity** NOAEL = 175 mg/kg bw/day **≥ 75 mg/kg bw/day**: ↓ fetal BW **@ 350 mg/kg bw/day**: ↑ incidence of 27th presacral vertebrae, ↑ incidence of 13th rudimentary and full ribs, ↑ incidence of unossified sternebra **No evidence of malformation or sensitivity of the young**
Prenatal Developmental (Gavage) NZW Rabbit PMRA#: 1161779	**Maternal Toxicity** NOAEL = 50 mg/kg bw/day **≥ 150 mg/kg bw/day**: ↑ reduced fecal output, ↑ soft/liquid feces, and ↑ blood on tray, ↓ BWG, ↓ FC **Developmental Toxicity** NOAEL = 50 mg/kg bw/day **≥ 150 mg/kg bw/day**: ↑ fetuses with one or more cardiovascular abnormalities **Evidence of malformation**
Genotoxicity Studies	
In vitro bacterial gene mutation assay (*Salmonella Typhimurium*) PMRA#: 1161785	Negative ≥ 1.3 mg/plate: Cytotoxicity (± S9)

Study Type/ Animal/ PMRA #	Study Results
In vitro bacterial gene mutation assay (*Salmonella Typhimurium*) PMRA #: 2391580	Negative @ 5000 µg/plate: Cytotoxicity (± S9)
In vitro bacterial gene mutation assay (*Salmonella Typhimurium*) PMRA# 1212019	Negative @ 5.0 mg/plate: Cytotoxicity (± S9)
In vitro bacterial gene mutation assay (*Salmonella Typhimurium* and *Escherichia Coli*) PMRA# 1212022	Negative ≥ 2.5 mg/plate: Cytotoxicity (± S9)
Dominant Lethal Assay CD-1 ♂ Mouse PMRA#: 1184728	Negative
In vitro Gene Mutation Assay, CHO cells PMRA#: 2391580	Negative @ 22.5 mg/ml: Cytotoxicity (± S9)
In Vitro Gene mutation / cytogenetics Assay Mouse Lymphoma Cells PMRA#: 1161781	Negative

Study Type/ Animal/ PMRA #	Study Results
In *vitro* Gene mutation / cytogenetics Assay Mouse Lymphoma Cells PMRA#: 1212020	Positive (@ cytotoxic doses) ≥ 1900 µg/ml (in the presence of metabolic activation): ↑ mutant frequency, total relative survival range 3-56% (cytotoxicity) ≥ 2400 µg/ml (in the absence of metabolic activation): ↑ mutant frequency, total relative survival under 10% (cytotoxicity)
In *vitro* Gene mutation / Cytogenetics Assay Mouse Lymphoma Cells PMRA#: 1212023	Negative ≥ 500 µg/ml (in the presence of metabolic activation): ↓ pH (range of 7.07 to 6.32 @ the top dose of 2000 µg/ml compared to 7.34 in the control group) ≥ 1000 µg/ml (in the presence of metabolic activation): ↑ cytotoxicity (% relative growth = 56-90%)
In vivo Bone Marrow Cytogenetics Study Sprague-Dawley Rats PMRA#: 2391580	Negative
In vivo Bone Marrow Cytogenetics Study Sprague-Dawley Rats PMRA#: 2391580	Negative
In vitro mammalian cell cytogenetics / clastogenicity assay Human lymphocytes PMRA#: 1212021	Negative ≥ 0.75 mg/plate: ↓ mitotic index (-S9)
In vitro mammalian cell cytogenetics / clastogenicity assay CHO Cells PMRA#: 1212025	Negative ≥ 500 µg/ml: ↑ cytotoxicity (30-47%) – S9 ≥ 1500 µg/ml: ↑ cytotoxicity (30-47%) + S9

Study Type/ Animal/ PMRA #	Study Results
In vivo micronucleus assay SPF mice bone marrow cells PMRA#: 1161784	Negative
In vivo micronucleus assay CD-1 mouse bone marrow cells PMRA#: 1212024	Negative
Neurotoxicity Studies	
Acute Neurotoxicity (Gavage) Wistar Rat PMRA#: 1212034	NOAEL = 1000 mg/kg bw/day (♂/♀) No treatment-related effect on landing foot splay, time to tail flick, grip strength data and motor activity habituation **≥ 1000 mg/kg bw/day**: ↓ motor activity **@ 2000 mg/kg bw/day**: ↑ incidence of clinical signs of toxicity/FOB findings (♂: ↑ reduced splay reflex, ♀: decreased activity, subdued behaviour, hunched posture, sides pinched in, tip-toe gait, reduced splay reflex and/or hypothermia for three females including the one died on day 2 and diarrhea for one further female 6hrs after dosing and full recovery by day 2, abnormal respiratory noise in another female on day 2), ↓ FC, ↓ motor activity; one death (♀) **No evidence of neurotoxicity**
90-Day Neurotoxicity (Diet) Wistar Rats PMRA#: 1212037	NOAEL = 617 mg/kg bw/day (♂) NOAEL = 672 mg/kg bw/day (♀) **≥ 617/672 mg/kg bw/day**: ↓ BWG, ↓ FE **@ 1546/1631 mg/kg bw/day**: ↑ decreased pupillary response to light, ↓ BW (♂); ↓ BWG, ↓ motor activity (♀) **No evidence of neurotoxicity**
Immunotoxicity Studies	
28-Day Immunotoxicity (Diet) $B6C3F_1$ Mouse PMRA#: 2223081	LOAEL = 150 mg/kg bw/day No treatment-related effects on spleen or thymus weights (absolute or relative) **≥ 150 mg/kg bw/day**: ↑ T-cell dependent antibody response as measured by IgM AFC/10^6 spleen cells, ↑ total spleen activity as measured by IgM AFC/spleen × 10^3 **Evidence of immunotoxicity**

Study Type/ Animal/ PMRA #	Study Results
	Special Studies (non-guideline)
14-Day Feeding Mechanistic Study (Induction of salivary gland lesions) F334 ♂ Rats PMRA#: 2391579	Softer and wetter feces were noted in glyphosate fed groups. Decrease in body-weight gains in the glyphosate-fed groups was noted compared to the other groups. Absolute parotid weight was increased in the group 2 (glyphosate-fed), group 3 (glyphosate-fed + propranolol), and group 4 (isoproterenol) compared to group 1 (control). Absolute submandibular/sublingual was increased in group 2, group 3, and group 4. Increased incidence of lesions in the parotid gland was observed in the in all groups compared to group 1 (control). Increased incidence of lesions was also observed in the submandibular gland of the groups 2 (glyphosate + vehicle) and 3 (glyphosate + propranolol) animals. Parotid lesions consisted of cytoplasmic basophilic change, fine vacuolation, and swelling of acinar cells, diagnosed collectively as cytoplasmic alterations. A distinct gradation in the severity of these lesions was reported which was based on the extent of involvement and degree of tinctorial alteration and cell enlargement present.
28-Day Oral Toxicity Study (Diet): Glyphosate Acid: Comparison of salivary gland effects in three strains of rat Wistar Rat Sprague-Dawley Rat Fischer 344 Rat PMRA #: 1212038	**Wistar Rats** **@ 1000 mg/kg bw/day:** ↓ BW (complete recovery after the 13th week recovery period), ↓ FC, ↑ salivary gland wt, ↑ salivary gland effect (small foci of cells). ↑ mucous metaplasia of parotid **Sprague-Dawley Rats** **@ 1000 mg/kg bw/day:** ↓ BW (complete recovery after the 13th week recovery period), ↓ FC, ↑ salivary gland effect (small foci of cells). **Fischer Rats:** **@ 1000 mg/kg bw/day:** ↑ salivary gland wt, ↑ pronounced salivary gland effect (diffuse cytoplasmic basophilia and enlargement of the parotid acinar cells). **Recovery Periods** Complete recovery in Wistar and SD rats starting after 4 weeks of recovery period from treatment-related effects. Starting after 4 weeks of recovery period, all treatment-related effects improved, but did not disappear in F344 rats, (focal changes in the salivary glands and increased salivary gland weight was evident).

Table III.1B Summary of Toxicology Studies for AMPA

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Effects on organ weights are known or assumed to reflect changes in absolute weight and relative (to bodyweight) weight unless otherwise noted.

Study Type/ Animal/ PMRA #	Study Results
Toxicokinetic Studies	
Toxicokinetic Single dose (Gavage) ♂ Wister Rats PMRA# 1184960	**Absorption**: Rapid (20%) **Distribution**: ≤ 0.01% of dose in most tissue, 0.02% in muscle and gut after 120 hrs (single dose) **Metabolism**: None since the compound was excreted in the unchanged form **Excretion**: Within 120 hr, 94% of administered dose (AD) was excreted as unchanged compound. 74% via the feces, 20% via the urine. < 0.1% excreted in the exhaled air, and < 0.06% was identified in the carcass.
Acute Toxicity Studies	
Acute Oral Toxicity Sprague-Dawley Rats PMRA#: 2391580	LD_{50} = 8300 mg/kg bw **Low acute toxicity**
Acute Oral Toxicity Wistar rats PMRA# 1212035	$LD_{50} \geq$ 5000 mg/kg bw Clinical signs included diarrhea, stains around the nose, lack of grooming, piloerection, and urinary incontinence (recover by 3-4 days post dosing). **Low acute toxicity**
Acute Oral Toxicity (Limit Dose) Sprague-Dawley Rats PMRA#: 1161753	LD_{50} > 5000 mg/kg bw Clinical signs 4h-3days post-dosing included piloerection, diarrhea, subdued behaviour, hunched appearance, and soiled anal and peri-genital areas. **Low oral toxicity**
Primary Eye Irritation Rabbits (Albino) PMRA#: 2391580	**Minimally Irritating**
Primary Dermal Irritation Rabbits (Albino) PMRA#: 2391580	**Non irritating**

Study Type/ Animal/ PMRA #	Study Results
Acute Dermal Toxicity Sprague-Dawley Rats PMRA#: 1161755	LD_{50} > 2000 mg/kg bw **Low dermal toxicity**
Skin Sensitization Hartley Guinea Pig ♀ PMRA#: 1161766	**Negative skin sensitizer**
Short-Term Toxicity Studies	
28-Day Oral Toxicity (Gavage) Range-finding Sprague-Dawley Rats PMRA# 1161791	**≥ 350 mg/kg bw/day:** ↑ kidney wt (♂)
90-Day Oral Toxicity (Diet) Sprague-Dawley Rats PMRA:# 1161769	NOAEL = 1000 mg/kg bw/day **@ 1000 mg/kg bw/day:** ↑ kidney wt (♂); ↓ BWG (♀)
90-Day Oral Toxicity (Diet) Sprague-Dawley Rats PMRA#: 1184722 Histopathology data was available only for high dose and concurrent control	NOAEL = 400 mg/kg bw/day **≥ 400 mg/kg bw/day:** ↓ liver wt (♂) **≥ 1200 mg/kg bw/day:**↑ mucosal hyperplasia of the bladder; ↓ BWG, ↓BW (♂) **@ 4800 mg/kg bw/day:** ↑ renal pelvic epithelial hyperplasia, ↑ lactate dehydrogenase, ↓ urinary pH, ↑ urinary calcium oxalate crystals; ↑ cholesterol (♂); ↓ BWG, ↓ BW, ↓ liver wt (♀)
30-Day Oral Toxicity (Capsules) Beagle Dogs PMRA# 1126881	NOAEL = 100 mg/kg bw/day **≥ 300 mg/kg bw/day:** ↓ RBC, ↓ HGB, ↓ HCT, ↑ reticulocyte count (♀) **@ 1000 mg/kg bw/day:** ↓ RBC, ↓ HGB, ↓ HCT, ↑ reticulocyte count (♂)

Study Type/ Animal/ PMRA #	Study Results
92-Day Oral Toxicity (Capsules) Beagle Dogs PMRA# 1126892 1149397	NOAEL = 300 mg/kg bw/day No treatment-related effects. No evidence of anemia.
Developmental/Reproductive Toxicity Studies	
Prenatal Developmental Toxicity Study (Gavage) ♀ Rats Range-Finding PMRA#: 2391580	No treatment-related effects. **Supplemental**
Prenatal Developmental Toxicity Study (Gavage) ♀ Rats PMRA#: 1126903	**Parental Toxicity**: NOAEL = 150 mg/kg bw/day **≥ 400 mg/kg bw/day:** ↑ hair loss, ↑ soft and mucoid feces **@ 1000 mg/kg bw/day:** ↓ BW, ↓ BWG, ↓ FC **Developmental Toxicity**: NOAEL = 400 mg/kg bw/day **@ 1000 mg/kg bw/day:** ↓ BW
Prenatal Developmental Toxicity ♀ Sprague-Dawley Rats PMRA#: 1161794	**Supplemental** **Parental Toxicity**: No treatment-related effects **Developmental Toxicity:** NOAEL= 350 mg/kg bw/day **@ 1000 mg/kg bw/day:** ↑ incidence of ↓ ossification (hyoid bone, skull bones and 2nd metacarpal) and ↑ skeletal variations (bipartite sternebrae hemicentres and caudal pelvic shift/asymmetric alignment of pelvic bones)
Genotoxicity Studies	
In vitro bacterial gene mutation assay (*Salmonella Typhimurium* and *Escherichia Coli*) PMRA# 1212018	Negative

Study Type/ Animal/ PMRA #	Study Results
In vitro bacterial gene mutation assay (*Salmonella Typhimurium* and *Escherichia Coli*) PMRA# 1161782	Negative
Unscheduled DNA synthesis Assay Rat hepatocytes PMRA# 1126905	Negative
Micronucleus Assay Mouse PMRA# 1156204	Negative
In *vitro* Gene mutation / cytogenetics Assay Mouse Lymphoma Cells PMRA# 1161780	Negative
Micronucleus Assay Mouse PMRA# 1161783	Negative

Table III.2 Toxicological Points of Departure for Use in Human Health Risk Assessment for Glyphosate Acid, AMPA, N-acetyl glyphosate and N-acetyl AMPA

	RfD	Study NOAEL (or LOAEL)	CAF or Target MOE and Rationale
ARfD (General Population)	1.0 mg/kg bw	NOAEL = 100 mg/kg bw/day **Rabbit developmental toxicity study** (Increased incidence of diarrhea: few/no feces, staining in genital area.)	CAF = 100 PCPA factor[1] = 1-fold
ARfD (female 13-49 years of age)	0.5 mg/kg bw	NOAEL = 150 mg/kg bw/day (for fetal cardiovascular malformations) **Rabbit developmental toxicity study** (Increased incidence of fetal cardiovascular malformations.)	CAF = 300 PCPA factor = 3-fold

	RfD	Study NOAEL (or LOAEL)	CAF or Target MOE and Rationale
ADI (All Populations)	0.3 mg/kg bw/day	NOAEL = 32/34 mg/kg bw/day (♂/♀) **26-month Chronic/Carcinogenicity Study in Rats** (No treatment-related effects were noted in this study. This was the highest (combined) NOAEL for the long-term toxicity studies in rats. The lowest (conbined) LOAEL was 100 mg/kg bw/day based on reduction in body weight in male rats in the interim sacrifice and increased incidences and severity of cellular alterations in the parotid and submandibular glands in a 24-month chronic toxicity and carcinogenicity study in rats. NOAELS/LOAELs are further supported by the NOAEL of 30 and LOAEL of 100 mg/kg bw/day in one-year studies in dogs.)	CAF/MOE = 100 PCPA factor = 1-fold
Aggregate (All Durations and Populations)			Target MOE = 100
Incidental Oral, Short-term Dermal and Inhalation (All Populations)	0.3 mg/kg bw/day	LOAEL = 30 mg/kg bw/day **90-Day Oral Study in Rats** (Increased incidence and severity of cellular alteration in the parotid gland. This LOAEL was considered to be at the threshold of toxicological adversity due to the mild nature of the cellular alteration in the parotid glands at this dose level. As a result, an uncertainty factor (UF_L) for extrapolating from a LOAEL to a NOAEL was not deemed necessary.)	Target MOE = 100
Intermediate and Long-term dermal, Inhalation. (All Populations)	0.3 mg/kg bw/day	NOAEL = 32/34 mg/kg bw/day (♂/♀) **26-month Chronic/Carcinogenicity Study in Rats** (No treatment-related effects were noted in this study. This was the highest (combined) NOAEL for the long-term toxicity studies in rats. The lowest (combined) LOAEL was 100 mg/kg bw/day based on reduction in body weight in male rats in the interim sacrifice and increased incidences and severity of cellular alterations in the parotid and submandibular glands in a 24-month chronic toxicity and carcinogenicity study in rats. NOAELS/LOAELs are further supported by the NOAEL of 30 and LOAEL of 100 mg/kg bw/day in one-year studies in dogs.)	Target MOE = 100
Cancer Assessment		Low level of concern due to benign nature of tumours observed at the limit dose and lack of oncogenicity in other studies	

1 PCPA factor = *Pest Control Products Act* factor

Appendix IV Dietary Exposure and Risk Estimates for Glyphosate

Table IV.1 Dietary Exposure and Risk Estimates for Glyphosate

Population Subgroup	MRL/Tolerance-Level							
	Acute Dietary (95th percentile)[1]				Chronic Dietary[2]			
	Food Only		Food + Water		Food Only		Food + Water	
	Exposure (mg/kg/day)	%ARfD	Exposure (mg/kg/day)	%ARfD	Exposure (mg/kg/day)	%ADI	Exposure (mg/kg/day)	%ADI
General Population	—	—	—	—	0.090925	28	0.095078	30
All Infants (< 1 year old)	0.310861	31	0.344347	34	0.125494	39	0.139108	44
Children 1-2 years old	**0.435005**	**44**	**0.446406**	**45**	**0.218341**	**68**	**0.224507**	**70**
Children 3-5 years old	0.401028	40	0.411654	41	0.213099	67	0.218872	68
Children 6-12 years old	0.283779	28	0.289644	29	0.147290	46	0.151272	47
Males[3] 13-19 years old	0.207897	21	0.210659	21				
Youth[3] 13-19 years old					0.090032	28	0.093034	29
Males[3] 20-49 years old	0.158854	16	0.176746	18				
Adults[3] 20-49 years old					0.073547	23	0.077423	24
Adults 50+ years old	0.116579	12	0.123514	12	0.058796	18	0.062875	20
Females 13-49 years old	0.146629	29	0.152714	31	0.068430	21	0.072290	23

[1]Acute reference dose (ARfD) of 0.5 mg/kg bw applies to females 13-49 years old; ARfD of 1.0 mg/kg bw applies to population subgroups other than females 13-49 years old.

[2]Acceptable daily intake (ADI) of 0.3 mg/kg bw/day applies to the general population and all population subgroups.

[3]Due to a specific ARfD for females 13-49 years old, acute exposure and risk estimates for males 13-19 and 20-49 years old were calculated separately by using the appropriate ARfD. Acute exposure and risk estimations for youth 13-19 years old and adults 20-49 years were not applicable. This separation was not necessary for chronic exposure and risk estimations as the same ADI applies to all population subgroups.

Appendix V Food Residue Chemistry Summary

V.1 Metabolism

V.1.1 General Considerations

Previously reviewed comparative studies have shown that there are no significant differences in the behaviour of aqueous solutions of glyphosate prepared from the acid form (in other words, technical glyphosate) and the different salts of glyphosate (for example, isopropylamine, ammonium or trimethylsulfonium salt). In these aqueous solutions, the glyphosate anion (in other words, the phosphonomethylglycine anion, denoted as PMG) and the cationic counterion exist as freely dissociated ions. Thus, with regard to the metabolic fate of the PMG moiety, all the glyphosate forms are considered to be equivalent when using ^{14}C-PMG radiolabelled material. The metabolism of the counterion is studied by using ^{14}C-counterion labelled test compound.

V.1.2 Animal Metabolism

Glyphosate

Livestock (goats and hens) metabolism studies were conducted with ^{14}C-PMG or ^{14}C-TMS labelled glyphosate salts. TMS (trimethylsulfonium) is the cationic group of glyphosate-TMS, the trimethylsulfonium salt of glyphosate. The studies were previously reviewed and deemed adequate. It was concluded that the biotransformation and degradation pathways of glyphosate (the PMG moiety) in the goat and hen are similar, producing essentially unchanged PMG and aminomethylphosphonic acid (AMPA); these pathways were also found to be similar to those established in rat metabolism.

N-acetylglyphosate

The metabolism of the metabolite *N*-acetylglyphosate, which is formed in the glyphosate *N*-acetyltransferase (GAT) crops (in other words, crops that were genetically modified to express the glyphosate *N*-acetyltransferase gene) treated with glyphosate, was also investigated in goats and poultry. The studies revealed that the molecule *N*-acetylglyphosate either remains unchanged or loses its *N*-acetyl group, forming parent glyphosate. Parent glyphosate is further metabolized into AMPA. To a certain extent *N*-acetyl AMPA was also formed, but was not detected in any tissue except in fat samples at low levels (average: 0.02 ppm in goat; 0.006 ppm in hen). AMPA was detected at low levels in milk, liver, fat, muscle and eggs.

V.1.3 Plant Metabolism

Glyphosate

The nature of glyphosate residues in plants has been investigated in a wide range of non-transgenic (conventional, glyphosate non-tolerant) crops (for example, wheat, grapes, corn, soybean and lemon) and in transgenic (glyphosate tolerant) crops containing the 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) gene and/or the glyphosate

oxidoreductase (GOX) gene (for example, soybean). The studies indicate that the uptake of glyphosate from soil is limited. The material that is taken up is readily translocated. Foliar applied glyphosate is readily absorbed and translocated throughout the trees or vines to the fruits. Conventional and transgenic crops containing EPSPS and/or GOX genes show a similar glyphosate metabolic pattern, producing mainly the parent compound (the PMG moiety) and the metabolite AMPA. However, in glyphosate-tolerant EPSPS/GOX crops, glyphosate was metabolized more rapidly to AMPA. For the most part, the ratio of glyphosate to AMPA is 9 to 1 but can approach 1 to 1 in a few cases (for example, soybeans and carrots).

N-acetylglyphosate

The metabolic fate of ^{14}C-PMG labelled glyphosate has also been investigated in soybean, corn and canola plants genetically modified to express the GAT gene. The studies were previously reviewed and deemed adequate. These studies revealed that, whereas conventional and glyphosate-tolerant crops containing the EPSPS and/or the GOX genes show a similar metabolic pattern that consists mainly of parent compound and AMPA, in crops containing the GAT gene, the major metabolic pathway is different. The parent compound is extensively metabolised to *N*-acetylglyphosate; to a lower extent *N*-acetyl AMPA and AMPA are also formed.

V.1.4 Residue Definition

Based on metabolism studies summarized above, the PMRA has previously determined that the residue definition (RD) in all conventional crops and in transgenic crops containing the EPSPS and/or the GOX genes is comprised of glyphosate and the metabolite AMPA. The RD in genetically modified crops containing the GAT gene (in other words, soybeans, corn and canola) is the sum of glyphosate and the metabolites *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA. The RD in animal commodities is the sum of glyphosate and the metabolites *N*-acetylglyphosate and AMPA. These RDs are used for both enforcement and dietary risk assessment purposes. No modification to the current RDs is proposed as the result of this re-evaluation, provided it is understood that all the metabolites included in the RDs are expressed as glyphosate (see Table VI.1). The residue of concern in drinking water for dietary risk assessment is defined as the sum of glyphosate and the metabolite AMPA. The acetylated metabolites are not included in the RD for drinking water because they are not formed in soil, in other words, *N*-acetylglyphosate is not applied to plants; it is a metabolite produced in GAT crops as a result of the application of glyphosate.

Table V.1 Residue Definitions

Transgenic GAT Crops	Conventional and Transgenic EPSPS/GOX Crops	Animal Commodities	Drinking Water
Residue Definition for Enforcement of MRLs			
Sum of glyphosate, *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA, expressed as glyphosate[1]	Sum of glyphosate and AMPA, expressed as glyphosate[1]	Sum of glyphosate, *N*-acetylglyphosate and AMPA, expressed as glyphosate[1]	Not applicable
Residue Definition for Risk Assessment			
Same as RD for enforcement	Same as RD for enforcement	Same as RD for enforcement	Sum of glyphosate and metabolite AMPA

[1] Molecular weight conversion factors (MWCF) for field trial residues: Glyphosate = 0.8 × *N*-Acetylglyphosate; 1.1 × *N*-Acetyl AMPA; 1.5 × AMPA.

V.2 Analytical Methods

The analysis of glyphosate and its major metabolites is complicated by the polar nature of the residues (in other words, insoluble in most organic solvents) and their similarity in properties to naturally occurring compounds such as amino acids. Nonetheless, several single analyte analytical methods have been reported for the analysis of residues in plant materials, animal tissues, milk and eggs. The methods used in field trials were similar to, or the same as those reported as suitable for enforcement purposes. The methods generally involve aqueous extraction of residues, typically with dilute acid, clean-up on cation and anion exchange columns, separation using GC or high performance liquid chromatography (HPLC) and derivatization prior to detection. The derivatisation reaction varies with the chromatographic method used for separation (GC, HPLC) and detection system employed (FPD, fluorescence detector, UV, MS or MS/MS). Satisfactory recoveries at limits of quantitation (LOQs) in the range of 0.025-0.05 ppm for glyphosate and its major metabolites were reported for numerous commodities. Some of those analytical methods have been successfully validated for enforcement purposes and are listed in United States Environmental Protection Agency's pesticide analytical methods (PAM)-Volume II or in the index of residue analytical methods (RAM) pending compilation in PAM-Volume II. Multiresidue methods in PAM-Volume I Appendix I were found to be inadequate for enforcement purposes and glyphosate is not listed in CFIA's Volume 7: Multiresidue Analytical Method Manual.

V.2.1 Supervised Residue Trial Analytical Methodology

Several single analyte analytical methods for the determination of the residues of glyphosate and its metabolites AMPA and the TMS cation in various plant and animal matrices have been previously reviewed and deemed adequate. Successfully validated methods are also available for the determination of glyphosate and its metabolites *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA in GAT-soybean, GAT-corn and GAT-canola and in animal commodities. The analyses were performed using reverse phase HPLC and a tandem LC-MS/MS system operating with an electrospray interface (ESI) in positive ion mode detection. The LOQ in each matrix examined was 0.05 ppm for plant commodities and in the range of 0.025-0.05 ppm for animal commodities.

V.2.2 Enforcement Analytical Methodology

The inter-laboratory validated data collection methods (see Section V.2.1) were determined to be acceptable for the enforcement of glyphosate MRLs including all the metabolites comprised in the residue definitions.

V.2.3 Independent Laboratory Validation (ILV)

See Section V.2.1.

V.2.4 Multi-Residue Analytical Methodology (MRM) Evaluation

Data from the Pestrak database (1990 and 2005) indicate that recoveries are not likely for glyphosate under USFDA PAM I Multiresidue Methods. *N*-acetylglyphosate was also tested according to Protocols A, B and C of the PAM I multiresidue methods. The test substance was not naturally fluorescent according to procedures outlined in Protocol A, and lacked suitable chromatographic properties according to the procedures outlined in Protocols B and C. Therefore, the multiresidue methods described in PAM I are not suitable also for the regulatory analysis of *N*-acetylglyphosate.

V.3 Food Residues

V.3.1 Storage Stability

V.3.1.1 Storage Stability of Working Solutions in Analytical Methodology

The storage stability of working solutions of glyphosate and its metabolites reported as part of the analytical methodology studies (see Sections V.2.1, V.2.2 and V.2.3) was deemed adequate.

V.3.1.2 Freezer Storage Stability

Glyphosate, AMPA – Reports on freezer storage stability of glyphosate and AMPA were previously reviewed for a variety of crops including soybean, soybean straw, wheat grain, sorghum grain, citrus fruits, grapes and bananas. It was concluded that glyphosate and AMPA (plant incorporated) appeared to be stable in the crops for the duration of the magnitude of residue (MOR) studies, which generally did not exceed 48 months. However, it was noted that the stability of AMPA in spiked samples was more matrix dependent, in other words, the residues remained stable in corn grain and tomatoes for up to 31 months, in soybean forage for up to 24 months, in sorghum straw for up to 9 months and in clover for only 6 months.

N-acetylglyphosate, N-acetyl AMPA – When stored at -20°C, residues of *N*-acetylglyphosate were stable for up to 12 months in soybean forage, seed and hay; corn green plant, forage and grain; and for 23 months in corn stover. Residues of *N*-acetyl AMPA were stable for at least 18 months in soybean forage, seed, and hay and for up to 23 months in corn green plant, forage, grain and stover. These stability periods were deemed adequate to support MOR studies.

V.3.2 Magnitude of Residue Studies

V.3.2.1 Supervised Residue Trial Studies

Conventional and transgenic EPSPS/GOX crops – All data requirements for the magnitude of the residue in conventional and in transgenic EPSPS/GOX plants have been evaluated in past petitions and deemed adequate. The submitted data originated from a number of field trials conducted side-by-side with different glyphosate salt formulations on numerous crops. The data support a maximum seasonal rate of 6.2 kg a.e./ha in pre-emergent applications and 0.9 kg a.e./ha in pre-harvest applications for forage crops (PHI of 3-7 days) and all other crops (PHI of 7-14 days). It was concluded that the magnitude of the residues resulting from application of any of the formulations was comparable.

Transgenic GAT crops – Data on residues of glyphosate, *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA in transgenic GAT-soybean, GAT-corn and GAT-canola support a combined maximum pre-emergent + post-emergent seasonal application rate of 6.98 kg a.e./ha and a PHI of 12-17 days for soybean seeds; 7.22 kg a.e./ha and a PHI of 7 ± 1 days for corn grain; and 2.53 kg a.e./ha and a PHI of 6-8 days for canola seeds.

V.3.2.2 Residue Decline Study

Residue decline studies were conducted concurrently with supervised residue trials. The studies were previously reviewed and deemed adequate to support the PHIs specified on the labels (see Section VI.3.2.1 above).

V.3.2.3 Confined Crop Rotation Trial Study

Confined rotational crop studies conducted with conventional, non-transgenic lettuce (leafy vegetable), wheat (cereal crop) and radish (root vegetable) using ^{14}C-PMG labelled glyphosate-trimesium were previously reviewed.These studies demonstrated similar metabolic pathways in all the studied secondary crops and showed that very low levels of the test compound were taken up by the plants. Similarly to the metabolism of glyphosate in primary crops, PMG and AMPA were the relevant major components of the radioactive residue found in rotational crops. The remaining radioactivity was largely incorporated into natural plant products. The studies were deemed adequate to support glyphosate label claims but no plant back intervals (PBIs) were specified on the labels. The PMRA concluded that, as glyphosate is registered for use as a "prior to planting" application on all crops (including rotated crops), no further plant back restrictions are required. Based on the same study, USEPA also concluded that the current language on glyphosate labels is sufficient with respect to plant back restrictions and that further plant back restrictions were not necessary.

V.3.2.4 Field Crop Rotation Trial Study

Conclusions from Section V.3.2.3 (above) waive the requirement for a field crop rotation trial study.

V.3.2.5 Processed Food/Feed

Processing studies were reviewed with past petitions for residues of glyphosate and AMPA in processed fractions of conventional or transgenic EPSPS/GOX soybean (hulls, meal, crude oil, refined oil, soapstock and aspirated grain fractions), wheat (bran, short, middlings, flour and aspirated grain fractions), barley (malt and beer), and canola (cake and oil). These crops are representative of all pre-harvest uses of glyphosate on crops that can be processed (in other words, soybean, canola, flax, wheat, barley and oats). Processing studies were also previously reviewed for residues of glyphosate, *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA in processed fractions of transgenic GAT-soybean, GAT-corn and GAT-canola. The use of experimental processing factors as a refinement was not necessary at this time; default processing factors were used in the exposure assessment.

V.3.2.6 Residue Data for Crops Used as Livestock Feed

Residue data for crops used as livestock feed have been previously reviewed. The data were used for the establishment of MRLs in animal commodities.

V.3.2.7 Livestock, Poultry, Egg and Milk Residue Data

Dairy cow, laying hen and swine feeding studies conducted with conventional and/or transgenic EPSPS/GOX crops have been previously reviewed and deemed adequate to support MRLs for residues of glyphosate, AMPA and TMS cation in livestock and dairy commodities. As MRLs for residues of the TMS cation are being proposed for revocation (see Section V.4), considerations related to this metabolite are not included in this discussion. Given that GAT crops (soybean, corn and canola) treated with glyphosate may be used as feed, livestock could be exposed not only to glyphosate and AMPA, but also to the new metabolites typical for these genetically modified varieties, namely *N*-acetylglyphosate and *N*-acetyl AMPA. Therefore, based on metabolism studies of *N*-acetylglyphosate in livestock, the residue definition (RD) for both enforcement and risk assessment of glyphosate residues in livestock has been amended in past petitions in order to take into account the possible presence of *N*-acetylglyphosate and *N*-acetyl AMPA. As *N*-acetyl AMPA was found to be a minor component of the residue in animal commodities, the RD was revised from glyphosate and AMPA, to glyphosate and the metabolites *N*-acetylglyphosate and AMPA, expressed as glyphosate. Based on results of livestock feeding studies conducted with GAT crops, the maximum theoretical dietary burden (MTDB) and consequently MRLs in livestock commodities were revised to the current status.

V.4 Data Gaps

Sufficient information was available to adequately assess the dietary exposure and risk from exposure to glyphosate (all registered, equivalent salt formulations). Given that all uses of glyphosate-TMS were voluntarily discontinued, risk assessments for glyphosate-TMS were not conducted. No deficiencies were identified in the residue chemistry database from previous PMRA reviews. No further data are required.

Appendix VI Supplemental Maximum Residue Limit Information, International Situation and Trade Implications

Maximum Residue Limits (MRLs) may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

VI.1 Canadian MRLs for Food Commodities

MRLs have been specified for residues of glyphosate including the metabolite AMPA in/on registered conventional and transgenic EPSPS/GOX genes containing crops as well as for residues of glyphosate including the metabolites *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA in/on transgenic GAT gene containing crops (in other words, corn, canola and soybeans). MRLs have also been specified for residues of glyphosate including the metabolites *N*-acetylglyphosate and AMPA in animal commodities. Separate MRLs have been specified for residues of the TMS cation (resulting from the use of glyphosate-trimesium) in plant as well as in animal commodities. PMRA's decision to regulate the TMS cation (detected as dimethyl sulfide and reported as TMS cation) separately was based on the fact that glyphosate-trimesium demonstrates a higher toxicity profile than the other glyphosate salts and, contrary to the counterions of the latter, the TMS cation is not a naturally occurring compound and leaves residues above the general regulation limit of 0.1 ppm [see Table VI.1]. Residues in/on all other crops appearing on the registered labels are regulated under Subsection B.15.002(1) of the *Food and Drugs Regulations* not to exceed 0.1 ppm (General MRL) for glyphosate (including metabolites) and 0.1 ppm for the TMS cation. Given that all glyphosate-trimesium (GPT) containing products have been discontinued, it is proposed that all MRLs for the TMS cation be revoked.

Table VI.1 Canadian Maximum Residue Limits

Commodity	MRL (ppm)	
	Glyphosate (Including Metabolites)	TMS Cation
Oat milling fractions (excluding flour)	35	15
Rapeseeds (canola)	20	10
Dry soybeans	20	13
Oats	15	10
Barley milling fractions (excluding flour)	15	*
Wheat milling fractions (excluding flour)	15	*
Barley	10	15
Sugar beet roots	10	*
Borage seeds	10	*
Cuphea seeds	10	*
Echium seeds	10	*
Gold pleasure seeds	10	*

Commodity	MRL (ppm)	
	Glyphosate (Including Metabolites)	TMS Cation
Hare's ear mustard seeds	10	*
Milkweed seeds	10	*
Mustard seeds (condiment type)	10	*
Mustard seeds (oilseed type)	10	*
Oil radish seeds	10	*
Poppy seeds	10	*
Sesame seeds	10	*
Sweet rocket seeds	10	*
Peas	5.0	3.0
Wheat	5.0	3.0
Beans	4.0	1.0
Dry lentils	4.0	1.5
Flax seeds	3.0	3.0
Field corn, sweet corn kernel plus cob with husks	3.0	*
Kidney of cattle, goats, hogs, horses and sheep	2.0	1.0
Kidney of poultry	2.0	0.1
Asparagus	0.5	*
Liver of cattle, goats, hogs, horses and sheep	0.2	0.5
Liver of poultry	0.2	0.1
Fat of cattle, goats, hogs, horses, poultry and sheep	0.15	*
Eggs	0.08	0.02
Meat of cattle, goats, hogs, horses and sheep	0.08	0.5
Meat of poultry	0.08	0.05
Milk	0.08	0.5
Meet byproducts of cattle, goats, hogs, horses and sheep	*	0.5
All other crops appearing on the registered labels	*	*

* Regulated under Subsection B.15.002(1) of the Food and Drugs Regulations not to exceed 0.1 ppm.

VI.2 International Regulatory Status

United States – In the United States, glyphosate is registered for use on a variety of fruit, vegetable and field crops as well as for aquatic and terrestrial non-food uses. Glyphosate is also registered for use on transgenic crop varieties such as canola, corn, cotton, soybeans, sugar beets and wheat. The registered forms of glyphosate include: glyphosate acid; glyphosate, isopropylamine salt; glyphosate, ethanolamine salt; glyphosate, sodium salt; glyphosate, potassium salt; glyphosate, ammonium salt; glyphosate, diammonium salt; and glyphosate, dimethylammonium salt. Glyphosate-trimesium (GPT, in other words, sulfosate or glyphosate-TMS) is not currently included in any pesticide products actively registered in the United States,

and is not, therefore, included in the current USEPA registration review program for glyphosate active ingredient. With regard to exposure and risk assessment, the USEPA considers all these active compounds as being equivalent, with glyphosate acid as the common moiety. Tolerances [see Table VI.2] are currently established under 40 CFR §180.364 for:

a) Residues of glyphosate, including its metabolites and degradates in/on registered conventional crops and transgenic EPSPS/GOX crops, resulting from the application of all registered forms of glyphosate. Compliance with those tolerance levels is to be determined by measuring only glyphosate (*N*-[phosphonomethyl] glycine). The USEPA determined that, based on toxicological considerations, the metabolite AMPA need not be regulated regardless of levels observed in food or feeds.

b) Residues of glyphosate, including its metabolites and degradates in/on registered transgenic GAT crops and in animal commodities, resulting from the application of all registered forms of glyphosate. Compliance with those tolerance levels is to be determined by measuring only glyphosate and its metabolite *N*- acetylglyphosate calculated as the stoichiometric equivalent of glyphosate. The metabolite *N*-acetylglyphosate is considered to be equally toxic as glyphosate. The metabolite *N*-acetyl AMPA, which is also formed in transgenic GAT crops, was excluded as residue of concern based on residue and toxicity considerations. However, the USEPA noted that the decision not to regulate AMPA and *N*-acetyl AMPA, regardless of levels observed in foods or feeds, may be revisited during the registration review process.

JMPR/Codex – Codex MRLs have been established in/on a range of plant commodities as well as in commodities of animal origin (see Table VI.2). The residue definitions (RDs) for compliance with MRLs are the same as those used by the USEPA for both transgenic GAT crops (in other words, the RDs exclude the metabolites AMPA and *N*-acetyl AMPA) and for conventional and transgenic non-GAT crops (in other words, the RDs exclude the metabolite AMPA). However, the residue for dietary risk assessment for plant (genetically modified or not) and animal commodities is defined as the sum of glyphosate, *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA, expressed as glyphosate. This RD is the same as the one used by the PMRA for both enforcement of MRLs and dietary risk assessment for transgenic GAT crops. Note that for risk assessment the PMRA excludes the acetylated metabolites from RDs in non-GAT crops (except corn, soybean and canola) as well as *N*-acetyl AMPA from RDs in animal commodities. There are no Codex MRLs for the TMS cation of glyphosate-trimesium.

EU – Glyphosate (including glyphosate-trimesium, in other words, sulfosate or glyphosate-TMS) has been approved for use in EU countries (in other words, is included in Annex I to Council Directive 91/414/EEC) until 12/31/15. The residue definitions for enforcement and risk assessment have recently been amended to accommodate new varieties of genetically modified (in other words, GAT gene-containing) soybeans and corn imported from the United States. For enforcement, the RD is expressed as glyphosate per se in all crops including transgenic GAT crops and in animal commodities. For dietary risk assessment, the RD is expressed as the sum of glyphosate, *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA, calculated as glyphosate for all plant commodities (including non-GAT crops) as well as for commodities of animal origin. No special consideration has been given to the TMS cation of glyphosate-trimesium with regard to the residue definition or MRLs, but a separate risk assessment has been conducted for glyphosate-TMS. Glyphosate-TMS has a lower ADI compared to the other glyphosate salts.

The residue definitions (see Table VI.3) and tolerance levels or MRLs (see Table VI.2) for a variety of commodities are not harmonized across the different regulatory jurisdictions.

Table VI.2 Canadian Maximum Residue Limits and International Tolerances / Maximum Residue Limits for Glyphosate

Commodity	CAN MRL[1] (ppm)	United States Tolerance[2] (ppm)	Codex MRL[3] (ppm)
Acerola	—	0.2	—
Alfalfa fodder	—	400 (Group 18)	500
Alfalfa, seed	—	0.5	—
Almond, hulls	—	25	—
Aloe vera	—	0.5	—
Ambarella	—	0.2	—
Animal feed, nongrass, group 18	—	400	—
Artichoke, globe	—	0.2	—
Asparagus	0.5	0.5	—
Atemoya	—	0.2	—
Avocado	—	0.2	—
Bamboo, shoots	—	0.2	—
Banana	—	0.2	0.05**
Barley	10	30 (Group 15, except field corn, popcorn, rice, sweet corn, and wild rice)	30 (Group 15)
Barley, bran	—	30 (Group 15, except field corn, popcorn, rice, sweet corn, and wild rice)	—
Barley milling fractions, except flour	15	—	—
Barley straw and fodder, dry	—	—	400
Bean fodder	—	—	200
Beans	4.0	5.0 (Group 6, except soybean and dry pea)	2.0 (dry)
Beat, sugar	10	10	—
Beet, sugar, dried pulp	—	25	—
Beet, sugar, roots	—	10	—
Beet, sugar, tops	—	10	—
Berry group 13	—	0.2	—
Betelnut	—	1.0	—
Biriba	—	0.2	—
Blimbe	—	0.2	—
Borage, seed	10	—	—

Commodity	CAN MRL[1] (ppm)	United States Tolerance[2] (ppm)	Codex MRL[3] (ppm)
Breadfruit	—	0.2	—
Cacao bean, bean	—	0.2	—
Cactus, fruit	—	0.5	—
Cactus, pads	—	0.5	—
Canistel	—	0.2	—
Canola, seed	20	20	20 (Rapeseed)
Carrot	—	5.0	—
Chaya	—	1.0	—
Cherimoya	—	0.2	—
Citrus, dried pulp	—	1.5	—
Coconut	—	0.1	—
Coffee, bean, green	—	1.0	—
Corn, field, forage	—	13	—
Corn, field, grain	3.0	5.0	5.0
Corn, field, stover	—	100	—
Corn, fodder, dry	—	—	150
Corn, pop, grain	3.0	0.1	5.0
Corn, sweet, kernel plus cob with husk removed		3.5	5.0
Cotton, gin byproducts	—	210	—
Cotton, undelinted seed	—	—	40
Cuphea seeds	10	—	—
Custard apple	—	0.2	—
Date, dried fruit	—	0.2	—
Dokudami	—	2.0	—
Durian	—	0.2	—
Echium seeds	10	—	—
Epazote	—	1.3	—
Feijoa	—	0.2	—
Fig	—	0.2	—
Fish	—	0.25	—
Flax, seed	3.0	—	—
Fruit, citrus, group 10-10	—	0.5	—
Fruit, pome, group 11-10	—	0.2	—
Fruit, stone, group 12	—	0.2	—
Galangal, roots	—	0.2	—
Ginger, white, flower	—	0.2	—
Gold pleasure seeds	10	—	—
Gourd, buffalo, seed	—	0.1	—
Governor's plum	—	0.2	—
Gow kee, leaves	-	0.2	—
Grain, cereal, forage, fodder and straw, group 16, except field corn, forage and field corn and stover	—	100	—

Commodity	CAN MRL[1] (ppm)	United States Tolerance[2] (ppm)	Codex MRL[3] (ppm)
Grain, cereal, group 15, except field corn, popcorn, rice, sweet corn and wild rice	Barley: 10 Corn (field and sweet): 3 Oat: 15 Sorghum (grain): 30 Wheat (grain): 5	30 (Group 15, except field corn, popcorn, rice, sweet corn, and wild rice)	30 (except corn and rice)
Grape	—	0.2	—
Grass, forage, fodder and hay, group 17	—	300	500
Guava	—	0.2	—
Hare's ear mustard seeds	10	—	—
Herbs subgroup 19A	—	0.2	—
Hop, dried cones	—	7.0	—
Ilama	—	0.2	—
Imbe	—	0.2	—
Imbu	—	0.2	—
Jaboticaba	—	0.2	—
Jackfruit	—	0.2	—
Kava, roots	—	0.2	—
Kenaf, forage	—	200	—
Lentils	4.0	5.0 (Group 6, except soybean and dry pea)	No Codex MRL (proposed EU MRL of 10 or 15 ppm, based on a single high residue value of 8.88 ppm whereas the rest of the residue trial values were in the range 0.5-4.17 ppm)
Leucaena, forage	—	200	—
Longan	—	0.2	—
Lychee	—	0.2	—
Mamey apple	—	0.2	—
Mango	—	0.2	—
Mangosteen	—	0.2	—
Marmaladebox	—	0.2	—
Mikweed seeds	10	—	—
Mioga, flower	—	0.2	—
Mustard, seed	10 (both condiment and oilseed types)	—	—
Noni	—	0.20	—
Nut, pine	—	1.0	—
Nut, tree, group 14	—	1.0	—

Commodity	CAN MRL[1] (ppm)	United States Tolerance[2] (ppm)	Codex MRL[3] (ppm)
Oats	15	30 (Group 15, except field corn, popcorn, rice, sweet corn, and wild rice)	30 (group 15)
Oats milling fractions	35 (excluding flour)	30 (Group 15, except field corn, popcorn, rice, sweet corn, and wild rice)	-
Oat straw and fodder, dry	—	—	100
Oil radish seeds	10	—	—
Oilseeds, group 20, except canola	—	40	—
Okra	—	0.5	—
Olive	—	0.2	—
Oregano, Mexican, leaves	—	2.0	—
Palm heart	—	0.2	—
Palm heart, leaves	—	0.2	—
Palm, oil	—	0.1	—
Papaya	—	0.2	—
Papaya, mountain	—	0.2	—
Passionfruit	—	0.2	—
Pawpaw	—	0.2	—
Pea hay or pea fodder (dry)	—	—	500
Peas	5.0	5.0 (Group 6, except soybean and dry pea)	—
Peas, dry	—	8.0	5.0
Peanut	—	0.1	—
Peanut, hay	—	0.5	—
Pepper leaf, fresh leaves	—	0.2	—
Peppermint, tops	—	200	—
Perilla, tops	—	1.8	—
Persimmon	—	0.2	—
Pineapple	—	0.1	—
Pistachio	—	1.0	—
Pomegranate	—	0.2	—
Poppy seeds	10	7.0 (Subgroup 19B)	—
Pulasan	—	0.2	—
Quinoa, grain	—	5.0	—
Rambutan	—	0.2	—
Rice, grain	—	0.1	—
Rice, wild, grain	—	0.1	—
Rose apple	—	0.2	—
Sapodilla	—	0.2	—

Commodity	CAN MRL[1] (ppm)	United States Tolerance[2] (ppm)	Codex MRL[3] (ppm)
Sapote, black	—	0.2	—
Sapote, mamey	—	0.2	—
Sapote, white	—	0.2	—
Sesame, seed	10	—	—
Shellfish	—	3.0	—
Sorghum straw and fodder, dry	—	—	50
Soursop	—	0.2	—
Soybean, dry	20	20 (seed)	20
Soybean, forage	—	100	—
Soybean, hay	—	200	—
Soybean, hulls	—	120	—
Spanish lime	—	0.2	—
Spearmint, tops	—	200	—
Spice subgroup 19B	10 (poppy seeds)	7.0	—
Star apple	—	0.2	—
Starfruit	—	0.2	—
Stevia, dried leaves	—	1.0	—
Strawberry	*	—	—
Sugar apple	—	0.2	—
Sugarcane, cane	—	2.0	2.0
Sugarcane, molasses	—	30	10
Sunflower, seed	—	—	7
Surinam cherry	—	0.2	—
Sweet potato	—	3.0	—
Sweet rocket seeds	10	—	—
Tamarind	—	0.2	—
Tea, dried	—	1.0	—
Tea, instant	—	7.0	—
Teff, forage	—	100	—
Teff, grain	—	5.0	—
Teff, hay	—	100	—
Ti, leaves	—	0.2	—
Ti, roots	—	0.2	—
Ugli fruit	—	0.5	—
Vegetable, bulb, group 3-07	—	0.2	—
Vegetable, cucurbit, group 9	—	0.5	—
Vegetable, foliage of legume, subgroup 7A, except soybean	—	0.2	—
Vegetable, fruiting, group 8-10 (except okra)	—	0.1	—
Vegetable, leafy, brassica, group 5	—	0.2	—
Vegetable, leafy, except brassica, group 4	—	0.2	—

Commodity	CAN MRL[1] (ppm)	United States Tolerance[2] (ppm)	Codex MRL[3] (ppm)
Vegetable, leaves of root and tuber, group 2, except sugar beet tops	—	0.2	—
Vegetable, legume, group 6 except soybean and dry pea	—	5.0	—
Vegetable, root and tuber, group 1, except carrot, sweet potato and sugar beet	—	0.2	—
Wasabi, roots	—	0.2	—
Water spinach, tops	—	0.2	—
Watercress, upland	—	0.2	—
Wax jambu	—	0.2	—
Wheat	5.0	30 (Group 15, except field corn, popcorn, rice, sweet corn, and wild rice)	30 (Group 15)
Wheat bran	—	30 (Group 15, except field corn, popcorn, rice, sweet corn, and wild rice)	20 (unprocessed)
Wheat milling fractions	15 (excluding flour)	30 (Group 15, except field corn, popcorn, rice, sweet corn, and wild rice)	—
Wheat straw and fodder, dry	—	—	300
Yacon, tuber	—	0.2	—
Edible offal of pigs	—	—	0.5
Edible offal of poultry	—	—	0.5
Egg	0.08	0.05	0.05**
Fat of cattle, goats, hogs, horses, sheep and poultry	0.15	—	—
Kidney of cattle, goats, hogs, horses, sheep and poultry	2.0	—	5.0 (mammalian except pigs)
Liver of cattle, goats, hogs, horses, sheep and poultry	0.2	—	5.0 (mammalian except pigs)
Meat byproducts of cattle, goats, hogs, horses and sheep	*	5.0	0.05** (from mammals other than marine mammals)
Meat byproducts of poultry	*	1.0	—
Meat of cattle, goats, hogs, horses and sheep	0.08	—	0.05** (from mammals other than marine mammals)
Meat of poultry	0.08	0.10	0.05**
Milk	0.08	—	0.05**

*Regulated under B.15.002(1) of the Food and Drugs Regulations not to exceed 0.1 ppm.

**At or about the limit of determination.
[1] Maximum Residue Limits for Pesticides webpage as of 12/10/13.
[2] Electronic Code of Federal Regulations.
[3] Codex Alimentarius webpage as of 12/10/13.

Table VI.3 Comparison of Residue Definitions derived by Canada, United States, JMPR/Codex and European Union

Commodity	Canada	United States	JMPR/Codex	European Union
Residue Definition for Enforcement of MRLs/Tolerances				
Transgenic GAT crops	Sum of glyphosate, *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA, expressed as glyphosate[1]	Sum of glyphosate and *N*-acetyl-glyphosate, expressed as glyphosate[1]	Same as United States	Glyphosate
Conventional and transgenic EPSPS/GOX crops	Sum of glyphosate and AMPA, expressed as glyphosate[1]	Glyphosate	Same as United States	
Animal commodities	Sum of glyphosate, *N*-acetylglyphosate and AMPA, expressed as glyphosate[1]	Sum of glyphosate and *N*-acetyl-glyphosate, expressed as glyphosate[1]	Same as United States	
Residue Definition for Risk Assessment				
Transgenic GAT crops	Sum of glyphosate, *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA, expressed as glyphosate[1]	Sum of glyphosate and *N*-acetyl-glyphosate, expressed as glyphosate[1]	Sum of glyphosate, *N*-acetylglyphosate, AMPA and *N*-acetyl AMPA, expressed as glyphosate[1]	Same as JMPR/Codex
Conventional and transgenic EPSPS/GOX crops	Sum of glyphosate and AMPA, expressed as glyphosate[1]	Glyphosate		
Animal commodities	Sum of glyphosate, *N*-acetylglyphosate and AMPA, expressed as glyphosate[1]	Sum of glyphosate and *N*-acetyl-glyphosate, expressed as glyphosate[1]		

[1] Molecular weight conversion factors (MWCF) for field trial residues: glyphosate = 0.8 × *N*-Acetylglyphosate; 1.1 × *N*-Acetyl AMPA; 1.5 × AMPA.

Appendix VII Agricultural Mixer/Loader/Applicator and Postapplication Risk Assessment

Table VII.1 Commercial Mixer/Loader/Applicator Exposure and Risk Assessment

Application Equipment	Scenario	Max. Rate	Area Treated per Day	Dermal Exposure[1] (mg/kg bw/day)	Inhalation Exposure[2] (mg/kg bw/day)	Dermal MOE[3]	Inhalation MOE[3]	Combined MOE[4]
Baseline PPE: Open M/L, Single Layer								
Groundboom (custom)	MLA	4.320 kg/ha	360 ha/day	0.060848	0.046294	490	650	280
Aerial	ML	4.320 kg/ha	536 ha/day	0.059208	0.046310	510	650	280
	A			0.011184	0.002026	2700	15000	2300
Airblast	MLA	4.320 kg/ha	20 ha/day	0.037988	0.007992	790	3800	650
Mechanically pressurized handgun	MLA	0.0096 kg/L	3800 L/day	0.101879	0.068856	290	440	180
Backpack	MLA	0.022 kg/L	150 L/day	0.008822	0.002515	3400	12000	2600
Cut stump application	MLA	0.36 kg/L	150 L/day	0.025471	0.030510	1200	980	540
ROW Sprayer	MLA	0.0096 kg/L	3800 L/day	0.016848	0.003010	1781	9968	1511

M/L = mix/load, A = apply, ATPD = area treated per day, MOE = margin of exposure, ROW = right-of-way

1 Dermal exposure (mg/kg bw/day) = (dermal unit exposure × ATPD × maximum application rate × 4% dermal absorption)/80 kg body weight

2 Inhalation exposure (mg/kg bw/day) = (inhalation unit exposure × ATPD × maximum application rate)/80 kg body weight

3 Based on a NOAEL of 30 mg/kg bw/day, target = 100

4 Combined MOE = 1/[1/dermal MOE + 1/inhalation MOE]

Table VII.2 Mixer/Loader Tree Injection Exposure and Risk Assessment

Application Equipment	Max. Rate (g/cm dbh)[1]	Amount Handled per Day (kg ai)[2]	Dermal Exposure (mg/kg bw/day)[3]	Inhalation Exposure (mg/kg bw/day)[4]	Dermal MOE[5]	Inhalation MOE[5]	Combined MOE[6]
Baseline PPE: Open M/L, Single Layer							
Injection	0.0364	0.1456	3.46×10^{-3}	2.91×10^{-4}	87[illegible]	1000000	47[illegible]

MOE = margin of exposure

[1] Maximum application rate: 0.182 g/5 cm depth breast height (dbh) = 0.0364 g per cm depth breast height (dbh).

[2] Amount handled per day: 0.0364 g/cm × 20 cm (max dbh) × 200 (maximum number of trees treated per day) × 0.001 (g to kg conversion).

[3] Dermal Exposure (mg/kg bw/day) = (Amount handled per day (kg) × Dermal Unit Exposure (µg/kg a.i.) × 4% dermal absorption)/80 kg body weight.

[4] Inhalation Exposure (mg/kg bw/day) = (Amount handled per day (kg) × Inhalation Unit Exposure (µg/kg a.i.))/80 kg body weight.

[5] Based on a NOAEL of 30 mg/kg/day, target MOE = 100.

[6] Combined MOE = 1/[1/dermal MOE + 1/inhalation MOE.

Table VII.3 Commercial Postapplication Exposure and Risk Assessment

Crop	Activity	TC[1] (cm^2/hr)	Rate (kg a.i./ha)	Number of Applications per Year	Interval Between Applications (Days)	MOE[2] (Day 0)	REI[3]
USC 4							
Forestry	Weeding (hand), grading/tagging	100	4.320	2	7	4700	12 hours
	Transplanting	230				2000	
	Scouting	580				810	
	Irrigation (hand set)	1750				270	
USC 7							
Canola (Roundup ready) seed production	Scouting	1100	0.902	2	5	1900	12 hours
USC 13							
Pearl Millet	Weeding (hand)	70	4.320	3	7	5800	12 hours
	Scouting	1100				370	
Forage grasses and legume	Weeding (hand)	70	4.320	4	7	5500	12 hours
	Scouting	1100				350	
	Irrigation (hand set)	1750				220	
Pasture	Scouting	1100	4.320	2	7	430	12 hours
	Irrigation (hand set)	1750				2670	
Apple	Weeding (hand), orchard maintenance	100	4.320	3	7	4100	12 hours
	Transplanting	230				1800	
	Scouting	580				700	
USC 14							
Corn (sweet)	Weeding (hand)	70	4.320	4	7	5500	12 hours
	Scouting (full foliage)	1100				350	
	Irrigation (hand set)	1750				220	
Dry Beans	Scouting	1100	4.320	6	7	330	12 hours
	Irrigation (hand set)	1750				210	
Lentils	Weeding (hand)	70	4.320	3	7	5800	12 hours
	Scouting	1100				370	
Sorghum	Weeding (hand)	70	4.320	3	7	5800	12 hours
	Scouting	210				1900	
Asparagus	Weeding (hand)	70	4.320	3	7	5800	12 hours
	Scouting	210				1900	
	Transplanting	230				1800	
	Irrigation (hand set)	1750				230	

Crop	Activity	TC[1] (cm^2/hr)	Rate (kg a.i./ha)	Number of Applications per Year	Interval Between Applications (Days)	MOE[2] (Day 0)	REI[3]
USC 14 (continued)							
Ginseng	Weeding (hand)	70	0.902	2	7	32000	12 hours
	Scouting	210				11000	
	Transplanting	230				9800	
	Irrigation (hand set)	1750				1300	
Strawberry	Weeding (hand)	70	4.320	4	7	5500	12 hours
	Scouting	210				1800	
	Transplanting	230				1700	
Blueberry (highbush)	Transplanting	230	4.320	3	7	1800	12 hours
	Scouting, weeding (hand), bird/frost control	640				640	
	Irrigation (hand set)	1750				230	
Blueberry (lowbush)	Weeding (hand)	70	4.320	3	7	5800	12 hours
	Scouting	1100				370	
	Irrigation (hand set)	1750				230	
Cranberry	Weeding (hand)	70	4.320	2	7	6700	12 hours
	Transplanting	230				2000	
	Scouting	1100				430	
Grapes	Transplanting	230	4.320	3	7	1800	12 hours
	Scouting, Weeding (hand), Bird control	640				640	
	Irrigation (hand set)	1750				230	
Filberts or Hazelnuts	Orchard maintenance	100	4.320	3	7	4100	12 hours
	Transplanting	230				1800	
	Scouting	580				700	
Walnut, Chestnut, Japanese heartnut	Orchard maintenance, weeding (hand)	100	4.320	2	7	4700	12 hours
	Transplanting	230				2000	
	Scouting	580				810	
USC 7, 13, 14							
Soybeans (and GPS tolerant soybeans	Weeding (hand)	70	4.320	6	7	5200	12 hours
	Scouting	1100				330	
Canola (and GPS tolerant canola)	Scouting	1100	4.320	5	7	340	12 hours
Flax	Scouting	1100	4.320	3	7	370	12 hours

Crop	Activity	TC[1] (cm^2/hr)	Rate (kg a.i./ha)	Number of Applications per Year	Interval Between Applications (Days)	MOE[2] (Day 0)	REI[3]
USC 7, 13, 14 (continued)							
Corn (and GPS tolerant corn)	Weeding (hand)	70	1.800	4	7	13000	12 hours
	Scouting	1100				830	
	Irrigation (hand set)	1750				520	
Mustard (yellow/white, brown, oriental)	Weeding (hand)	70	4.320	3	7	5800	12 hours
	Scouting	210				1900	
	Transplanting	230				1800	
	Irrigation (hand set)	1750				230	
Sugar Beets	Weeding (hand), thinning	70	4.320	3	7	5800	12 hours
	Scouting	210				1900	
Summer Fallow	Scouting	1100	4.320	1	n/a	630	12 hours
	Irrigation (hand set)	1750				400	
USC 13, 14							
Wheat, Barley, Oats	Weeding (hand)	70	4.320	4	7	5500	12 hours
	Scouting	1100				350	
Rye	Weeding (hand)	70	0.902	1	n/a	48000	12 hours
	Scouting	1100				3000	
Peas	Weeding (hand)	70	4.320	3	7	5800	12 hours
	Scouting	1100				370	
	Irrigation (hand set)	1750				230	
Sugar beets (Roundup ready)	Weeding (hand), thinning	70	0.902	4	10	31000	12 hours
	Scouting	210				10000	
Chickpeas, Lupin (dried), Fava bean (dried)	Weeding (hand)	70	4.320	3	7	5800	12 hours
	Scouting	1100				370	
	Irrigation (hand set)	1750				230	
Apricot, Cherry (sweet/sour), Peaches, Plums, Pears	Orchard maintenance, propping, bird control, weeding (hand)	100	4.320	3	7	4100	12 hours
	Transplanting	230				1800	12 hours
	Scouting	580				700	12 hours
USC 16							
Non-cropland and industrial uses	Scouting	1100	4.320	3	7	370	12 hours
	Irrigation (hand set)	1750				230	
Recreational and public areas	See residential assessment						

Crop	Activity	TC[1] (cm^2/hr)	Rate (kg a.i./ha)	Number of Applications per Year	Interval Between Applications (Days)	MOE[2] (Day 0)	REI[3]
USC 4, 27							
Shelterbelts, Nursery stock, Woody ornamentals, short rotation intensive culture	All activities except irrigation	230	4.320	4	7	1700	12 hours
	Irrigation (hand set)	1750				220	
USC 30							
Turf (prior to establishment or renovation)	Scouting	1000	4.320	2	7	18000	12 hours

USC = use site category, REI = restricted entry interval.

Since no DFR or TTR studies were submitted, a peak default DFR value of 25% or a peak default TTR value of 10% of the application rate were used.

[1] TC = transfer coefficient. Values from PMRA memo (PMRA, 2012d).

[2] Based on an oral NOAEL of 30 mg/kg bw/day and a target MOE of 100.

[3] If the target MOE is met, the minimum REI for agricultural uses was set at 12 hours.

Appendix VIII Non-Occupational Risk Assessment

Table VIII.1 Adult Short-Term Residential Applicator Exposure

Application Equipment	Maximum Application Rate[1]	ATPD[2]	Unit Exposure (mg/kg a.i. Handled)		Exposure[3] (mg/kg bw/day)		MOE[4]		Combined MOE[5]
			Dermal	Inhalation	Dermal	Inhalation	Dermal	Inhalation	
Lawns and Turf: Liquid Product (Adult)									
Manually pressurized handwand	28 g a.i./L	18.927 L/day	138.89	0.04	3.68×10^{-2}	2.65×10^{-4}	820	110000	820
Backpack	28 g a.i./L	18.927 L/day	286.60	0.31	7.59×10^{-2}	2.05×10^{-3}	400	15000	400
Sprinkler can	0.700 g a.i./m^2	93 m^2/day	29.54	0.049	9.62×10^{-4}	3.99×10^{-5}	31000	750000	31000
RTU – Trigger-pump sprayer	28 g a.i./L	5 L/day	187.61	0.13	1.31×10^{-2}	2.28×10^{-4}	2300	130000	2300
Gardens and Trees: Liquid Product (Adult)									
Manually-pressurized handwand	28 g a.i./L	18.93 L/day	138.89	0.04	3.68×10^{-2}	2.65×10^{-4}	820	110000	820
Backpack	28 g a.i./L	18.93 L/day	286.60	0.31	7.60×10^{-2}	2.05×10^{-3}	400	15000	400
Sprinkler can	28 g a.i./L	18.93 L/day	127.87	0.0031	3.39×10^{-2}	2.05×10^{-5}	890	1500000	890
RTU – Trigger-pump sprayer	28 g a.i./L	10 L/day	187.61	0.13	2.63×10^{-2}	4.55×10^{-4}	1100	66000	1100

ATPD = area treated per day; MOE = margin of exposure.
Homeowner PPE consists of: short-sleeved shirt, shorts, and no gloves.

[1] Application rate was provided as 0.7 g a.i./m^2. This value was converted to g ai/L using a spray volume of 0.025 L/m^2 (PMRA, 2012).

[2] Default values from USEPA Residential SOP (USEPA, 2012). For lawns and turf RTU-trigger-pump sprayer the default value is 1 container/day and for gardens and trees RTU-trigger-pump sprayer the default value is 2 containers/day. The largest container size of 5 L was used in the risk assessment.

[3] Exposure (mg/kg bw/day) = (Unit exposure (mg/kg a.i.) × ATPD × maximum application rate × 4% dermal absorption factor)/BW (80kg for adults).

[4] Based on a dermal NOAEL of 30 mg/kg bw/day , target MOE is 100.

[5] Calculated using the following equation: Combined MOE = 1/(1/dermal MOE + 1/inhalation MOE).

Table VIII.2 Adult, Youth and Children Short-term Postapplication Exposure and Risk Assessments on Lawns and Turf

Scenario	TC[1] (cm^2/hr)	Duration (Hours)	Dermal Exposure[2] (mg/kg bw /day)	Dermal MOE[3]
1 Application of Glyphosate				
High-Contact Lawn Activities				
Adult	180000	1.5	0.0945	320
Youth	148000	1.3	0.0945	320
Children (1 to < 2)	49000	1.5	0.1871	160
Mowing Turf				
Adult	5500	1.0	0.0019	16000
Youth	4500	1.0	0.0022	14000
2 Applications of Glyphosate (7-day interval)				
High-Contact Lawn Activities				
Adult	180000	1.5	0.1397	220
Youth	148000	1.3	0.1397	220
Children (1 to < 2)	49000	1.5	0.2766	110
Mowing Turf				
Adult	5500	1.0	0.0028	11000
Youth	4500	1.0	0.0033	9200

TC = transfer co-efficient; BW = Body Weight (80 kg for adults, 57 kg for youth, and 11 kg for children [1 to < 2 years old]).

[1] Transfer coefficient are based on the USEPA Residential SOPs (USEPA, 2012). Transfer coefficients based on a body weight of 80 kg were scaled for the surface area of youth and children (1 to < 2 years old) using the correction factors of 0.82 and 0.27 respectively.

[2] Dermal Exposure (mg/kg bw/day) = (TTR (μg/cm^2) × TC (cm^2/hr) × Duration × DA (4%))/BW (kg).

[3] Adult, youth and children short-term MOEs are based on a NOAEL of 30 mg/kg bw/day with a target of 100.

Table VIII.3 Adult, Youth and Children Short-term Postapplication Exposure and Risk Assessments on Golf Course Turf

Scenario	TC[1] (cm^2/hr)	Duration (Hours)	Dermal Exposure[2] (mg/kg bw /day)	Dermal MOE[3]
1 Application of Glyphosate				
Postapplication Exposure to Golf Course Turf				
Adult	5300	4	0.0074	4000
Youth	4400	4	0.0086	3500
Children (6 to < 11)	2900	4	0.0102	3000
2 Applications of Glyphosate (7-day interval)				
Postapplication Exposure to Golf Course Turf				
Adult	5300	4	0.0110	2700
Youth	4400	4	0.0128	2300
Children (6 to < 11)	2900	4	0.0150	2000

TC = transfer co-efficient; BW = Body Weight (80 kg for adults, 57 kg for youth, and 32 kg for children [6 to < 11 years old]).

[1] Transfer coefficient are based on the USEPA Residential SOPs (USEPA, 2012). Transfer coefficients based on a body weight of 80 kg were scaled for the surface area of youth and child (6 to < 11 years old) using the correction factors of 0.82 and 0.55 respectively.

[2] Dermal Exposure (mg/kg bw/day) = (TTR (μg/cm^2) × TC (cm^2/hr) × Duration × DA (4%))/BW (kg).

[3] Adult, youth and children short-term MOEs are based on a NOAEL of 30 mg/kg bw/day with a target of 100.

Table VIII.4 Incidental Oral Exposure Estimates and MOEs for Hand-to-Mouth Transfer to Children

Formulation	Surface	Hand Residue (mg/cm^2)[1]	Oral Dose (mg/kg bw/day)[2]	MOE[3]
1 Application of Glyphosate (7-day TWA)				
Liquid	Lawns/Turf	0.0077	0.0732	410
2 Applications of Glyphosate (7-day interval)				
Liquid	Lawns/Turf	0.0152	0.1451	210

TWA = time weighted average.
[1] Fraction of residue on the hands (mg/cm^2) is the residue available for transfer.
[2] Where Oral Dose (mg/kg bw/day) = [Hand Residue (mg/cm^2) × (Fraction of hand mouthed/event (0.06) × Surface Area of one hand (150 cm^2)) × (Exposure Time (hr) × Replenishment Intervals (4/hr)) × (1 – (1 – Saliva Extraction Factor (0.48)) Number events per hour (13.9)/Replenishment Intervals (4/hr))]/ Body Weight (11 kg).
[3] MOE = margin of exposure; For children (1 to < 2 years old), the short-term MOE was based on a NOAEL of 30 mg/kg bw/day with a target of 100.

Table VIII.5 Incidental Oral Exposure Estimate and MOE for Object-to-Mouth Transfer to Children

Formulation	Surface	Object Residue ($\mu g/cm^2$)[1]	Oral Dose (mg/kg bw/day)[2]	MOE[3]
2 Applications of Glyphosate (7-day interval)				
Liquid	Lawns/Turf	1.034	0.0047	7000

[1] Where Object Residue ($\mu g/cm^2$) was calculated using the TTR equation. 2 applications of glyphosate with a 7 day interval were assumed.
[2] Where Oral Dose (mg/kg bw/day) = [Object Residue ($\mu g/cm^2$) × 0.001 mg/µg × Surface Area Object Mouthed (10 cm^2/event) × (Exposure Time (hr/day) × Replenishment Intervals (4/hr)) × (1 – (1 – Saliva Extraction (0.48)) Number of object-to-mouth events (8.8/hr)/Replenishment Intervals (4/hr))]/ Body weight (11 kg).
[3] MOE = margin of exposure; for children (1 to < 2 years old), short-term MOE was based on a NOAEL of 30 mg/kg bw/day with a target of 100.

Table VIII.6 Bystander Exposure and Risk Assessment

Crop	Activity	TC[1] (cm^2/hr)	Rate (kg a.i./ha)	Dermal Exposure[2] (mg/kg bw/day)	MOE[3] (Day 0)
Forestry[4]	Hiker – Adult	580	4.320	0.0093	3200
	Hiker – Youth	476		0.0107	2800
	Hiker – Child (6 to < 11 years old)	319		0.0127	2400
Non-cropland and Industrial Uses[5]	Hiker – Adult	580	4.320	0.0107	2800
	Hiker – Youth	476		0.0123	2400
	Hiker – Child (6 to < 11 years old)	319		0.0147	2000

[1] TC = transfer coefficient. Value is based on scouting in an orchard. Values from PMRA memo (PMRA, 2012d).
[2] Since no DFR or TTR studies were submitted, a peak default DFR value of 25% of the application rate was used.
[3] Based on an oral NOAEL of 30 mg/kg bw/day and a target MOE of 100.
[4] Based on 2 applications per year with a 7 day interval.
[5] Based on 3 applications per year with a 7 day interval.

Appendix IX Aggregate Risk Assessment

Table IX.1 Aggregate Risk Assessment

Population	M/L/A Scenario	PA Scenario[1]	Total Dermal + Inhalation Exposure (mg/kg bw/day)[2]	Incidental Oral Exposure (mg/kg bw/day)	Chronic Dietary Exposure (mg/kg bw/day)[3]	Total Exposure (mg/kg bw/day)[4]	Aggregate MOE[5]
Lawns and Turf Scenario							
Adult	Manually pressurized handwand	High Contact Lawn Activities	0.1316	—	0.0377	0.1692	190
	Backpack		0.1725	—		0.2102	150
	Sprinkler can		0.0955	—		0.1332	240
	Trigger pump sprayer		0.1079	—		0.1455	220
	Manually pressurized handwand	Mowing	0.0390	—		0.0767	420
	Backpack		0.0799	—		0.1176	270
	Sprinkler can		0.0029	—		0.0406	790
	Trigger pump sprayer		0.0153	—		0.0530	600
	—	Golfing	0.0074	—		0.0451	710
Youth	—	High Contact Lawn Activities	0.0945	—	0.0548	0.1493	210
	—	Mowing	0.0022	—		0.0570	560
	—	Golfing	0.0086	—		0.0634	500
Children (6 to < 11)	—	Golfing	0.0102	—	0.0815	0.0917	350

Population	M/L/A Scenario	PA Scenario[1]	Total Dermal + Inhalation Exposure (mg/kg bw/day)[2]	Incidental Oral Exposure (mg/kg bw/day)	Chronic Dietary Exposure (mg/kg bw/day)[3]	Total Exposure (mg/kg bw/day)[4]	Aggregate MOE[5]
Children (1 to < 2)	—	High Contact Lawn Activities	0.1394[6]	0.0732[6]	0.1125	0.3251	98

M/L/A = Mixer, Loader, Applicator; PA = postapplication.

[1] Based on 1 application of glyphosate.

[2] Total Dermal + Inhalation Exposure (mg/kg bw/day) = Sum of Dermal and Inhalation Exposures from Handler and Postapplication Scenarios (See Tables III.1 to III.4).

[3] See Section 3.5.2.

[4] Total Exposure (mg/kg bw/day) = (Total Dermal + Inhalation Exposure) + Incidental Oral Exposure + Chronic Dietary Exposure.

[5] Based on an oral NOAEL of 32 mg/kg bw/day and a target MOE of 100.

[6] 1 application of glyphosate along with a 7-day time-weighted DFR average was used (the average residues of glyphosate were calculated over a 7-day span) for this lifestage (see Table III.5).

Appendix X Environmental Fate, Toxicity and Risk Assessment of Glyphosate

Table X.1 Fate and Behaviour of Glyphosate, Its Transformation Product AMPA and the Formulant POEA in the Terrestrial Environment

Property	Test Substance	Material	DT_{50} (Days)	DT_{90} (Days)	Rep $t_{1/2}$ (days)	Kinetic Models	Major Transf. Prod.	Comments [1]
Phototransformation in soil	Glyphosate	Sandy loam, pH7.6, O.M. 1.6%. 22.2°C	90.2 (96.3 dark)	NR	NR	SFO	None	Not a major route of transformation in the environment
		Ray siltt loam, pH 8.2, O.M. 1.2%	45.0	NR	NR	SFO	None	
		Les Evouettes silt loam, pH 6.1, O.M. 2.4%	402.0	NR	NR	SFO?	None	
		Visalia sandy loam, pH 8.3, O.M. 0.6%	6.5 (6.6 dark)	NR	NR	SFO	AMPA	
	AMPA	California sandy loam	AMPA was detected at 19.9% AR and 24% AR in irradiated and dark samples at study termination from exposition of glyphosate to sunlight. The presence of AMPA was linked to microbial activity rather than photolytic process. Phototransformation is unlikely to be major route of dissipation					
Phtotransformation in air	Glyphosate	NR	Glyphosate is considered to be non-volatile, having a very low vapour pressure and low Henry's law constant. Photransformation is not expected to be a major route of transformation					
	AMPA	NR	Glyphosate is unlikely to be volatile since it is formed in soil and bind strongly to soil particles. Photransformation is not expected to be a major route of transformation					
Aerobic soil biotransformation (non-sterile soils)	Glyphosate	**Lab dissipation**						
		Drummer silty clay loam, pH 6.2, O.M. 5.6%	15.4-16.8	NR	NR	NR	AMPA	
		Spinks sandy loam, pH 4.7, O.M. 2.3%	11.2-14.7	NR	NR	NR	AMPA	
		Aerobic biotransformation						
		Drummer silty clay loam, pH 7.0, O.M. 6.0%	25-27.0	NR	NR	NR	AMPA	Non-persistent to moderately persistent. A major route of transformation in the environment
		Ray silt loam, pH 6.5, O.M. 1.0%	3.0	NR	NR	NR	AMPA	
		Norfolk sandy loam, pH 5.7, O.M. 1.0%	130.0	NR	NR	NR	AMPA	
		Kickapoo sandy loam, pH 7.3, O.M. 2.8%	1.9	16.8	5.1	IORE	AMPA	
		Dupo silt loam, pH 7.5, O.M.1.0%	2.1	10.9	3.3	IORE	AMPA	
		Les Evouettes II silt loam, pH 6.1, O.M. 2.4%	18.8	243	77.1	DFOP	AMPA	
		Visalia sandy loam, pH 8.3, O.M. 0.6%	1.0	6.8	2.0	IORE	AMPA	
		Washington sandy loam, pH 8.2, O.M. 1.2%	7.5	NR	NR	SFO	AMPA	
		Sandved, Denmark, pH 6.5, O.M.2.7%	9.0	101	NR	FOMC	AMPA	
		Lorraine sandy loam, pH 5.1, O.M. 1.4%	19.3	64.2	13.6	SFO	AMPA	
		Lorraine silty clay loam, pH 6.3, O.M. 2.5%	12.4	91.1	19.4	IORE	AMPA	
		Lorraine clay loam, pH 7.9, O.M. 3.3%	7.8	25.9	5.5	SFO	AMPA	
		Nantuna sand top soil, pH 7.4, O.M. 2.0%	16.9	56.2	NR	SFO	AMPA	
		Nantuna sand sub soil, pH 6.4, O.M. 1.0%	36.5	121	NR	SFO	AMPA	

Property	Test Substance	Material	DT_{50} (Days)	DT_{90} (Days)	Rep $t_{1/2}$ (days)	Kinetic Models	Major Transf. Prod.	Comments [1]
		Lanna clay top soil, pH 7.2, O.M. 4.4%	110.0	365	NR	SFO	AMPA	
		Lanna clay subsoil, pH 7.4, O.M. 0%	151.0	501	NR	SFO	AMPA	
		Châlon silty clay, pH 8.2, O.M. 3.5%	< 1.0	NR	NR	SFO	AMPA	
		Dijon clay soil, pH 8.2, O.M. 2.8%	0.8	NR	NR	SFO	AMPA	
		Toulouse loam, pH7.6, O.M. 1.6%	3.7	NR	NR	SFO	AMPA	
	AMPA	Visalia sandy loam, pH 8.3, O.M. 0.6%	107.0	356.0	107.0	SFO	NR	Moderately persistent
		Kickapoo sandy loam, pH 7.3, O.M. 2.8%	48.5	161.0	48.5	SFO		
		Dupo silt loam, pH 7.5, O.M. 1.0%	2.1	570.0	263.0	DFOP		
		Sandved, Denmark, pH 6.5, O.M.2.6%	32.0	106	NR	FOMC		Moderately persistent
		Unknown	151	NR	NR	NR		
		Nantuna sand top soil, pH 7.4, O.M. 2.0%	60.4	NR	NR	SFO		Non-persistent
		Nantuna sand sub soil, pH 6.4, O.M. 1.0%	91.3	NR	NR	SFO		
		Lanna clay top soil, pH 7.2, O.M. 4.4%	34.9	NR	NR	SFO		Slightly persistent
		Lanna clay subsoil, pH 7.4, O.M. 0%	97.6	NR	NR	SFO		
		Châlon silty clay, pH 8.2, O.M. 3.5%	25.0	NR	NR	SFO		Moderately persitent
		Dijon clay soil, pH 8.2, O.M. 2.8%	34.0	NR	NR	SFO		
		Toulouse loam, pH7.6, O.M. 1.6%	75.0	NR	NR	SFO		
	POEA	Ray silt loam, pH 6.5, O.M. 1.0%	1-14	NR	NR	SFO	NR	Non-persistent
		Drummer silty clay, pH 7.0, O.M. 6.0%	< 7-14	NR	NR	SFO		
		Norfolk sandy loam, pH 5.7, O.M. 1.0%	< 7-14	NR	NR	SFO		
Anaerobic soil biotransformation	Glyphosate	European Water phase Soil 1 European System Soil 2	3 1699	NR	NR	NR	NR	Non-persistent to persistent
Foliar dissipation	Glyphosate	15 tested foliage values	2.5-26.6 Average = 10.7	NR	90^{th} pcentile 14.4	NR	N/A	Non persistent

Property	Test Substance	Material	Kd (mL/g)	Koc (mL/g)	Comments [1]
Adsorption/ desorption	Glyphosate	Ray silty Loam	73.7	10592	Low mobility
		Drummer silty clay loam	56.9	2886	Low mobility
		Spinks sandy loam	70.4	5059	Low mobility
		Lintonia sandy loam	16.4	4041	Low mobility
		Cat tail swamp sediment	164.0	18852	Low mobility
		Houston clay loam	Kf = 76.0	4872	Slight mobility
		Muskinum silt loam	Kf = 56.0	3415	Slight mobility
		Sassafras sandy loam	Kf = 33.0	2661	Slight mobility
		Montmorilloite clay	Kf = 138.0	NR	NR
		Illite clay	Kf = 115.0	NR	NR
		Kaolinite clay	Kf = 8.0	NR	NR
		Silty clay loam	900	60 000	Immobile
		Silt loam	34	3 800	Slight mobility
		Loamy sand	245	22 300	Immobile
		Greenan sand	263	32 830	Immobile
		Auchincruive sandy loam	810	50 660	Immobile
		Headley sandy clay loam	50	3 598	Slight mobility
		Californian loamy sand	5.3	884	Low mobility
		Les Evouettes II silt loam	47	3 404	Slight mobility
		Darnconner sediment	510	17 819	Immobile
		Unknown	NR	2660-12930	Slight to immobile
		Silt loam	33	NR	NR
		Silty clay	324	NR	NR
		Unknown	NR	500	Moderately mobile
		Unknown	NR	2640	Slightly mobile
		Lilly Field sand	70	23093	Immobile
		Visalia sandy loam	8.3	1426	Low mobility
		18 acres sandy loam	559.8	24771	Immobile
		Wisborough Green silty clay loam	111.1	6170	Immobile
		Champaign silty clay loam	710.3	33037	Immobile
		Sandy muck soil	133	NR	Immobile
		Muck soil	1188	NR	Immobile
		Sandy profile (0-1m)	27-385	NR	NR
		Clay rich till	72-1140	NR	NR
		Sandy Achaia soil (Greece)	5.9	NR	NR
		Ap horizon	227.8	NR	NR
		Bs horizon	762	NR	NR
		ECNR	172.9	NR	NR

Property	Test Substance	Material	Kd (mL/g)	Koc (mL/g)	Comments [1]
		ECR	251.9	NR	NR
		E4G	152.6	NR	NR
		E20GSP	193.1	NR	NR
		Nantuna sand top soil	124.9	NR	NR
		Nantuna sand sub soil	Kf = 40	NR	NR
		Lanna clay top soil	Kf = 28.7	NR	NR
		Lanna clay subsoil	Kf = 118	NR	NR
			Kf = 165	NR	NR
	AMPA	SLI Soil # 1 clay loam	76.0	3640	Slight mobilility
		SLI Soil # 2 sand	1554.0	8310	Immobile
		SLI Soil # 4 sand	15.0	1160	Low mobility
		SLI Soil # 5 clay loam	30.0	3330	Slight mobilility
		SLI Soil # 9 loamy sand	111.0	6920	Immobile
		SLI Soil # 11 sand	74.0	24800	Immobile
		Visalia sandy loam	9.5	1645	Low mobility
		18 acres sandy loam	85.8	4764	Slight mobility
		Lily filed sand	172.6	59510	Immobile
		Champaign silty clay loam	306.8	14272	Immobile
		Wisborough Green silty clay loam	700.9	31014	Immobile
	POEA	Sandy loam	NR	2500	Slight mobility
		Silt loam	NR	6000	Immobile
		Clay loam	NR	9600	Immobile
		Unknown	NR	15400	Immobile

Property	Test Substance	Material	% recovery and detection at different depth					Comments [1]
			0-10 cm	10-20 cm	20-30 cm	> 30 cm		
Soil column leaching	Glyphosate	**Unaged soils**					**Max. depth detect.**	
		Lintonia sandy loam, pH 6.5, O.M. 0.7%					45 cm	
		Ray silt, pH 8.1, O.M. 1.2%	58.7	27.7	7.1	1.4	45 cm	
		Spinks sandy loam, pH 4.7, O.M. 2.4%	48.8	32.5	9.2	4.8	25 cm	
		Leon sand, pH 4.8, O.M. 1.0%	96.7	2.2	0.2	0	65 cm	
		Drummer silty cl loam, pH 6.2, O.M. 3.4%	41.0	30.9	17.1	10.0	45 cm	
		Hilo sandy clay loam, pH 5.7, O.M. 9.5%	94.3	16.7	0.7	0.6	20 cm	
		Molokai clay, pH 7.0, O.M. 3.0%	99.7	0.3	0	0	20 cm	
		Speyer 2.1 sand, pH 6.0, O.M. 0.8%	99.5	0.4	0	0	40 cm	
		Speyer 2.2 loamy sand, pH 6.0, O.M. 4.4%	0	0	0	1.45	40 cm	
		Speyer 2.3 sandy loam, pH 6.6, O.M. 1.3%	0	0	0	0.12	40 cm	
			0	0	0	0.63		
		Aged soil						
		Ray silt, pH 8.1, O.M. 1.2%					65 cm	
		Molokai clay, pH 7.0, O.M.3.0%	31.4	0.76	0.41	0.61	60 cm	
		Hilo sandy clay loam, pH 5.7, O.M.3.4%	40.6	0.12	0.11	0.14	30 cm	
			97.6	0.04	0.02	0		

Property	Test Substance	Material	Rf value	Mobility Index	Comments [1]
Soil TLC (Helling mobility index)	Glyphosate	Spinks sandy loam, pH 6.1, O.M. 2%	0.04	1	Immobile
		Toledo clay loam, pH 7.4, O.M. 3.8%	0.07	1	Immobile
		Toledo clay loam, pH 7.6, O.M. 3.8%	0.13	2	Low mobility
		Hillsdale sandy cl loam, pH 4.6, O.M. 1.5%	0.04	1	Immobile
		Hillsdale sandy cl loam, pH 5.6, O.M.1.3%	0.06	1	Immobile
		Hillsdale sandy cl loam, pH 6.7, O.M. 1.5%	0.08	1	Immobile
		Sandy loam topsoil, pH 6.7, 1.3% OC	0.05	1	Immobile
		Sandy loam subsoil, pH 6.7, 1.3% OC	0.03	1	Immobile
		Muck top soil (0-15 cm, pH 4.7, 30.5% OC	0.02	1	Immobile
		Muck subsoil (15-25 cm, pH 4.7, 30.5% OC	0.05	1	Immobile
		Norfolk sandy loam, pH 5, O.M.7.1%	< 0.09	1	Immobile
		Ray silt loam, pH 6.5, O.M. 1.0%	< 0.09	1	Immobile
		Drummer silty cl loam, pH 7.0, O.M.6.0%,	< 0.09	1	Immobile

Property	Test Substance	Criteria	Value	Criteria Met	Comments [1]
Leaching potential (Leaching criteria of Cohen *et al.* 1984)	Glyphosate	Solubility > 30 mg/L	12000 mg/L	Yes	Low potential for leaching.
		K_d < 5 and usually < 1 or 2	5.3-1188 mL/g	No	
		K_{oc} < 300	500-58000 mL/g	No	
		Henry's law constant < 10^{-2} atm m^3/mol	2.07×10^{-14} atm m^3/mole	Yes	
		pKa = Negatively charged	0.8, 2.35, 5.84, 10.84	No	
		Hydrolysis $t_{1/2}$ > 140 d	$t_{1/2} \leq$ 1627 days at pH 7	Yes	
		Soil phototransformation $t_{1/2}$ > 7 d	DT50: 90 d. irr. (96.3 d. dark)	Yes	
		Soil biotransformation $t_{1/2}$ > 14 to 21 d	DT_{50} = 1-19.3 days	No	
	AMPA	Solubility > 30 mg/L	5800 mg/L	Yes	Some potential for leaching.
		K_d < 5 and usually < 1 or 2	9.5-1554 mL/g	No	
		K_{oc} < 300	1160-59510 mL/g	No	
		Henry's law constant < 10^{-2} atm m^3/mol	1.58×10^{-6} atm m^3/mole	Yes	
		pKa = Negatively charged	0.9, 5.6, 10.2	No	
		Hydrolysis $t_{1/2}$ > 140 d	Unknown, assumed stable	Yes	
		Soil phototransformation $t_{1/2}$ > 7 d	DT50: 90 d. irr. (96.3 d. dark)	Yes	
		Soil biotransformation $t_{1/2}$ > 14 to 21 d	DT_{50} = 2.13-151 days	Yes	
	POEA	Solubility > 30 mg/L	0.082 mg/L	No	Low potential for leaching.
		K_d < 5 and usually < 1 or 2	NR	N/A	
		K_{oc} < 300	2500-15400 mL/g	No	
		Henry's law constant < 10^{-2} atm m^3/mol	2.5×10^{-13} atm m^3/mole	Yes	
		pKa = Negatively charged	Protonated at ambient pH	No	
		Hydrolysis $t_{1/2}$ > 140 d	Stable at pH 7	Yes	
		Soil phototransformation $t_{1/2}$ > 7 d	Unknown	N/A	
		Soil biotransformation $t_{1/2}$ > 14 to 21 d	DT_{50} = 1-14 days	No	

Property	Test Substance	GUS Score Range	Comments [1]
GUS Score	Glyphosate	-1.46 to 2.46	Non-leacher to borderline leacher.
	AMPA	-1.67 to 2.03	Non-leacher to boredline leacher.
	POEA	-0.22 to 0.69	Non-leacher.

Property	Test Substance	Criteria	Interpretation	Comments [1]
Volatility	Glyphosate	Vapour pressure (1.3×10^{-7} Pa at 20°C)	Low	Expected to be relatively non-volatile under field conditions.
		Henry's law constant (2.0×10^{-14} atm m3/mole)	Low	
		Presence of volatile in gas traps of soil lab experiments	Non-volatile in soil lab experiments	
		Soil biodegradation	Non-persistent to slightly persistent	
			Strongly binds to soil particles	

		Adsorption			
	AMPA	Vapour pressure (8.35 = Pa (25°) Henry's law constant (1/H :1.55 × 10^4) Microbial activity Adsorption	Intermediate to highly Slightly volatile from a water surface water or moist soil Need microbial activity to transform glyphosate into AMPA Strongly bind to soil particles		Unlikely to be volatile since it is formed in soil and bind strongly to soil particles.
	POEA	Vapour pressure (6.97 × 10^{-12} Pa at 20°C) Henry's law constant (I/H: 9.8 × 10^{10}) Soil biodegradation Adsorption	Low Low Non-persistent Strongly bind to soil particles		Expected to be relatively non-volatile under field conditions.
Property	**Test Substance**	**Material**	**Max. Soil Depth Detection (cm)**	**DT_{50} Value (days)**	**Comments**
Agricultural Canadian (and Equivalent Ecoregion) Field Studies	Glyphosate	Fredonia, New York, U.S.A., gravel loam	0-15	Detection after 300 days	Persistent
		Casselton, North Dakota, U.S.A., clay loam	0-15	9.0	Non-persistent
		Canard, Nova Scotia, Canada sandy loam	0-15	16.2 (IORE)	Slightly persistent
		Canadian soil	NR	6-21	Non-persistent to slightly persistent
		Manitoba, Canada Ontario, Canada Alberta, Canada	NR NR NR	11 16 63	Non-persistent Slightly persistent Moderately persistent
		St-Davids, Ontario, Canada, silty clay Carman, Manitoba, Canada, loamy sand Grandora, Saskatchewan, Canada, clay loam Speers, Saskatchewan, Canada, silty clay loam Brooks, Alberta, Canada, loam	0-30 0-15 0-12.5 0-12 0-15	NR 60 NR 87 155	N/A Moderately persistent N/A Moderately persistent Moderately persistent
	AMPA	Manitoba, Canada Ontario, Canada	NR NR	128 185	Moderately persistent Persistent
		Canard, Nova Scotia, Canada, sandy loam	0-15	55.1 (DFOP)	Moderately persistent
Forestry Canadian (and Equivalent Ecoregion) Field Studies	**Glyphosate**	Nanaimo sandy (gravelly) soil (mean station I, II and III)	7-12	< 60-80	Moderately persistent
		Carnation Creek, British Columbia, sandy clay loam 0-5 cm Carnation Creek, British Columbia, sandy clay loam 5-15 cm Carnation Creek, British Columbia, sandy clay loam 15-35 cm	0-15	45-60	Slightly to moderately persistent

		Carnation Creek, BC, sandy loam 0-5 cm Carnation Creek, BC, sandy loam 5-15 cm Carnation Creek, BC, sandy loam 15-35 cm			
		Harker, On, sandy soil Lamplugh, On, clay soil	0-15 NR	24 Low recovery	Slightly persistent
	AMPA	Chassell, MI, USA	Exposed soil (0-15) Under litter (15-30)	NR NR	N/A
Foreign Agricultural Field studies (Non-equivalent Ecoregions to Canada)	**Glyphosate**	France Sweden	NR	5-197.3 1.2-24.3	Non persistent to persistent Non-persistent to slightly persistent
		Holdenville, OK, USA, loam Shawnee, OK, USA, loam Tumbleton, AL, USA, sandy loam Mankato, MN, USA, silty clay loam Adel, Iowa, USA, silty clay loam Olathe, KS, USA, silty clay loam	0-15 0-15 15-30 15-30 15-30 0-15	36.2 27.3 35.0 43.5 34.0 55.5	Slightly persistent Slightly persistent Slightly persistent Slightly persistent Slightly persistent Moderately persistent
		Clinton, IL, USA, clay loam Joes, CO, USA, loamy sand Twin Falls, ID, USA, silt loam Henderson, KY, USA, silty clay loam Perrysburg, OH, USA, clay loam Chickasha, OK, USA, loam Memphis, TN, USA, silty loam Mission, TX, USA, sandy loam Downs, CA, USA, sandy clay loam Mankato, MN, USA, sandy clay loam	0-15 0-15 0-15 ND ND 0-15 0-15 0-15 0-15 0-15	17.0 4.4 17.1 95.6 1.8 15.3 12.0 1.6 68.4 174	Slightly persistent Non-persistent Slightly persistent Moderately persistent Non-persistent Slightly persistent Non-persistent Non-persistent Moderately persistent Moderately persistent
		Opelika, AL, USA, sandy clay loam Lake Alfred, FL, USA, astatula fine sand Woolvine, VA, USA, clay loam Grand Rapid, MI, USA, silty loam Selah, WA, USA, sandy loam Wapato, WA, USA, sandy loam The Dalles, OR, USA, sandy loam Hood River, OR, USA, sandy loam Five points, CA, USA Milton, WI, USA Champaign , IL, USA	15-30 15-30 0-15 0-15 0-15 0-15 0-15 15-30 0-15 0-15 15-30	NR	N/A
		USA, Texas, sandy loam USA, N. Carolina, sandy clay loam USA, Minnesota, loam USA Colorado, silt loam	0-15 0-15 0-15 0-15	2 16 122-174 NR	Non-persistent Slightly persistent Moderately persistent NA

		Texas	0-15	2.6	Non-persistent
		Ohio	0-15	ND	N/A
		Georgia	0.15	ND	N/A
		California	0-15	ND	N/A
		Arizona	0-15	28.7	Slightly persistent
		Minnesota	0-15	127.8	Moderately persistent
		New York	15-30	140.6	Moderately persistent
		Iowa	0-15	ND	N/A
		California, USA	NR	43.6	Slightly persistent
		California, USA, sandy loam	0-15	2.8	Non-persistent
		N. Carolina, USA, sandy loam	0-15	31	Non-persistent
		Leland, Mississippi, USA, loam bareground	0-15	3.9	Non-persistent
		Leland, Mississippi, USA, loam turf	0-15	1.4	Non-persistent
		California, USA, sandy loam bareground	0-15	19	Slightly persistent to Non-persistent
		California, USA, sandy loam turf	0-15	12	
		California, USA	NR	44-60	Slightly to moderately persistent
		Ohio, USA,	0-15	7 - 7.3	Non-persistent
		Georgia, USA, sandy loam	0-15	8.3 - 9	Non-persistent
		California, USA	0-15	12.6 - 13	Non-persistent
		Arizona, USA	0-15	17.1	Slightly persistent
		Minnesota, USA	0-15	24.7 - 31	Slightly persistent
		New York, USA	0-15	106 - 114.3	Moderately persistent
		Iowa, USA, silt loam	15-30	NR	N/A
		Texas, USA	0-15	1 – 1.7	Non-persistent
		Germany, 5 sites	NR	12	Non-persistent
		Switzerland, 7 sites	NR	21	Slightly persistent
		Finland, Janakala sandy loam	28	90-180	Moderately persistent to persistent
		Finland, Pernio clay	8-28	< 210	
		Michigan, USA	NR	35-158	Slightly to moderately persistent
		Georgia, USA	NR		
		Oregon, USA	NR		
	AMPA	Germany	NR	218	Persistent
		Switzerland	NR	135-139	Moderately persistent
		Ohio, USA	0-15	119	Moderately persistent
		Texas, USA	15-30	131	Moderately persistent
		Arizona, USA	46-61	142	Moderately persistent
		New York, USA	0-15	240	Moderately persistent
		Georgia, USA	0-15	896	Persistent

		Minnesota, USA	15-30	302	Persistent
		California, USA	0-15	958	Persistent
Foreign Forest Field Studies (Non-equivalent Ecoregions to Canada)	**Glyphosate**	**Pacific Northwest Watershed, USA**			
		Foliage	NR	9.5	Non-persistent
		Shrubs	NR	11.6	Non-persistent
		Herbs	NR	14.3	Non-persistent
		Leaf litter	0-5	9.6	Non-persistent
		Corvallis, OR, USA, sandy clay loam	15-30	< 14	Non-persistent
		Cuthbert, GA, sandy loam	15-30	< 1	Non-persistent
		Oregon Coast Range	—		
		Foliage	2-0	10.4	Non-persistent
		Litter	0-7.5	26.6	Slightly persistent
		Covered loam	0-7.5	29.2	Slightly persistent
		Exposed loam		40.2	Slightly persistent
	AMPA	Corvallis, OR, USA, exposed soil	15-30	NR	N/A
		Corvallis, OR, USA, under litter	0-15	NR	
		Cuthbert, GA, USA, Exposed soil	0-15	NR	
		Cuthbert, GA, USA, under litter	0-15	NR	

[1] = Persistence classification of pesticides in soil according to Goring et al. (1975), Persistence classification of pesticides in water according to McEwen and Stephensen (1979), Adsorption/desorption mobility class according to McCall et al. (1981), TLC mobility class according to Helling and Turner (1968), Leaching potential based on the criteria of Cohen et al. (1984), and Ground Ubiquity Score (GUS) based on Gustafson (1989).