Agriculture Canada

Food Production and Inspection Branch | Direction générale de la production et de l'inspection des aliments

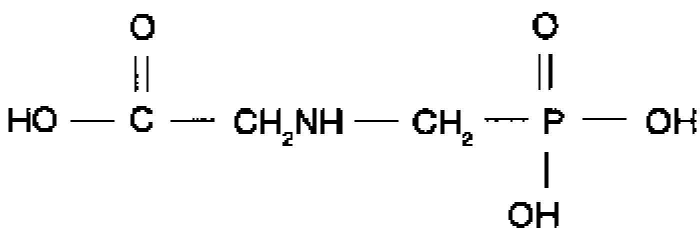
Pesticides Directorate | Direction des pesticides

Canada

Discussion Document

D91-01

PRE-HARVEST USE OF GLYPHOSATE



HERBICIDE

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DISCUSSION DOCUMENT

PREHARVEST APPLICATION

OF

GLYPHOSATE (Roundup^{R})

HERBICIDE

by
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Product Manager
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EXECUTIVE SUMMARY

The purpose of this Discussion Document is to provide a summary of the data reviewed and outline regulatory considerations and options for the preharvest application of glyphosate herbicide in wheat, barley, soybeans, peas, lentils, canola, forage crops (e.g., alfalfa), and flax.

At this time, aerial application is not being considered. However, recognizing that interested parties are likely to raise the question of aerial use, Agriculture Canada has made a preliminary examination of this matter.

We welcome your views on the subject matter of this document. Please address your comments within 60 days of the issue date of this document, to the Provincial Spokesperson, as directed in the Introduction section of the Discussion Document.

Glyphosate, a non-selective herbicide, is the active ingredient in the commercial herbicide products Roundup® and Vision® and (in combination with 2,4-D) Rustler®. A variety of home and garden herbicide products containing glyphosate are also registered.

Preharvest application of glyphosate has been registered since the early 1980s in many other countries on a variety of food crops. International Maximum Residue Limits (MRLs) in these crops have been adopted by the Codex Alimentarius Commission.

Agriculture Canada, with the assistance of advisors from Health and Welfare Canada, Environment Canada, the Canadian Grain Commission, and the Department of Fisheries and Oceans, has completed an assessment of the data submitted by the registrant in support of the preharvest use of glyphosate.

Agronomic and Economic Benefits

The preharvest use of glyphosate would provide an alternative application timing for the control of perennial weeds and, in some areas, could help reduce the use of cultivation as a means of weed control. Therefore, preharvest glyphosate application may be a valuable tool with respect to soil conservation.

The preharvest application of glyphosate is also potentially useful as a harvest management tool (desiccant). This treatment may speed up crop and weed drydown, thereby allowing for an earlier and/or easier harvest. This, in turn, may result in a reduction of the risk of crop loss and downgrading caused by adverse weather and harvesting conditions. The registrant has not conclusively demonstrated the effectiveness of preharvest glyphosate use in producing the harvest aid effects described in the proposed label text.

A consultant's study conducted for the registrant concluded that the principal economic benefit of preharvest application would be enhanced crop yield. This enhancement in crop yield would occur because of the reduction in competitive perennial weeds in areas where the use of currently registered herbicide treatments is not practical. No attempt was made to quantify any harvest management benefits.

Health Aspects

Health and Welfare Canada has reviewed the glyphosate toxicology data base, which is considered to be complete. The acute toxicity of glyphosate is very low. The submitted studies contain no evidence that glyphosate causes mutations, birth defects or cancer.

The potential for worker exposure should not change as a result of the registration of preharvest glyphosate application, because this application is only a change in timing. The amount of glyphosate per hectare that would be applied is less than or equal to the amount applied for currently registered uses.

Residues

Maximum residue limits (MRLs), are being proposed for inclusion in the Food and Drugs Regulations to cover any possible glyphosate residues remaining in harvested crops and other agricultural commodities. Residues such as those represented by these MRLs are not considered to pose a health hazard to consumers.

Due to the dilution of treated grain by untreated grain in the channels of trade, and to the partitioning effects of processing, any glyphosate residues found in commercial flour or beer are likely to be lower than those found in treated wheat or barley. For example, The Canadian Grain Commission assessment concludes that, in reality, it is likely that residues in commercial beer would be, for all practical purposes, non-detectable.

Marketing Considerations

The Canadian Grain Commission (CGC) has assessed the proposed uses with respect to any risks they might present for export trade in grain, oilseed (e.g., canola) or pulse (e.g., lentil) crops. The CGC does not object to ground only preharvest application of glyphosate to these crops. Due to the uncertainties inherent in predicting the extent of use, levels and frequencies of residues in commercial shipments, and buyer acceptance of these residues, the CGC would prefer to see a period of temporary registration to allow for evaluation of any actual impacts of the registration on trade.

The Canadian Grain Commission is opposed to the registration of aerial application of glyphosate in any crop before the actual impacts of the ground only applications have been evaluated.

Environmental Aspects

Glyphosate is not expected to pose a hazard to birds, mammals, soil or aquatic microorganisms, earthworms or bees. Glyphosate itself is not toxic to fish or aquatic invertebrates; the surfactant used in the Roundup® formulation is more so. However, the preharvest use of Roundup® by ground application should not result in significant effects on fish or fish habitat provided a 15-m buffer zone is observed.

Glyphosate is not mobile in soil and it is not taken up by plant roots. While field dissipation studies have been carried out in forest soils, there are no Canadian field data available on dissipation from soil in agricultural areas. The registrant has now initiated the requested studies.

Because glyphosate is a non-selective herbicide, there is concern about the potential impact of overspray or drift on non-target vegetation and on wildlife habitats.

Aerial application may be convenient and avoids yield losses from tractor wheel damage caused by use of ground application equipment in mature crops, but there is the possibility of an increase in drift. The possibility of greater drift increases the potential risk of impact on non-target vegetation and wildlife habitats.

Label Directions/Limitations

The proposed label for the preharvest use of glyphosate includes statements on: (1) correct timing of application; (2) avoiding contamination of water bodies; (3) keeping a 15-m buffer zone around non-target areas; and (4) avoiding drift or overspray to non-target vegetation and wildlife habitats. The label also contains a statement prohibiting application by aircraft.

Regulatory Considerations

Agriculture Canada has already granted a temporary registration for the preharvest use of glyphosate by ground application on flax only. Agriculture Canada has three regulatory options available for the preharvest use of glyphosate: (1) to grant registration; (2) to grant temporary registration; or (3) not to register. It is possible to make different regulatory decisions for the various proposed uses.

Responses to this Discussion Document and commitments to provide additional information that may be requested will be taken into consideration in making the necessary regulatory decision regarding preharvest ground application of glyphosate. Registration of preharvest glyphosate by aerial application is not currently under consideration.

TABLE OF CONTENTS

1. **INTRODUCTION**

The purpose of this document is to provide a summary of the data reviewed and to outline regulatory considerations and options for the preharvest application of glyphosate herbicide in wheat, barley, soybeans, peas, lentils, canola, forage crops (e.g., alfalfa), and flax.

Aerial application of preharvest glyphosate is not under consideration at this time. However, recognizing that interested parties (such as farm organizations and aerial applicators) are likely to raise the question of aerial use, Agriculture Canada has taken this opportunity for a preliminary examination of this matter.

We welcome your views on the subject matter of this document. Please address your comments within 60 days of the issue date of this document, to:

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2. PESTICIDE NAME AND PROPERTIES

2.1 Pesticide Name

Common name:	glyphosate
Chemical name:	N-phosphonomethylglycine
Trade name:	Roundup[R] (isopropylamine salt formulation)
CAS Registry No.:	38641-94-0

2.2 Physical and Chemical Properties

Empirical formula: $C_3H_8NO_5P$

Structural formula:

```
 O              O
  V              V
HOSQCSQCH2NHSQCH2S)QPSQOH
                 R
                OH
```

Molecular weight:	169.1
Physical form:	solid
Colour:	white
Odor:	odorless
Melting point:	200°C (with decomposition)
Boiling point:	not determined
Vapour pressure:	<10^{-8} mm Hg at 25°C
Octanol/water partition coefficient (K_{ow}):	0.0006 - 0.0017
Solubility:	water - 1.57% at 25°C organic solvents - insoluble
Bulk density:	1.74
Storage Stability:	no change in assay after 1 year storage

3. DEVELOPMENT AND USE HISTORY

Glyphosate is a non-selective post-emergence foliar-applied herbicide developed and manufactured by Monsanto Company. It has been registered for use in many countries, and is one of the most widely used herbicides in the world.

In Canada, glyphosate was first registered in 1976, as Roundup[R], an isopropylamine formulation. This product is used for pre-plant and post-harvest control of annual and perennial weeds in continuous, summerfallow and minimum tillage cropping systems. It is also registered for control of woody brush and trees on rights-of-way, and for directed application in orchards, vineyards and shelterbelts. Vision®, a similar formulation, is registered for control of undesired woody and herbaceous species for site preparation and conifer release in forestry and woodland sites and in forest nurseries. Rustler®, a pre-mix formulation of glyphosate and 2,4-D isopropylamine salts, is registered as an alternative to cultivation for weed control in summerfallow. Several dilute formulations of glyphosate isopropylamine salt are registered for home and garden use.

Preharvest application of glyphosate has been registered in the U.K., Netherlands, Belgium, France, Germany, Norway, Denmark, Luxembourg, Czechoslovakia, Poland, New Zealand and Australia since the early 1980's (see Table 1). Crops approved for preharvest application include cereals, pulses, canola and hay. Registration and amended tolerances are presently being sought for preharvest use in the United States. International Maximum Residue Limits (MRLs) have been adopted by the Codex Alimentarius Commission (see Table 2).

TABLE 1

GLYPHOSATE HERBICIDE

GLOBAL REGISTRATION STATUS

PREHARVEST USE

Country	Initial Registration Date	CROP							
		Wheat	Barley	Oats	Rye	Peas	Beans	Canola	Hay
U.K.*	Feb 1980	X	X	X	–	X	X	X	X
Netherlands	Sept 1983	X	X	X	X	X	X	–	X
Belgium	March 1983	X	X	X	X	X	X	–	X
France	March 1982	X	X	–	X	–	–	–	–
W. Germany	March 1981	X	X	X	X	–	–	–	X
CSSR**	June 1983	X	X	X	·	–	–	–	–
Poland	–	X	X	X	X	–	·	–	–
Denmark	June 1982	X	X	X	X	X	X	X	X
Norway	April 1984	–	X		–	–	–	–	–
Luxembourg	July 1983	X	X	–	–	·	–	–	–
New Zealand	–	X	X	X	–	X	–	–	–
Australia	–	Sorghum							

* In the U.K., preharvest glyphosate is also registered for use on triticale and linseed.

** In Czechoslovakia, it is also registered for use on corn.

TABLE 2

INTERNATIONAL MAXIMUM RESIDUE LIMITS FOR GLYPHOSATE (adopted by the Codex Alimentarius Commission)

Crop	Codex Maximum Residue Limit
Wheat	5 ppm
Barley	20 ppm
Rapeseed (Canola)	10 ppm
Flax	---
Peas (dry)	5 ppm
Lentils	---
Soyabean (dry)	5 ppm
Hay or fodder (dry) of grasses	50 ppm
Straw and fodder (dry) of cereal grains	100 ppm
Wheat bran, unprocessed	40 ppm*
Wheat flour	0.5 ppm*
Wheat whole meal	5.0 ppm*

* proposed

Canadian efficacy and residue trials for preharvest glyphosate use have been conducted in various crops. Monsanto Canada submitted initial residue data and requested that Health and Welfare Canada set Maximum Residue Limits under the Food and Drugs Act in November, 1987. Monsanto's submission for registration of preharvest use under the Pest Control Products Act was received by Agriculture Canada in December, 1988.

4. **REGULATORY CONSIDERATIONS**

Agriculture Canada, with the assistance of advisors from Health and Welfare Canada, Environment Canada, the Canadian Grain Commission and the Department of Fisheries and Oceans, has completed an assessment of the data submitted by the registrant in support of preharvest use of glyphosate.

4.1 Summary of Reviews

a) Agronomic Benefits

Preharvest use of glyphosate provides a valuable alternative time of application for control of the perennial weeds quackgrass, Canada thistle, and perennial sow-thistle. These difficult-to-control weeds cause significant reductions in crop yields; currently registered treatments for their control are not suitable to all areas and circumstances (see 6.3 Control of Perennial Weeds, below). Weed control via preharvest glyphosate application has the potential to reduce the use of cultivation to control quackgrass and Canada thistle in areas where chemfallow (i.e., use of herbicide treatment instead of cultivation in summerfallow) is not practiced or desirable. Preharvest glyphosate application is thus of potential value with respect to soil conservation in those areas.

Preharvest use of glyphosate is also potentially useful as a harvest management tool (desiccant), reducing the period of time from crop maturity to harvest by speeding up crop and weed drydown. It must be emphasized that preharvest application of glyphosate will not shorten the time required for the crop to reach physiological maturity. Faster drydown would allow for an earlier and/or easier harvest and serve as an alternative to swathing. Earlier harvest reduces the risk of crop loss and downgrading due to damage caused by adverse weather and harvesting conditions. The merits of desiccant applications are often more difficult to document than are those of herbicidal treatments. The registrant has not conclusively demonstrated effectiveness of preharvest glyphosate use in producing the harvest aid effects described in the proposed label text. Crop desiccation is especially beneficial in harvesting of indeterminate crops such as lentils, canola, peas, flax, and some varieties of soybeans.

The combination of perennial weed control with the harvest management benefits attributed to preharvest glyphosate application have led to considerable farmer interest in this use. This interest has been expressed via resolutions requesting registration from such farmer organizations as the Canadian Federation of Agriculture, Alberta Canola Growers Association (now the Alberta Canola Producers Commission), Alberta Conservation Tillage Society, and the Western Barley Growers Association.

b) Economic Benefits

A consultant's study conducted for the registrant concludes that the primary source of economic benefits would be enhanced crop yield resulting from improved control in western Canada of two weeds: Canada thistle and quackgrass. The annual net benefits from weed control of preharvest application of glyphosate are estimated as being in the $31.6 to $35.8 million range. This estimate was derived through the use of a wide range of data (e.g., five year averages for crop prices) and assumptions (e.g., that improved weed control would result exclusively from treatment of acreage infested with perennial weeds and not treatable with current methods). No attempt was made to quantify harvest management benefits.

c) Health Aspects

Health and Welfare Canada has reviewed the glyphosate toxicology data base, which is considered to be complete. Based on inclusion in the data base of the recently available repeat long-term rat study, the Acceptable Daily Intake (ADI) for glyphosate has been revised upward to 0.75 mg/kg bw/day. Health and Welfare Canada has concluded that there is no evidence of glyphosate-caused mutagenicity, teratogenicity or cancer induction in the submitted studies; the acute toxicity of glyphosate is very low.

The potential for worker exposure from the requested uses (i.e., preharvest application by ground equipment) is not likely to be greater than that of currently registered uses since only a change in timing of application is involved. Furthermore, the rate of application is equal to or lower than current label rates.

d) Residues

Close-to-harvest treatment entails an assessment of the potential for residues in harvested crops and corresponding processed foods. Health and Welfare Canada has assessed residue data submitted by the registrant. Maximum residue limits (MRLs), listed in the Health and Welfare section of this document, are being proposed for inclusion in the Food and Drugs Regulations to cover any possible glyphosate residues remaining in the following harvested crops and other agricultural commodities: wheat, barley, wheat and barley milling fractions, soybeans, soybean oil, peas, lentils, rapeseed (canola), rapeseed (canola) oil, and flax. Feeding of treated cereal and oilseed grain, grain fractions or meal to livestock is not expected to cause significant residues in meat, meat fat or milk. Residues such as those represented by the proposed MRLs are not considered to pose a health hazard to consumers.

Residue data submitted for beans, mustard, and forage crops are insufficient to support the proposed use. Therefore, registration on these crops is not presently under consideration. No data were provided to support the multiple use of glyphosate on a crop in one crop year, i.e., pre-plant plus preharvest, etc.

The proposed MRLs will be published in Part I of the Canada Gazette in the near future. Any comments on these proposed MRLs and their implications for downstream milled products or processed foods can be addressed to Health and Welfare Canada via the Canada Gazette Part I provisions for public comment on regulatory changes.

According to the data reviews provided by Health and Welfare Canada and the Canadian Grain Commission, glyphosate is not destroyed on milling, but instead is redistributed in the mill fractions. Much of the residue is retained in the bran, with lower levels ocurring in flour. Moreover, to the extent that treated grain is diluted by untreated grain in the channels of trade, levels of glyphosate in commercial flour are likely to be lower than those in flour made entirely from treated grain. Processing data for barley indicate that, theoretically, glyphosate residues might be found in beer produced from barley that had been treated at the recommended application rate and stage of development. In reality, however, due to the dilution of treated grain by untreated grain in the channels of trade, it is likely that the residues in commercial beer would be, for all practical purposes, non-detectable.

e) Marketing Considerations

The presence of residues, even the same as or lower than the international MRLs adopted by the Codex Alimentarius Commission, might have implications for Canada's export markets, especially with such major trading partners as the United States and Japan. The Canadian Grain Commission (CGC) has assessed the proposed uses with respect to any risks they might present for export trade in grain, oilseed, and pulse crops.

The Canadian Grain Commission does not object to ground only preharvest application of glyphosate to wheat, barley, canola, lentils, soybeans and peas as per the conditions set forth in the proposed label. However, due to uncertainties pertaining to residue levels and their frequency of occurrence in commercial shipments and uncertainties with respect to buyer acceptance of these residues, the CGC recommends only a temporary registration. The CGC is opposed to registration of aerial application of glyphosate for wheat, barley and canola. While the Commission eventually might not object to aerial application of glyphosate on lentils, soybeans and peas, they are opposed to approval of these use patterns before the actual impacts of ground only application have been evaluated.

The assessments of the CGC are based on predictions about the degree of mixing of treated with untreated crop in the channels of trade. The views of the CGC are also based on the assumptions that glyphosate will be used in compliance with label directions and that the market potential estimates provided by the registrant are reasonably accurate. Should it turn out that there is widespread use of glyphosate at inappropriate moisture levels or if there is widespread illegal aerial application or if the extent of use turns out to be significantly higher than anticipated by the registrant, the predictions that have been made may require revision.

f) Environmental Aspects

The potential use expansion associated with preharvest application of glyphosate warranted updated reviews of environmental impact by Environment Canada and the Department of Fisheries and Oceans. Despite high solubility of the isopropylamine salt in water, glyphosate is strongly adsorbed to soils and is thus not mobile. Laboratory studies conducted at 25°C indicate that there is rapid transformation of glyphosate in aerobic soil and aerobic aquatic systems, but that glyphosate is persistent in anaerobic systems. U.S. field data indicate that glyphosate dissipates rapidly in regions with warm climates but less so in areas with cool climates, and that leaching in soils is minimal. While field dissipation studies have been carried out in forest soils, no Canadian field data on dissipation from soil in agricultural areas are available. The registrant has now initiated the requested studies.

Glyphosate is not expected to pose acute or chronic hazards to birds, mammals, soil microorganisms, earthworms, bees or *Daphnia magna*. As glyphosate is a non-selective herbicide, there is concern about the potential impact on nontarget terrestrial and aquatic vegetation from spray drift from ground or aerial applications. The Canadian Wildlife Service feels that, given the large potential treatment area represented by the crops on the proposed label, more information on the effects of low doses of glyphosate is needed to assess thoroughly the impacts of overspray or drift on wildlife habitats in the vicinity of sprayed fields.

Aerial application of glyphosate would be convenient, and would avoid yield loss caused by tractor wheel damage (specialized application equipment, and/or the use of tramlines, can reduce such wheel damage). However, the possibility of greater drift increases the potential risk of impact on wildlife habitat and on non-target plants, such as late-maturing crops, shelterbelts and ornamentals.

The extent to which preharvest glyphosate would, in practice, be applied by ground equipment is not known, and would be expected to vary with the crop. In flax, peas, and possibly canola, the advantages of glyphosate use might outweigh any damage associated with the use of ground application equipment in a mature crop. The extent to which the treatment area may be reduced by restriction to ground equipment has implications for the economic benefits predicted for the use, and for the significance of the potential risks that have been identified.

Glyphosate, the active ingredient in Roundup^{R}, is not acutely or chronically toxic to fish or aquatic invertebrates. The Department of Fisheries and Oceans is concerned, however, about the Roundup^{R} formulation because it contains a surfactant component which is toxic to aquatic fauna. Exposure of riparian and emergent aquatic vegetation to glyphosate is also a concern. However, the preharvest use of Roundup^{R} should not result in significant effects on fish and fish habitat if the potential for Roundup^{R} deposition on fish habitat is reduced by limiting the application to ground equipment and by observing a 15 m buffer zone. The preharvest use of Roundup^{R} by aerial application may result in significant effects on fish and fish habitat due to the increased risk of deposit on sensitive habitat.

g) Label Directions/Limitations

The proposed label includes the following wording to mitigate any hazard to fish or wildlife:

> "Overspray or drift to important wildlife habitats such as bodies of water, shelterbelts, woodlots, vegetated ditchbanks and other cover on the edges of fields should be avoided. Leave a 15-meter buffer zone between the last spray swath and the edge of any of these habitats."
>
> "Do not contaminate any body of water or non-target vegetation by direct application, spray drift, or when cleaning and rinsing spray equipment."

The proposed label also states:

> "DO NOT APPLY BY AIRCRAFT."

4.2 Regulatory Management Process

Agriculture Canada uses a regulatory management process in making significant or complex registration decisions on pesticides. This approach involves a consideration of both the scientific and public policy aspects of the risks and values associated with pesticide use. The value component involves assessment of:

1) the performance of the material;

2) sustainable considerations (e.g., is it more environmentally friendly than the current product(s), practice or problem?); and

3) economic benefits.

The potential value of preharvest use of glyphosate includes both weed control and harvest management advantages. As with all biological responses, the performance and economic merits of the two value components can be scientifically measured, within certain practical limits, and assessed by experts. However, in a public policy context, these value components also merit comments from other parties, including users, by whom they will ultimately be judged. This same principle applies to the sustainable considerations involved with preharvest use of glyphosate, i.e., reduction of soil erosion.

The potential risks associated with preharvest glyphosate include:

1) residues in a staple food item (cereals);

2) environmental impact considerations associated with such use expansion; and

3) possible impact of food residues tolerances on export markets.

Potential risks can also be measured scientifically and assessed by experts. However, as is the case with values, in a public policy context they also merit comment from other parties, including the food sector, the public and users. It is against this background, and in keeping with recognized decision-making procedures, that the Department is undertaking public consultation via this Discussion Document, prior to registration of preharvest use of glyphosate in most of the crops sought by the applicant.

Preharvest use by ground application in flax has been granted temporary registration, pending generation of further supporting data on effectiveness for control of perennial sow-thistle and as a harvest management tool. Flax is a relatively small acreage crop, and most of the flax grown in Canada is used for such non-food industrial products as linseed oil and linoleum. Preharvest glyphosate application thus does not entail the range nor the intensity of considerations that emerge regarding its use on the other proposed crops. Reviews were received from all advisor agencies, and none indicated any concerns regarding the temporary registration of glyphosate applied by ground equipment in flax.

Responses to this Discussion Document and commitments to provide additional information that may be requested will be taken into consideration in making the necessary regulatory decision regarding preharvest application of glyphosate. Registration of preharvest glyphosate by aerial application is not currently under consideration.

4.3 Regulatory Options

a) General Options

In general, three basic regulatory options are available to Agriculture Canada, as set out in the Pest Control Products Act and Regulations. These are:

1) registration, pursuant to Section 13 of the Regulations;

2) temporary registration for a specified period, pursuant to Section 17 of the Regulations, conditional upon the provision of additional supporting information;

3) no registration, pursuant to Section 18 of the Regulations.

b) Preharvest Glyphosate Application: Considerations and Information Needs

Review of the submission for preharvest glyphosate use has identified a variety of considerations and information needs related to this label expansion. Several of these have already been resolved. For example, the registrant has initiated field dissipation studies in Canadian agricultural soils, to provide additional information regarding persistence of glyphosate under Canadian conditions. The Department of Fisheries and Oceans' concern about toxicity of the Roundup[R] formulation to fish has been mitigated by the addition of a label requirement for a 15-m buffer around fish-bearing waters. The label will carry a statement directing users not to apply glyphosate to crops grown for seed. The various aspects identified in this Discussion Document as outstanding will be addressed via the dialogue and responses triggered by this publication.

c) Specific Regulatory Options

The proposed new use covers preharvest glyphosate application in a variety of crops, for control of three weeds and for harvest management. Certain considerations (e.g., the need for field dissipation data in Canadian agricultural soils) apply to all crops more or less equally; others (such as international trade implications and harvest management effectiveness) can be expected to vary among crops. It is theoretically possible to make different regulatory decisions for the various proposed uses. In other words, for each crop, harvest management and control of each weed (quackgrass, Canada thistle, perennial sowthistle) can separately be granted registration, temporary registration, or no registration.

5. BIOLOGICAL PROPERTIES

Glyphosate is a broad spectrum herbicide, which is absorbed through foliage and translocated throughout the plant. It is relatively non-selective in its action (higher rates are required for control of some species). Translocation to underground parts of perennial species prevents regrowth. Glyphosate is tightly bound in the soil, and hence is not taken up by plant roots.

The primary mode of action of glyphosate is the inhibition of biosynthesis of aromatic amino acids, by the inhibition of the EPSP (5-enolpyruvylshikimate-3-phosphate) synthase enzyme of the shikimic acid pathway. This enzyme and metabolic pathway are not present in mammals.

Visible effects normally occur on annual species in 2-4 days, and on perennial species in 7-10 days. Woody species may require 1-2 weeks, and if treated in the late fall may not show results until the following spring. The most common symptom is development of yellow or yellow-orange color, followed by browning of leaves. At higher rates, wilting is followed by overall yellowing, mottling, browning and eventual death of the plant. With sublethal doses or in regrowth, leaf and stem deformities can occur.

6. AGRONOMIC BENEFITS OF PREHARVEST ROUNDUP[R] APPLICATION

6.1 Use Properties and Application Instructions

The proposed use is the application of glyphosate to wheat, barley, soybeans, peas, lentils, canola, forage crops, and flax for control of quackgrass, season-long control of Canada thistle and perennial sow thistle, and to the listed crops (except forages) for harvest management (desiccation of crop and weeds).

Glyphosate should be applied preharvest at 0.9 kg active ingredient/hectare in 50 - 100 L/ha of clean water, by ground application only. The application should take place only when grain or seed moisture content is 30% or less. This stage typically occurs 7 - 14 days before harvest. Earlier application may reduce crop yield and/or quality. For best weed control results, quackgrass should be actively growing and have at least 4 - 5 green leaves. Canada thistle and perennial sow thistle should be actively growing and at, or beyond, the bud stage for best results. Preharvest application for weed control must take place at the correct stage of both weed and crop. The registrant's proposed label text carries a statement warning users not to apply glyphosate to crops grown for seed.

6.2 Timing of Application

Correct time of preharvest application is critical for both weed control and harvest management. Weeds must be actively growing at time of application, and sufficient time must elapse before harvest for glyphosate to be translocated to underground parts of the plant. The proposed label specifies that application must take place 7-14 days before harvest and when seed/grain moisture content is less than 30%. Application at higher moisture content may produce excess glyphosate residues in the crop and decreased crop yield and/or quality.

Monsanto has proposed visual indicators of 30% seed moisture content as follows:

wheat/barley	hard dough stage - a thumb nail impression will remain
canola	pods are yellow to green and most seeds are yellow to brown
flax	75-80% of pods are brown
lentils/peas	75-80% of pods are brown
soybeans	stems are green to brown in colour and pods are black

Information must be provided to substantiate the correlations between seed moisture content and these visual indicators (as they are interpreted by farmers). It would also be useful to have information relating these proposed application times with the usual stage at which each crop is swathed. In crops with indeterminate growth patterns, the proposed visual indicators could span a week or more. Variable crop maturity in a given field would add to this uncertainty. The margin of safety of these visual indicators, with respect to crop damage or excessive glyphosate residues, must therefore be verified.

6.3 Control of Perennial Weeds

a) Significance of Perennial Weeds

Perennial weeds, particularly quackgrass and Canada thistle, infest millions of acres of Canadian cropland and cause extensive crop damage, both in terms of yield loss and crop quality reduction. The prevalence of perennial weeds such as quackgrass and Canada thistle is greatest under conditions of reduced tillage/continuous cropping and relatively moist conditions throughout the year.

Incidence of Canada thistle is highest in the eastern provinces and lowest in the areas west of central Saskatchewan. While Canada thistle can be found in the drier areas of the southern prairies, infestations in the prairie provinces are generally heavier in the parkland region. Continuous cropping practices common in this region make control of perennial weeds more difficult than in summerfallowed dryland areas. Surveys cited in the economic benefits study submitted by the applicant estimate more than 2.7 million acres of cropland to be infested with Canada thistle in the three prairie provinces. However, in many instances, thistles can be managed using tillage and currently available chemical treatments.

The highest densities and most extensive quackgrass infestations in the prairie provinces are found in the black and dark grey soil zones located in northern agricultural areas and in southern Manitoba. The National Quackgrass Action Committee (NQAC) 1989 survey of farm organizations, extension and research workers, and agrichemical industry personnel reported 42.7% of fields in western Canada to be infested with quackgrass, with an average of 17.3% of the field surface infested. Prevalence and density of quackgrass is even greater in Atlantic and central Canada, where the same survey reported 51.8% and 57.6% of fields to be infested, respectively, with an average of 30% of the field surface infested. [The registrant's economic benefits analysis considers this survey to overestimate total area infested with quackgrass, but this criticism does not refer to the estimated percentage of fields infested or average field surface area infested.]

Competition from weeds often leads to significant reductions in crop yield. The amount of this yield loss depends on many factors, including relative competitiveness of crop and weed, weed density, environmental conditions and crop management practices. With perennial weeds, such as quackgrass, viability and vigour of underground rhizomes are other important determinants of competitive ability. The NQAC survey reported Canada-wide average yield losses to quackgrass ranging from 21.8% for pulse crops to 13.7% for potatoes. Losses in wheat were reported to average 16.1%, barley 15.8%, canola 16.7%, flax 21.0%, soybeans 20.8%, and alfalfa 20.1%.

Zero and minimum tillage systems are valuable practices in reducing soil erosion. These tillage systems, however, have been shown to lead to increases in quackgrass infestations. The presence of quackgrass, thus, can limit the use of these soil conserving practices.

b) <u>Availability of Alternative Control Methods</u>

Perennial weeds are generally controlled by repeated cultivation, herbicides, or a combination of the two. The ability to control quackgrass and thistles with currently registered products depends largely upon cropping sequences, soil type and geographic location. Table 3 is a profile of the products currently registered for control of quackgrass, Canada thistle and perennial sow thistle in various crops. Chemical controls are usually supplemented by spring and/or fall tillage. Infestation and yield loss estimates cited above indicate that, even with presently available control methods, quackgrass remains a significant problem. No selective herbicide controls both quackgrass and Canada thistle. The use of cultivation for weed control (especially when repeated, as is often the practice in summerfallow) is considered to be a major cause of the soil erosion now prevalent in many cropland areas. Registration of preharvest glyphosate application could reduce reliance on cultivation and hence contribute to soil conservation efforts in some areas.

TABLE 3

ALTERNATIVE PRODUCTS

PRODUCT	WEED	CROP
On Summerfallow		
Glyphosate	QG & CT & PST	N/A
Dicamba	CT & PST	N/A
2,4-D	CT* & PST*	N/A
Mechanical Tillage	QG & CT	N/A
Clopyralid	CT & PST*	N/A
Pre-Planting		
Glyphosate	QG & CT & PST	All
In Crop		
Diquat	Desiccation	Peas, Lentils, Alfalfa, Canola, Flax, Soybeans, Mustard,Forage Legumes
Clopyralid	CT & PST*	Wheat, Barley, Canola, Flax, Seedling & Established Timothy (seed crop)
Dicamba	CT* & PST*	Wheat, Barley, Red Fescue
2,4-D	CT* & PST*	Wheat, Barley, Forage Legumes, Flax

PRODUCT	WEED	CROP
2,4-D/2,4-DP	CT* & PST*	Wheat, Barley
Chlorsulfuron + 2,4-D	CT*	Wheat, Barley
Sethoxydim	QG	Canola, Peas, Forage Legumes, Soybeans, Creeping Red Fescue, Lentils, Flax
Fluazifop-butyl Fluazifop-P-butyl	QG	Canola, Flax, Soybeans, Creeping Red Fescue, Forage Legumes
Glyphosate	QG & CT & PST	All - spot treatments or before crop emerges
Post Harvest		
Glyphosate	QG & CT & PST	N/A
Dicamba	CT & PST	N/A
2,4-D	CT* & PST*	N/A

* = Topgrowth suppression or control
QG = Quackgrass
CT = Canada Thistle
PST = Perennial Sow-thistle

Preharvest glyphosate application would not, however, be expected to eliminate the need for other methods of perennial weed control. For example, much of the quackgrass and Canada thistle would have set and/or dispersed seed by this time; subsequent infestations would require treatment.

The registrant considers the most important potential area for preharvest glyphosate use to be in Manitoba and the parkland region of western Canada. Feasibility of post-harvest or pre-plant herbicide application is limited by the short growing season in this area. Thistle and quackgrass plants must be actively growing for herbicide treatment to be effective. Waiting for the weeds to resume active growth in the spring leads to undesirable delays in seeding; spring quackgrass growth can deplete soil moisture during this period. In many years not enough time elapses between harvest and freeze-up for perennial weeds to regrow sufficiently to be controlled by fall herbicide application. Preharvest application of glyphosate could provide valuable flexibility in the timing of herbicide use, and thus constitute an effective control option in areas where infestations are not currently being treated.

c) Efficacy of Preharvest Application For Weed Control

The efficacy of glyphosate in controlling quackgrass is well-established. The registrant's summary of the trials carried out with each of the three application timings shows that quackgrass control with pre-harvest glyphosate was equal to or better than pre-seeding or post-harvest treatments. Consistency of control, as measured by the number of trials in which "commercial levels" of control (80% or better) were obtained, was reported to be greater for preharvest treatment than for the currently registered application timings. A total of 41 trials conducted in a variety of crops over a period of 6 years showed an average of 90% quackgrass control one year after treatment. There was no evidence of reduced efficacy due to interference from the canopy in any crop.

Roundup® is currently registered for control of Canada thistle and perennial sow thistle at different application timings and for sow-thistle at higher rates. Trials submitted for Canada thistle indicated good season-long control in most instances. Limited data submitted for perennial sow-thistle indicated good season-long control after preharvest application. Additional trials will be required to support efficacy in perennial sow-thistle.

Only a small number of aerial application trials were conducted. Further evidence of effective canopy penetration would be required should the registrant wish to make a submission for registration of this application method.

6.4 Harvest Management (Crop Desiccation)

a) Significance of Harvest Management

The proposed label carries the following text: "Application for harvest management can reduce the period of time from crop maturity to harvest by speeding up crop and weed drydown, and may therefore speed up harvesting time and efficiency by replacing the need for swathing or artificial drying. Earlier harvest may provide improved crop quality and recoverable yields by reducing the risk of direct losses and downgrading due to damage caused by adverse weather and harvesting conditions."

Quality and yield of crops can be adversely affected by cool, moist conditions and variable weather at the end of the growing season. To overcome this problem, many farmers swath (windrow) their crops when physiological maturation is complete but the grain/seed is too moist to be stored safely. Swathing also dries green weeds and crop foliage, making combine operation more efficient when a large quantity of vegetative growth is present. Harvesting is completed by combining, usually when grain/seed moisture levels have declined sufficiently for safe storage.

Unfavourable late-season conditions occur more frequently in the parkland areas of the prairies, and crop maturity is often slower and more uneven than in more southerly areas.

Swathing is costly in time, fuel and equipment. Depending on crop, cultivar and growing conditions, swathing may increase or reduce crop loss due to shattering of heads/pods. If harvest conditions are wet, as frequently occurs in northern areas, swathing can inrease sprouting, weathering, mildew, etc., and thus lead to serious losses in crop yield and quality.

Early frost damage to physiologically mature standing crops which are too moist to harvest can be another cause of downgraded quality and hence significant financial loss. If crop maturity is uneven, green kernels could be damaged by frost leading to downgrading of the whole field (see Table 4. Canadian Wheat Board payments for various grades of wheat).

TABLE 4 CANADIAN WHEAT BOARD PAYMENTS FOR VARIOUS GRADES OF WHEAT

Canadian Wheat Board Initial Payments (in store Thunder Bay or Vancouver)

Grade	1988/89	1989/90	1990/91	1991/92
		($'s/tonne)		
#1 CWRS[a]	150.00	155	135	95
#2 CWRS	144.21	149.21	129.21	89.21
#3 CWRS	130.21	135.21	117.21	80.00
Can. Western Feed	110.00	100.00	95.00	71.00

Canadian Wheat Board Final Realized Prices
(in store Thunder Bay or Vancouver)

#1 CWRS	197.14	172.11	-	-
#2 CWRS	191.19	168.08	-	-
#3 CWRS	182.11	161.13	-	-
Can. Western Feed	161.06	138.08	-	-
			Year not over yet	

[a] Canadian Western Red Spring Wheat

Source: Agriculture Canada
Grains and Oilseeds Branch
August 2, 1991

Effective desiccant application could provide an attractive alternative to swathing, under ideal weather conditions. (It must be emphasized that preharvest application of glyphosate will not shorten the time required for the crop to reach physiological maturity.) Swathing is a more conservative approach, in that swathed grain can eventually be recovered (although possibly with some loss or damage) after a period of wet weather. Harvesting of a standing crop cannot be delayed as long as can that of a swathed crop.

Lentils, canola, peas, flax and some varieties of soybeans are characterized by indeterminate growth. Plants with this pattern of development continue to produce new growth and flowers while the earliest seeds are maturing. Uneven maturity at harvest results in the presence of immature seeds, which can lead to grade reduction of the crop. These crops are also particularly susceptible to yield loss from pod shatter, which can occur during swathing or while swaths are drying in the field. Heavy green vegetative growth in peas and soybeans interferes with harvesting machinery. Application of a desiccant would reduce these problems by halting growth, drying out immature seeds, and drying down the uncut crop.

Recognizing the operational challenges and limitations discussed above, it is not surprising that the possibility of glyphosate's being an effective harvest management tool has aroused considerable interest among farmers.

b) <u>Availability of Alternative Products</u>

Diquat, a fast-acting contact herbicide, is currently registered for desiccation of canola, mustard, field peas, flax, soybeans and lentils. It is widely used in lentils and peas for this purpose. While diquat is effective in drying down these crops, under some conditions it can increase a crop's propensity to shatter. Diquat is not particularly effective in controlling perennial weeds, and it is not registered for use on cereals.

c) Efficacy of Preharvest Roundup® Application for Harvest Management

Since the merits of desiccation focus largely on practical situations encountered under operational scale conditions, it is difficult to conclusively prove the value of desiccation via the small-plot replicated trials traditionally used to establish efficacy of herbicides. Effects of glyphosate application on such characteristics as the speed of crop drydown may be too small or variable to be apparent in small-plot trials. It is much more difficult to develop quantitative comparisons of ease of combine operation than to count the number of weeds killed by a herbicide. It is also very difficult to measure the contribution of the treatment to farm operations under the time pressures of threatening weather or the need to harvest a variety of crops.

It is for these reasons that scientifically demonstrating (e.g., via replicated trials) whether glyphosate is actually effective as a desiccant has proven to be quite challenging. It is, therefore, understandable that there is not universal agreement among experts regarding the value of desiccant applications.

The registrant has not conclusively demonstrated effectiveness of preharvest glyphosate application in producing the harvest management effects described in the proposed label text. Demonstration of harvest management performance in the numerous crops proposed involves a large and complicated experimental program. However, Section 9 of the Pest Control Products Regulations requires that the applicant provide information that will allow a determination of the safety, merit and value of the product.

Crop characteristics important in assessing a harvest management treatment include yield, quality, date of maturation, speed of drydown, amount of shattering, and speed/convenience of combine operation. In addition, the possibility of decreased seed germination or seedling vigour must be considered. Effects of glyphosate application on these crop parameters may be relatively small, and yet of importance to farmers.

Treatments must be carried out at the appropriate herbicide rate and seed moisture content. Seed moisture content at times of swathing and harvesting should also be reported.

The choice of swathing or straight-cut harvesting can affect all the crop parameters listed above. Since preharvest application is claimed to be an alternative to swathing, both swathed (windrowed) and straight-cut untreated checks should be included for comparison. Timing of the various operations introduces another complexity into the experimental design. For an appropriate yield comparison, should the check be swathed at the best time or at the same time as the herbicide is applied to the treatment plots? Similarly, should swathed checks and straight-cut treated plots be harvested at the same time or at the best time for each?

Herbicide-induced differences in crop parameters will be very difficult to separate from variability within and between trials caused by both environmental and experimental factors. The particular variety used in a trial can influence the results, since tendencies to shatter differ substantially among varieties. Losses due to shattering will vary with cutting height and with seed/grain moisture content at time of swathing and/or combining. The effects of herbicide treatment and harvesting method are likely to be sensitive to weather conditions between herbicide application and harvest.

The data package submitted by the registrant provides some useful information regarding the effects of preharvest glyphosate application. For example, no significant negative effects of the treatment on such measurements of crop quality as 1000 kernel weight and oil number (flax) and proportion of green seed (canola) were found.

The registrant's summary of germination trials carried out on seed from treated plots indicates no negative effects on barley, wheat, canola, flax or lentils. Early germination (6 days) was reduced in treated seed peas, but by the 16th day, germination was excellent.

The question of seed viability is particularly crucial in barley. By far the highest prices are paid for malting barley, which is germinated under precisely controlled conditions for the production of beer. Any negative effect of glyphosate treatment on germination would therefore be a significant contraindication to use on barley.

Some positive results for crop yield and rate of seed drydown were reported. However, these results were not consistent throughout the relatively small number of trials conducted at the appropriate herbicide application times. In wheat, results were submitted for five trials where glyphosate was applied at the appropriate grain moisture. Of these, two trials showed no treatment-correlated decrease in grain moisture content at harvest; in three trials, slightly lower moisture contents were observed in the glyphosate-treated grain than in the untreated checks. Results were also variable in one out of the six in which glyphosate was applied at the correct grain moisture content of barley, and in the six similar trials in canola.

Pod shatter in canola was variable, with a treatment-correlated increase of 10-11% in one of the two trials in which this characteristic was assessed. In flax, some trials showed a significant decrease in shatter and increase in yield in comparison to a swathed check. There was no signficant difference in shatter of barley in the one trial in which this characteristic was assessed.

Drydown of annual and perennial weeds and of crop vegetative growth was also variable. In some of the seventeen trials in which drydown was assessed, glyphosate treatment was correlated with increased drydown of crop and/or at least one weed species, relative to an untreated straight-cut check. Trial details, such as weather conditions, which might have provided the means for interpreting some of the observed variations in results, were not discussed in the data package.

The fact that it is difficult to conclusively demonstrate harvest management effectiveness tends to explain differences of opinion held by various researchers and other experts. However, this difficulty does not necessarily mean that preharvest treatment will not be useful. This treatment may well prove to be valuable in certain geographic areas and under specific crop/weed/weather combinations, particularly in difficult to harvest crops such as flax, lentils and peas.

Since the factors that drive this assessment are diverse, complex, interdependent, highly variable, and heavily influenced by practical operating conditions on individual farms and fields, farmers themselves may well be the best judges of this question. Clearly, they are the ultimate arbiters in any case, since they alone decide whether this or any treatment has value for them in their business operations.

There are several approaches to dealing with this type of complexity and uncertainty:

1) require the registrant to conduct additional small plot trials;

2) require the registrant to evaluate and better document harvest management performance under various commercial conditions of use (e.g., via research permit and/or during a period of temporary registration);

3) revise or limit the product label to reflect a harvest management claim which is supported by the available data;

4) warn the user, via a statement on the product label, that this type of harvest management claim is not completely supported by scientific research;

5) provide a general label reference to the uncertainties and complexities inherent in desiccation, e.g., as per the currently proposed label text; or

6) register the use and allow users to make their own determinations of effectiveness.

7. ECONOMIC BENEFITS: AGRICULTURE CANADA POLICY BRANCH INPUT

7.1 Primary Source of Benefits

a) Description

A consultant's study conducted for Monsanto Canada Inc. concludes that the primary source of benefits would be enhanced crop yield resulting from improved control in western Canada of two weeds: Canada thistle and quackgrass. The annual net benefits from weed control of preharvest application of Roundup[R] are estimated in the report as being in the $31.6 to $35.8 million range. Approximately 64% of these benefits would be associated with additional wheat production, 17% with added barley, and the remaining 19% with enhanced yield of canola, flax, peas and lentils combined. The benefits in question would accrue in the form of additional income to farmers resulting from the gain in productivity associated with this new pesticide use.

b) Key Assumptions / Data Sources

The data and assumptions employed in deriving the above estimates of annual net benefits were obtained and developed through extensive use of available scientific/economic information and consultation with industry experts. The following is an illustrative list:

1) It is assumed that improved weed control would result exclusively from the preharvest treatment of infested areas that are currently untreated. Treatment in these currently untreatable areas would be possible due to the potential for preharvest applications providing a "wider window of application timing" as discussed in Section 5.1 of this document.

2) Two alternative assumptions were employed with respect to the percentage of infested/untreated areas which would be treated by Roundup[R] (preharvest). In one scenario, this is assumed to be 85%, while in the other it is assumed to be 75%. This is the only instance in which alternative assumptions were employed and, accordingly, it accounts for the fact that the annual net benefits are expressed as a range rather than a point estimate.

3) The weed densities for quackgrass and Canada thistle in infested/untreated areas are assumed to be 180/m^2 and 30/m^2 respectively. These assumptions were based on "discussions with industry contacts and a review of relevant literature." They are particularly important because a number of other estimates are dependent on them.

4) It is assumed that 50% of the application would be by ground with the remainder applied aerially.

5) For each crop and province, data were obtained regarding planted area, yield, production and price. Five-year averages were used for each of these variables.

c) <u>Validity of Assumptions / Data Sources Employed</u>

As noted above, there was considerable reliance placed on available scientific/economic information and consultations with industry experts. Such efforts contribute greatly to ensuring that the assumptions and data employed are valid and, accordingly, that the potential benefits are estimated with as much accuracy as possible. These estimates may tend to be conservative because, as the report notes, the most conservative of available data sources was employed in a number of instances. Nevertheless, certain qualifications should be noted and discussed.

Aerial vs. Ground Application:

The report was prepared prior to Monsanto's amendment of its request for a label change that would limit proposed preharvest usage to ground application. As a result, the assumption of only 50% ground application is clearly inappropriate and a reconsideration of the estimated benefits is in order. If one assumes that the limitation of preharvest Roundup[R] use to ground treatment only would not reduce the number of acres treated, calculations based on the information contained in the report suggest that net benefits would be reduced only slightly.[1] However, it appears quite possible that the limitation in question would reduce the number of acres treated. The report notes that some of the experts who were consulted raised the following issues:

1) The availability of ground application equipment may, in the short term, limit application.

2) Some question may exist as to the feasibility of product use without aerial application.

These considerations create additional uncertainty regarding whether the benefits estimated would be fully realized. It appears safe to conclude that net benefits would be at least somewhat smaller as a result of the limitation to ground treatment only.

Interpretation of the Upper and Lower Bounds of the Range:

As noted above, the upper and lower bound estimates of annual net benefits are based on varying the assumed percentage of currently untreated infested acres which would be treated by preharvest Roundup[R] from 75% to 85%. However, one should take care not to regard the upper and lower bounds of the

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[1] These calculations are incomplete because not all of the information required to make the necessary calculations is contained in the report. Accordingly, their reliability is in some doubt.

estimated range as representing extreme "best-case" and "worst-case" scenarios. This caution is necessary due to two considerations:

1) The degree of uncertainty regarding the percentage of currently untreated acres which would be treated by preharvest Roundup[R] may be greater than the assumed range of 75-85% implies. Some uncertainty is caused, as in most situations of this type, by the difficulty which exists in assessing the relationship between the price of the pesticide and usage.

2) The values assumed and held constant between the two scenarios (e.g., weed densities in infested/untreated areas) are also open to some debate. Ideally, it would have been useful to have scenarios which varied some of these other assumptions.

7.2 Other Sources of Benefits

In addition to the weed control benefits described above, the report identifies substantial potential harvest management benefits. While these are not quantified, some of the experts interviewed in the course of conducting the study expressed the view that the harvest management benefits could outweigh the weed control benefits.

7.3 Additional Issue

The report notes that real and perceived residues could be constraints to the level of benefits and discusses matters related to, among other things, the impact of residues on product quality, price, distribution and marketing. This discussion gives no basis for concluding that any problems associated with residues would threaten or undermine the benefits of preharvest Roundup[R] use as described above. However, it is not clear that all of the relevant issues have been fully addressed. For example, the question of whether exports to key markets could potentially be affected by residues is not specifically dealt with. This matter is dealt with in Section 8 of this document.

7.4 Conclusions

The analyses and conclusions of the consultant's study appear to be soundly based, although the qualifications noted above should be kept in mind. Additional caution is required because all of the benefits at issue are potential in nature as the usage in question has not yet been approved.

In any case, the study's conclusions, as summarized above, provide very useful and balanced evidence of the nature and general magnitude of the potential economic benefits of the preharvest use of Roundup[R].

8. MARKETING CONSIDERATION (WHEAT, BARLEY, CANOLA, LENTILS, SOYBEANS, PEAS) : CANADIAN GRAIN COMMISSION INPUT

8.1 Summary

a) Introduction

This report outlines the views of the Canadian Grain Commission (CGC) with respect to marketing risks associated with licensing of glyphosate for pre-harvest use on wheat, barley, canola, lentils, soybeans and peas. This assessment is based on evaluation of available information, most of which has been provided by Monsanto Canada Inc. As requested by Pesticides Directorate, comments related to both ground and aerial application have been included.

b) Summary of CGC Comments

The CGC does not object to ground only pre-harvest application of glyphosate to wheat, barley, canola, lentils, soybeans and peas as per the conditions set forth in the proposed label. However, due to uncertainties pertaining to residue levels and their frequency of occurrence in commercial shipments and uncertainties with respect to buyer acceptance of these residues, the CGC recommends only a TEMPORARY REGISTRATION. The CGC is opposed to registration of aerial application of glyphosate for wheat, barley and canola. While the Commission eventually may not object to aerial application of glyphosate on lentils, soybeans and peas, it is opposed to approval of these use patterns before the actual impacts of ground only application have been evaluated.

c) <u>Background Considerations</u>

1) <u>Assessing Marketing Risks Associated With Pesticide Use</u>

In assessing potential marketing risks associated with pre-harvest use of glyphosate on Canadian grain it is important to ask three questions:

i) What types of marketing problems could be encountered?

ii) What are the probabilities that these potential problems could become a reality?

iii) How serious are these marketing risks in terms of the potential cost to the Canadian grain industry?

As far as export sales of Canadian grain are concerned, the potential extent of any marketing problems that might be associated with pesticide use are generally a function of two major factors:

i) Residue levels and their frequency of occurrence in commercial shipments; and

ii) The views of foreign buyers with respect to the acceptability of such residues in shipments.

Prediction of residue levels in commercial shipments and buyer acceptance of the presence of residues in grain is not a straightforward matter, however, and requires that certain understandings, assumptions and realities be taken into consideration. Accordingly, it is important to realize the conditional nature of such predictions and to view them in their proper perspective.

The views of the CGC as set forth in this document are based on the assumptions that glyphosate will be used in compliance with label directions and that the market potential estimates provided by Monsanto are reasonably accurate. Should it turn out that there is widespread use of glyphosate at inappropriate moisture levels or if there is widespread illegal aerial application or if the extent of use turns out to be significantly higher than anticipated by Monsanto, the predictions that have been made concerning residue levels in commercial shipments may require revision.

Prediction of residues in commercial shipments also involves other assumptions. One is that the variability of average residue levels in cargo shipments will be minimal due to the blending effect of the bulk handling system. The blending effect is primarily a function of the size of the Canadian commercial grain handling system and the fact that it may take more than 2,000 producer deliveries to fill a cargo of 20,000 tonnes. In essence, blending of producer deliveries from across western Canada should serve to dilute any farm incurred residue that may be present in some deliveries and to keep the range of average levels in cargo shipments to a minimum.

Certain assumptions are also necessary with respect to prediction of customer acceptance to residues in shipments and prediction of customer response to objectionable levels. In assessing the marketing risks associated with pre-harvest use of glyphosate, we have made two important assumptions in this regard:

i) Discriminating buyers will not alter their buying patterns for the grains in question on account of the presence of glyphosate residues at levels up to 0.20 ppm (the Japanese limit for glyphosate in rice).

ii) United States officials will not take regulatory action on shipments from Canada found to contain levels of glyphosate that are many times below accepted international tolerances. Even though the presence of an insignificant but detectable level might be in technical violation of current guidelines, under the circumstances, it is unlikely that these guidelines would be enforced in the case of glyphosate.

There are two reasons why this is unlikely. One is the low toxicity of glyphosate which would make it impossible to make a case that low levels in grain constitute a health hazard. The second reason centres around the expectation that glyphosate may soon be licensed for pre-harvest use on grains in the USA. Once this occurs, US tolerance limits will be more in line with accepted international limits and low levels of glyphosate in shipments to the USA will no longer be a potential issue.

Another reality which makes prediction of marketing risks related to pesticide use somewhat tenuous and which makes it even more important to proceed with caution when licensing new pesticides, is the absence of specific official tolerance limits for pesticide residues in many market countries. In the absence of an official tolerance limit for any given pesticide in any given grain, one can never be certain about the maximum allowable level in imported shipments. In the case of glyphosate, few countries have official tolerance limits for grains. Subsequently, for some markets, prediction of buyer acceptance of glyphosate residues is strictly an educated guess.

On the other hand, however, absolute certainty about the overall acceptability of residues in foreign shipments is not a realistic expectation either. Realistically, we must expect to live with some degree of risk. Accordingly, in assessing new pesticides proposed for use in the grain industry, the CGC strives to ensure that the potential risks are minimal and that they will not seriously jeopardize the quality or marketability of Canadian grain.

8.2 Potential Marketing Problems Associated with Pesticide Use

The three major types of potential marketing problems associated with food safety issues affecting grain are: rejection of shipments; claims for compensation against shipments containing objectionable levels of an undesirable substance; and lost sales.

Theoretically, where food safety issues are involved, there are at least four reasons why a shipment could be rejected or a claim could arise against a shipment. These are:

1) Noncompliance with either legislated tolerance limits or accepted international tolerance limits for toxic substances in grain.

2) Noncompliance with grain purchase contract specifications relating to toxic substances.

3) Nonacceptance or objections to the presence of certain substances in shipments at levels above a buyer's arbitrary quality control standards.

4) Evidence that a particular shipment may be responsible for health and safety-related problems in either humans or animals following use of all or part of the shipment.

In the event of an actual or perceived problem with respect to the safety of Canadian grain, export sales would undoubtedly be affected. Lost sales of Canadian grain due to food safety issues affecting grain could arise for a number of reasons:

1) The inability of Canadian grain to comply with the standards of a given country.

2) The inability of Canadian grain to meet the purity demands of buyers representing highly discriminating customers within a given country.

3) Concern or perception that Canadian grain may be contaminated and therefore unfit for human or animal consumption.

8.3 Residues of Glyphosate and AMPA in Harvested Grain

Field trial residue data provided by Monsanto Canada Inc. clearly show the presence of highly detectable levels of glyphosate in most samples of all grains harvested from treated plots. Generally, the amounts detected varied considerably from study to study, from location to location, and according to the glyphosate application rate and grain moisture level at time of application.

For application of glyphosate at a rate of approximately 0.9 kg AI/ha and at grain moisture levels under 30%, the range of mean concentrations of glyphosate residues over all studies and the average mean levels were as follows:

Mean Glyphosate residues Over All Studies (ppm)

Grain	Minimum	Maximum	Average
Wheat	0.5	2.6	1.1
Barley	2.5	3.4	3.0
Canola	2.1	14.6	4.8
Lentils	3.6	3.6	3.6
Soybeans	1.9	1.9	1.9
Peas	3.1	3.1	3.1

Note: The above values are means and do not reflect the range of results for individual trials within each study. In dealing with bulk shipments, it is more important to consider average residue levels in treated fields than individual test results within a study.

Aminomethylphosphonic acid (AMPA), the major metabolite of glyphosate, was detected at relatively low levels in some samples of wheat, barley, canola and soybeans, but was undetectable in samples of lentils and peas. Reportable levels in wheat and barley were generally associated with high application rates and application to grain at moisture contents above 30%. Overall, AMPA residues do not appear to be a concern.

8.4 Effect of Processing on Retention of Residues

Glyphosate is not destroyed on milling, but instead is redistributed in the mill fractions. Much of the residue is retained in the bran, however, with levels in flour generally ranging between 16% and 29% of the concentration in the whole grain.

Processing data for barley show a loose linear relationship between level of glyphosate in the grain, the concentration in the malt, and retention of glyphosate in beer. In one study, the retention of glyphosate in malt ranged from 0.8% to 4.1% of the level in the grain and averaged 2.0%. Higher retentions in malt, up to 42.1%, were generally associated with treatment of immature crops and excessive application rates. Retention of glyphosate in beer generally averaged between 11.6% and 16.0% of the level in the malt. Theoretically, the maximum level of glyphosate that might be found in beer produced from barley treated at the recommended application rate and stage of development is 0.02 ppm. In reality, however, the level of glyphosate in commercial beer would be considerably less, and for all practical purposes, would be nondetectable.

In processing of canola and soybeans, glyphosate is retained in the meal of the former and in the meal and hulls of the latter. Residues in the oil were virtually nondetectable. For canola, levels in the meal averaged approximately 1.6 times the level in the seed. For soybeans, the level in the meal was similar to the level in the whole seed, but the concentration in the hulls was almost five times the level in the seed.

8.5 Predicted Residues in Commercial Shipments

In assessing potential marketing problems associated with pre-harvest use of glyphosate, it is necessary to examine the different types of shipments that could feasibly occur.

Average levels of glyphosate in cargo shipments are predicted to be as follows:

Predicted ppm Glyphosate in Cargo Shipments

Grain	Ground Only Application	Ground and Aerial Application
Wheat	<0.05	0.06
Barley	0.09	0.27
Canola	0.10	0.30
Lentils	[a]	[a]
Soybeans	<0.05	<0.05
Peas	<0.05	<0.05

[a] not shipped in bulk

For wheat, barley, canola and soybeans, glyphosate concentrations would likely be higher in carlot shipments than in cargoes. This is primarily due to differences in the amount of blending that occurs with these different types of shipments. In some cases, particularly producer cars, the levels in carlots could approach concentrations previously listed for grain harvested from treated fields. On the average, however, since some degree of blending would normally occur, the concentration of glyphosate in carlots is more likely to be somewhere between levels predicted for cargo shipments and levels typically found in grain from treated fields.

The frequency of occurrence of glyphosate residues in carlot shipments is very difficult to predict, but would be much higher than the percent of total crop treated. This is basically because it only takes one contaminated trucklot delivery to contaminate an entire carlot. A rough estimate of the frequency of occurrence of residues in carlots is 10% to 15% for each 1% of total crop treated. With ground only application, the majority of carlots of wheat, barley, canola and soybeans would be essentially free of glyphosate residues. However with aerial application almost all carlots of wheat, barley and canola would be positive and average levels would be significantly higher.

In the case of baglots, the primary means of shipping lentils and one of the ways that peas and soybeans may be shipped, the frequency of occurrence of glyphosate residues would be very low, but when present, the concentration would likely be significant. This is basically due to the lack of blending that occurs before bagging. Without any significant blending, the average level of glyphosate in baglots from treated fields could be close to average levels observed in field trials. On the other hand, however, baglots from untreated fields would likely be essentially free of glyphosate residues. In general, due to the lack of blending, the frequency of occurrence of glyphosate in baglots should not greatly exceed the percent of total crop treated.

8.6 International Tolerance Limits

Crop	FAO/WHO	Italy	Japan	United States	Canada[a]
Barley	20.0	0.1	0.2	0.1	10.0
Beans	2.0			0.2	[b]
Canola	10.0				[c]
Lentils				0.2	4.0
Peas	5.0			0.2	5.0
Rice	0.05	0.1	0.2		---
Soybeans	5.0			6.0	6.0
Wheat	5.0	0.1	0.2	0.1	5.0

[a] Proposed limits--not official tolerances.
[b] No limit proposed due to insufficient data.
[c] No limit proposed because available data indicate that there is no significant retention in canola oil.

8.7 Assessment of Potential Marketing Problems

Bulk Cargo Shipments -- No serious marketing problems are expected for cargo shipments of wheat, barley, canola, canola meal, soybeans and peas as a consequence of pre-harvest use of glyphosate. Minor protests or objections may come from some highly discriminating buyers, particularly with respect to use of glyphosate on wheat, barley and canola, but these should be of little consequence. Given the high FAO/WHO tolerance limit for glyphosate in wheat, the low relative toxicity of this compound and the low predicted levels in cargoes, complaints, rejected shipments, claims for compensation and lost sales with respect to cargo shipments are improbable.

On the other hand, with approval of aerial application, potentially serious marketing problems are possible with respect to cargo shipments of wheat, barley, canola and canola meal. Basically, approval of aerial application would result in an increase in the percent of total crop treated which, in turn, would mean less untreated crop available for dilution of residue levels in treated crop. The end result would be higher residue levels in cargo shipments. With the generally higher residue concentrations associated with aerial application, and the variability of levels that would be encountered in cargoes, occasional shipments could contain levels above limits deemed acceptable by some highly discriminating buyers. Approval of aerial application for lentils, peas and soybeans, however, is not likely to cause any serious marketing problems for these grains.

Carlot Shipments to the USA -- One of the main concerns with respect to marketing risks associated with pre-harvest use of glyphosate on wheat, barley and canola is the possible rejection of carlot shipments to the United States. This risk will likely persist until US tolerance limits come more in line with established international limits. In theory, as the rules stand, any carlot shipment in which glyphosate is detected could feasibly be rejected. This would also apply to carlot shipments of canola meal. In practice, however, for reasons stated previously, mass rejection of carlot shipments as a result of ground only use of glyphosate is considered highly unlikely. It is possible that occasional carlot shipments of these commodities could be rejected by US authorities, but the overall situation should be quite acceptable.

Given the higher residue levels and the higher frequencies of occurrence of residues in carlot shipments that are predicted for aerial application, approval of this use could result in a rash of rejected carlots. If this were to occur, it could constitute a major problem for the grain industry. Accordingly, prudence dictates that this use be deferred at least until the situation pertaining to US tolerance limits has been clarified.

<u>Baglot Shipments to Foreign Destinations</u> -- The only marketing concerns for baglot shipments of lentils, peas and soybeans centre around shipments to the United States and Japan. For reasons mentioned above, however, as far as ground only use of glyphosate is concerned, none of these concerns are expected to amount to any serious problems. We are not as confident, however, about the possibilities surrounding approval of aerial application. Accordingly, prudence dictates that this use be deferred at least until the situation pertaining to US tolerance limits has been clarified.

<u>Shipments to Canadian Destinations</u> -- Overall, ground only pre-harvest use of glyphosate on wheat, canola, lentils, peas and soybeans is not likely to cause any domestic marketing problems. Generally, commercial shipments should easily comply with the tolerance limits being considered by the Health Protection Branch of Health and Welfare Canada.

However, there is a domestic marketing problem that could possibly befall the barley industry as a result of registration of glyphosate. Domestic malt plants could refuse to accept malting barley treated with glyphosate. Regardless of the reasons for imposing such a standard and whether or not they have any solid basis, if the malting and brewing industries choose to go in this direction, the domestic marketability of treated malting barley could be severely affected. However, since the issues involved relate more to yet-to-be-determined industry quality control standards than to safety issues, the CGC does not regard this as sufficient grounds to preclude pre-harvest use of glyphosate for the entire barley industry. Instead, should the malting and brewing industries choose to impose a ban of this nature, it would be up to individual producers to decide whether or not it would be in their best interests to use glyphosate.

9. **TOXICOLOGY, OCCUPATIONAL EXPOSURE AND FOOD RESIDUES: HEALTH AND WELFARE CANADA INPUT**

9.1 Identification

Title: Glyphosate Herbicide (Roundup[R], Vision[R])

Directorate: Food and Environmental Health

Structure:

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        O              O
        V              V
    HOSQCSQCH2NHSQCH2S)QPSQOH
                       R
                      OH
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9.2 Background

Glyphosate, N-phosphonomethyl glycine, is a systemic, non-selective, post-emergent herbicide. The major international use patterns of the herbicide include pre-plant to crops; directed spray to control unwanted vegetation in tree and vine crops; silvicultural site preparations and conifer release; fallow and reduced tillage systems; general land management in non-crop situations and preharvest application to cereals and oilseeds.

The formulation Roundup[R] contains the isopropylamine salt of glyphosate (356 grams as glyphosate acid equivalent per liter of product) and is presently registered in Canada for control of annual and perennial weeds in non-crop and crop land as a pre-plant or post-harvest treatment, using ground application equipment; as a directed application to control weeds between crop rows and between fruit trees; and for spot treatment in crops and on industrial and publicly accessible properties using various types of equipment. There are currently no registered uses for glyphosate directly on any growing food crops because such uses would likely kill the crops. Residues of glyphosate on crops resulting from existing uses are covered by the general Regulation B.15.002.(1) of the Food and Drugs Regulations.

Monsanto Canada Inc. have now applied to Agriculture Canada for registration of the same formulation (Roundup[R]) for control of perennial grasses and crop desiccation on wheat, barley, rapeseed, mustard, soybean, flax, lentils, peas, beans and forage crops as a close-to-harvest (preharvest) treatment. This use will kill and desiccate the crop, aiding the harvesting of the grain or seed borne by these crops. It will also control perennial grasses such as quackgrass and Canada thistles and prevent regrowth of these weeds in the following season. In addition, Monsanto Canada has requested that Health and Welfare Canada establish Maximum Residue Limits to cover residues on imported commodities that may contain residues on glyphosate from countries in which these preharvest treatments are already registered.

A second formulation identical to Roundup[R], but registered under the trade name Vision[R], is used for brush and weed control in silviculture sites, using aerial and ground application equipment.

9.3 Evaluation

a) Product Chemistry

The technical material (glyphosate as an acid) has a purity of 98.0%. All major impurities have been identified and are related to the active material. The formulated product is produced by converting the glyphosate acid to its isopropylamine salt. All major metabolites have been identified and these individual impurities range from 0.2% to 1% of the technical material on a weight per weight basis. The formulation also contains water and a surfactant.

The presence of a contaminant (1,4-dioxane) in a surfactant used in the Roundup[R]/Vision[R] formulation has been identified by some public interest groups as a concern in forestry (aerial) applications. This chemical has been identified as a carcinogen and has been confused with dioxins. A separate Status Report will be prepared concerning the toxicology of 1,4-dioxane.

N-nitrosoglyphosate (NNG) has been identified as a micro-contaminant of the technical active ingredient (0.1 to 0.4 ppm[2]). The current level of this contaminant is below the present level of detection in the formulated product of 0.05 ppm. An evaluation of the available toxicology database for NNG has been included in this document.

b) Toxicology

i) Product Chemistry

The major toxicity studies used technical material containing 94%-99.7% purity. The formulation Roundup^R/Vision^R containing the isopropylamine salt of glyphosate is rapidly converted to the acid.

Aminomethylphosphonic acid (AMPA) is a metabolite found in soil treated with glyphosate. An evaluation of the available toxicology database for this metabolite has been included in this document.

ii) Acute Toxicity - Technical

Oral Toxicity

The technical material (given as a 25% aqueous solution - w/v) was classified practically non-toxic in a gavage study using five Wistar rats/sex/dose level. The LD_{50} was 5.6 (4.9-6.3, 95% confidence interval) g/kg bw. Gastro-intestinal changes in animals which died and pale liver and kidney in terminal sacrifice animals were noted. Reactions (piloerection and lethargy) persisted up to 7 days in animals which recovered.

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[2] Detection limit was 0.1 to 0.2 ppm.

In a valid IBT gavage study using 2 female rabbits/dose, administration resulted in ulceration and intestinal haemorrhages. The LD_{50} was 3.8 (2.836-5.092, 95% confidence interval) g/kg bw. The technical was practically non-toxic to rabbits by the oral route.

Dermal Toxicity

Two New Zealand White rabbits/sex/dose level were exposed to 5 g/kg bw as a 25% aqueous solution for 24 hours on abraded skin. Slight (2 rabbits) or well defined (2 rabbits) erythema was observed at 24 hours. No deaths occurred. Clear nasal discharge persisted for up to 6 days post-dosing in all rabbits.

Dermal Irritation

Six New Zealand White rabbits were exposed to 0.5 ml of 25% aqueous solution on abraded and intact sites. Slight erythema on one intact and one abraded site (different rabbits) was observed. The technical material was not deemed to be a skin irritant.

In a repeated insult patch test on human volunteers (various ages), a 1:45 dilution of technical glyphosate was applied to an upper arm skin site three times a week for a total of fifteen applications on the same site. No reactions characteristic of a primary irritant were noted.

Dermal Sensitization

In a delayed contact hypersensitivity study (Buehler) in Hartley guinea pigs, glyphosate did not demonstrate any potential to produce dermal sensitization.

In the repeated insult patch test on human volunteers described above, a challenge application was applied 2 weeks after the fifteenth sensitizing dose. There were no observed skin changes.

Eye Irritation

Glyphosate (0.1 ml of 25% aqueous solution) was instilled into one eye of each of 9 rabbits. Three of these eyes were washed with water, 20 seconds after treatment. The technical was observed to be minimally irritating to the eye (unwashed). Washing with water did not appear to be ameliorative, the response after washing was moderately irritating. Recovery in all cases occurred by day 7.

In an earlier study technical glyphosate applied as a finely ground powder followed by warm saline wash caused minimal irritation at one hour, recovery was complete by 72 hours.

iii) Acute Toxicity - Roundup^R Formulation Glyphosate, Isopropylamine Salt

Oral Toxicity

In a rat gavage study, the formulation was observed to be virtually non-toxic. The oral LD_{50} was determined to be 5.4 (4.6-6.2, 95% confidence interval) g/kg bw. Severity of gastrointestinal irritation increased with dose.

Dermal Toxicity

Two New Zealand White rabbits/sex/dose were exposed for 24 hours on abraded skin to 5 g/kg bw. At 24 hours, well defined erythema was observed. There were no deaths. The dermal LD_{50} was greater than 5 g/kg bw, the compound was non-toxic.

Inhalation Toxicity

Eleven groups of Sprague-Dawley (Crl:CD(SD)BR) rats, 5/sex/ dose level, were exposed to the formulation for 4 hours. LC_{50} values (analytical levels) were 3.05 (2.78-3.89) mg/L air for males, 3.33 mg/L air for females, and 3.28 (3.0 -4.1) mg/L air for combined sexes . Signs of toxicity were seen in all test groups. Body weight loss was noted in all groups for 2-3 days post-exposure, with recovery to normal weight gains by day 7.

Dermal Irritation

Six New Zealand White rabbits were exposed to the formulation on abraded and intact sites for 24 hours at 0.5 ml/site. Erythema and edema were noted at 24 hours and increased by 72 hours. Abraded skin reactions were slightly greater than those on intact skin. Recovery was variable (one rabbit was still affected on day 14). The compound was declared to be a moderate skin irritant.

Dermal Sensitization

In a delayed contact hypersensitivity study (Buehler) in Hartley guinea pigs, Roundup[R] did not demonstrate any potential to produce dermal sensitization.

Eye Irritation

The formulation (undiluted or diluted to end use concentration) applied to rabbit eyes was minimally irritating, with or without eye wash.

iv) Short Term Toxicity - Technical

Mouse - Oral

Fifteen CD-1 COBS mice/sex/dose were fed diets containing 0, 5000, 10,000 or 50,000 ppm glyphosate for 3 months. Histopathology in this pilot study was limited to 10 mice/sex at 0 and 50,000 ppm. Body weight gain was depressed at 50,000 ppm. No clinical chemistry, haematology or urinalysis were performed. The probable no observable effect level (NOEL) was 10,000 ppm (equal to 1900 mg/kg bw/day).

Rat - Oral

Fifteen Charles River rats/sex/dose level were fed diets containing 0, 200, 600 or 2000 ppm glyphosate for 13 weeks. No adverse effects were observed on body weight, haematology, clinical chemistry, organ weights (absolute and relative) or histopathology (based on 10/sex/dose level at 0 and 2000 ppm). The NOEL appears to be greater than 2000 ppm (equivalent to 100 mg/kg bw/day).

Dog - Oral

Four beagle dogs/sex/dose level were fed diets containing 0, 200, 600 or 2000 ppm glyphosate for 90 days. No adverse effects were seen on body weight gain, haematology, clinical chemistry, urinalysis, organ weights, gross examination or histopathology. The NOEL appears to be greater than 2000 ppm (equivalent to 50 mg/kg bw/day).

Six beagle dogs/sex were administered glyphosate by gelatin capsule at dose levels of 0, 20, 100 or 500 mg/kg bw/day for one year. No mortality occurred. Clinical signs of toxicity were comparable across all groups. Ophthalmology was unaffected by glyphosate. Body weight, food intake, haematology and urinalysis were unaffected. Tubular degeneration of the kidney, of questionable biological significance, was observed in all test groups. A conservative no observable adverse effect level (NOAEL) of 100 mg/kg bw/day was based on increased incidence of lymphoid nodules observed in epididymis at the top dose level.

Four beagle dogs/sex (aged about 6 months) were fed diets containing 0, 30, 100 or 300 ppm glyphosate for 2 years. This study was performed by IBT. It should be noted that although deemed to be valid there were unanswered questions relating to evidence of diet preparation and absence of detailed data on clinical chemistry, gross pathology and histopathology therefore, the study was considered inadequate.

Rabbit - Dermal

Five New Zealand White rabbits/sex were treated with 0, 100, 1000 or 5000 mg/kg bw/day on intact or abraded skin sites for 6 hours/day, 5 times weekly for 3 weeks. No adverse effects were reported with respect to body weight, body weight gain, haematology, clinical chemistry, food consumption nor absolute and relative organ weights. No compound related gross or histopathological changes were observed. Slight dermal irritation was noted at 5000 mg/kg bw/day only. The NOEL for systemic toxicity was determined to be in excess of 5000 mg/kg bw/day.

v) Short Term Toxicity - Roundup^{R} Formulation Glyphosate, Isopropylamine Salt

Rabbit - Dermal

Ten male New Zealand White rabbits were treated on abraded or non-abraded skin sites at dose levels of 0, 76 and 114 mg of Roundup^{R}/kg bw/day for 6 hours/day, 5 times weekly for 3 weeks. 50% of the animals were killed at 21 days and the remainder were observed for a further 28 days. Slight to moderate erythema and dermal thickening were noted in all treated groups during weeks 2 and 3, the severity being increased slightly in abraded groups. Complete recovery occurred by 4 weeks post-dosing. At 21 days only, the testicular weights in the 114 mg/kg bw/day group with intact skin were significantly increased. Histopathology of these testes was comparable to controls. The probable NOEL for systemic toxicity is in excess of 114 mg/kg bw/day.

Rat - Inhalation

Male and female Sprague Dawley rats were exposed to 0, 0.05, 0.16 or 0.36 mg/L for 6 hours per day, 5 days per week for 4 weeks. No signs of toxicity were observed during exposure. There were no mortalities or clinical signs observed during or after administration. Necropsy and histopathology findings indicated no treatment related differences between controls and treatment groups. The NOEL was determined to be greater than 0.36 mg/L in this study.

vi) Long Term Toxicity - Technical

Mouse - Oral

Fifty Charles River, CD-1 COBS mice/sex/dose level were fed diets containing 0, 1000, 5000 or 30,000 ppm glyphosate for 2 years. No toxic signs or effects on mortality, food and water consumption, organ weights or gross

pathology were observed. Body weight was reduced in both sexes at 30,000 ppm and leucocyte cell counts were reduced significantly in males at 12 months only. Histopathological examination indicated a slight increase in liver necrosis in males at 30,000 ppm. There was no evidence of tumour induction. A NOEL of 5000 ppm (equal to 714 mg/kg bw/day) was determined.

Rat - Oral

Fifty Sprague-Dawley CD Charles River rats/sex/dose level were fed glyphosate in the diet to yield intakes of 0, 3.0, 10.3 or 31.5 mg/kg bw/day for males and 0, 3.4, 11.2

or 34 mg/kg bw/day for females for 26 months. No adverse effects were observed which appeared to be of biological significance with respect to mortality, clinical signs, haematology, clinical chemistry, urinalysis, food and water intake, absolute or relative organ weights or histopathology. The incidence of interstitial cell testicular tumours was not dose related, and unlikely to be treatment related. An increased incidence of thyroid C-cell carcinomas was observed in females (2.1, 0, 4, and 12.8% in control, low, mid and high dose). Three independent consultant pathologists selected by the Health Protection Branch (HPB), two external and one from HPB, discounted the relationship between treatment and the occurrence of thyroid C-cell tumours.

A repeat two-year rat chronic/oncogenicity study, utilizing Sprague Dawley rats fed diets containing nominal levels of 0, 2000, 8000 or 20,000 ppm for 2 years was conducted to resolve the uncertainty of the tumorigenic potential of glyphosate. In this study, there was no indication of any tumorigenic activity resulting from glyphosate exposure, confirming the independent pathologists' advice that glyphosate was not oncogenic. A NOAEL of 8000 ppm (equal to 362 mg/kg bw/day) was determined for chronic toxicity, based on minimal changes related to stomach irritation in females at this dose level. At 20,000 ppm, female body weights and weight gains were reduced while decreased urinary pH and increased incidence of cataractogenic effects and testicular effects (typical of ageing rats) were noted in males, and an increased incidence of stomach irritation in both sexes was observed.

vii) Teratogenicity - Technical

Rat

Four groups of 25 mated Charles River COBS CD strain rats/dose level (0, 300, 1000 or 3500 mg/kg bw/day) were dosed by gavage on days 6-19 of gestation (day 0 - copulatory plug or sperm detection). Sacrifice was on day 20 of gestation. Six females at 3500 mg/kg bw/day died. Body weight of maternal animals was reduced at 3500 mg/kg bw/day. Pup weights were reduced at 3500 mg/kg bw/day. Also at 3500 mg/kg bw/day, absent kidneys and ureters were noted in 3 pups (2 litters), as was a slight increase in skeletal variants. The NOEL was determined to be 1000 mg/kg bw/day, based on evidence of terata (slight) and fetotoxicity at the maternally toxic doses of 3500 mg/kg bw/day.

Rabbit

Four groups of 16 artificially inseminated Dutch Belted rabbits were administered (by gavage) 0, 75, 175 or 350 mg/kg bw/day on days 7-27 of gestation. Mortality of parental females was 0, 1, 2 and 10, respectively. Clinical signs of toxicity and transient maternal body weight reduction were observed in dams at 175 and 350 mg/kg bw/day during the dosing period. Malformations observed in each of the treatment groups were not dose-related and did not exceed historical control values.

Increased incidence of skeletal variations were observed at the top dose level only. A NOEL of 75 mg/kg bw/day was based on maternal toxicity at 175 and 350 mg/kg bw/day and fetotoxicity at 350 mg/kg bw/day. Glyphosate did not demonstrate any teratological potential in this study.

viii) <u>Reproductive Toxicity - Technical</u>

A rat multigeneration study performed by IBT was deemed to be invalid, based on lack of diet preparation data, and substitution of animals during the first 10 weeks of the study.

Charles River Sprague-Dawley CD rats were fed dietary levels of glyphosate to yield intakes of 0, 3, 10, or 30 mg/kg bw/day for 3 generations, producing 2 litters/generation. No biologically significant effects were observed in parental animals with respect to mortality, clinical signs, body weight, organ/body weight or food consumption. Initial histopathology examination was limited to 0 and 30 mg/kg bw/day dose groups. Renal tubular dilation was increased in high-dose F3b pups, the toxicological significance of this finding is uncertain. Additional histopathology data at intermediate dose levels indicated a possible NOEL of 10 mg/kg bw/day.

In a repeat two-generation study (1 litter in the first generation and 2 litters in the second generation), Charles River SD CD rats were given glyphosate in diets at dose levels of 0, 2000, 10,000 and 30,000 ppm equivalent to 0, 100, 500 and 1500 mg/kg bw/day. A NOEL was set at 100 mg/kg bw/day based on clinical signs of toxicity, decreased adult and pup weight at 1500 mg/kg bw/day in both generations and reduced maternal body weight in F1 females and F2a pups at 500 mg/kg bw/day. In the absence of treatment related renal histopathology it would be appropriate to select the overall NOEL of 100 mg/kg bw/day for reproductive effects from this study rather than the previous study.

ix) Absorption, Distribution, Excretion and Metabolism - Technical

Oral - Single Dose

Glycine moiety labelled (14C) glyphosate was administered to 4 female and 8 male Wistar SPF rats by gavage as an aqueous solution at 6.7 mg/kg bw. In males 14% and 81% of the administered dose appeared in urine and faeces respectively within 48 hours. Carcass retention at 120 hours was 0.65%. Expired CO_2 accounted for 0.5% of the dose. In females, 35-40% of the dose appeared in urine by 48 hours, 1% in the carcass at 120 hours, and 0.7% as expired CO_2.

Seven male New Zealand White rabbits dosed orally with doses ranging from 5.7-8.8 mg/kg bw (depending on site of ^{14}C label) excreted 90% of the administered dose in 5 days. 80% appeared in faeces and 7-10% in urine. Less than 1% appeared as CO_2. Tissue residues were highest in gut (2.5%), muscle (0.01-0.8%) and liver (0.04-0.18%).

Intraperitoneal (i.p.) - Single Dose

Following i.p. administration of doses between 2.3 and 3.6 mg/kg bw, to 9 male rats, 74-78% was excreted in urine within 12 hours, 6-14% appeared in faeces and 0.8% as CO_2. Tissue retention at 120 hours was about 1%.

Dietary

Four groups of rats were fed 0 (12/sex), 1, 10 or 100 ppm (16/sex) glyphosate in the diet for 14 days, followed by a 10-day withdrawal period. Two rats/sex were sacrificed on days 2, 6, 10 or 14 of treatment and 1, 2, 6 and 10 days after withdrawal of exposure for tissue analysis. Equilibrium in tissues was attained by 10 days. Excretion equalled intake by 6 days.

Metabolite Identification

Following single oral or i.p. dose or multiple oral doses administration of glyphosate to rats, the major radioactive component excreted remains unchanged glyphosate.

Dermal Absorption

In an *in vivo* dermal absorption study in Rhesus monkeys only 16% of the applied dose was recovered which left a large proportion unaccounted for. It was not possible to use this study to estimate percent dermal absorption.

In a recent publication, Wester *et al*. (1991) reported on *in vivo* percutaneous absorption of Roundup[R] spiked with ^{14}C glyphosate administered to monkey abdomen. The study showed that glyphosate was poorly absorbed, approximately 5.5% and 3.7% (values corrected for 75% recovery) for the low and high dose (25 and 270 g/cm^2) respectively.

In an *in vitro* dermal absorption study, penetration of three glyphosate products (MON 0139, Roundup[R] and Roundup[R] spray solution) was measured in fresh human abdominal skin (unfrozen). The results showed that glyphosate was poorly absorbed. The total absorbed dose was 0.028, 0.063 and 0.152% for MON 0139, Roundup[R] and Roundup[R] spray solutions respectively. Data from the *in vitro* model for dermal absorption is not routinely used to calculate systemic dose as the model has not yet been validated.

Mutagenicity - Technical

In a dominant lethal assay male CD-1 mice were administered single oral doses of 0, 200, 800 or 2000 mg/kg bw. A positive control group received 240 mg/kg bw of Cytoxan, i.p. Each treated male was paired with 2 females weekly for 8 weeks. No evidence of mutagenic activity, as assessed by number of living embryos/litter, number of implantations/litter, early or late resorptions/litter, number of corpora lutea/female, pregnancy rate or post implantation losses were observed, except in positive controls (increase in post-implantation losses/litter).

No evidence of mutagenic activity was observed in three mammalian studies (CHO/HGPRT gene mutation assay, _in vivo_ bone marrow cytogenetics in Sprague-Dawley rats and a primary rat hepatocyte assay for unscheduled DNA synthesis (UDS) nor in three microbial studies (two reverse mutation assay in _Salmonella typhimurium_ and a rec-assay in _Bacillus subtilis_).

x) _Genotoxicity - Roundup[R] Formulation Glyphosate, Isopropylamine Salt_

In a published genotoxicity study, the formulation Roundup[R] was investigated for genotoxic potential (sister chromatid exchange) in a human lymphocyte cell line. (Vigusson, N.V. and E.R. Vyse, 1980) At doses ranging from 0.25 to 25 mg/ml there was evidence that Roundup[R] was a weak genotoxin.

xi) _Neurotoxicity - Technical_

Two groups of ten 9-month old hens were dosed twice a day, orally with glyphosate, for 3 consecutive days, this dosing regime being repeated starting on day 21 of the study. Sacrifice was on day 42. TOCP was used as a positive control. No clinical signs of toxicity or nerve tissue histopathological lesions were seen in glyphosate treated hens. TOCP induced expected changes.

xii) AMPA (CP 50435) - (soil metabolite)

Acute Toxicity

Oral Toxicity

Single doses of 40% solution administered to rats (strain unspecified) at 5010, 6310, 7940 or 10,000 mg/kg bw indicated an LD_{50} of 8,300 mg/kg bw.

Dermal Irritation

AMPA was found to be non-irritating when applied to intact skin sites on three rabbits (two males and one female) for twenty-four hours.

Eye Irritation

In a rabbit study, AMPA applied as a finely ground powder followed by warm saline wash caused minimal irritation at one hour, recovery was complete by 120 hours.

xiii) Short Term Toxicity

Rat - Oral

Four groups of 20 Charles River CD rats/sex/dose level were fed diets to yield 0, 400, 1200 or 4800 mg/kg bw/day for 12-13 weeks. Blood samples were obtained from fasted rats. Body weight gain was depressed in males at 4800 mg/kg bw/day. Haematology was unaffected. LDH (lactic dehydrogenase) showed a significant dose-related increase in males at 1200 and 4800 mg/kg bw/day. In females significantly increased LDH values were observed at all dose levels when compared to contemporary controls, but were within normal ranges at 400 and 1200 mg/kg bw/day when compared to historical values. Urinary pH was decreased in both sexes at 4800 mg/kg bw/day. Histopathology revealed dose-related increases in the incidence of mucosal hyperplasia of the bladder in both sexes at 1200 and 4800 g/kg bw/day and a low incidence of kidney pelvic epithelial hyperplasia at 4800 mg/kg bw/day.

Decreased absolute liver weights were observed in all treated males but relative liver weights were only decreased at 4800 mg/kg bw/day. The NOEL was estimated to be 400 mg/kg bw/day.

Absorption, Distribution, Excretion and Metabolism

In a gavage study, following a single oral dose (6.7 mg/kg bw) of radiolabelled AMPA, male rats excreted 94% of the compound unchanged within 120 hours, 74% of the dose via the fecal route and 20% via the urinary route. Less than 0.1% of the dose activity was excreted via exhaled air and less than 0.06% was found in the carcass.

xiv) NNG, Sodium Salt

Acute Toxicity

Oral Toxicity

Single doses of 20% solution administered to three Sprague-Dawley rats at 6, 320, 7960 or 10,020 mg/kg bw indicated an LD_{50} of 7,600 mg/kg bw.

xv) Short Term Toxicity

Mouse - Oral

Groups of 15 mice/sex/dose level (strain not specified) were intubated daily with 0, 50, 150 or 500 mg sodium NNG/kg bw/day for 90 days. In females, spleen weight was increased at 500 mg/kg bw/day. Histopathology at 500 mg/kg bw/day showed inflammatory cell infiltrates in livers, kidneys, lungs, salivary glands, and uteri, peribronchial lymphocytic accumulation and uterine endometrial fibroplasia. The NOEL was 150 mg/kg bw/day.

Rat - Oral

Five weanling Sprague-Dawley rats/sex/dose level were intubated with 0, 100, 300 or 1000 mg/kg bw/day for 14 days. No treatment-related effects were noted.

Groups of 25 rats/sex/dose level were intubated with 0, 200, 600 or 2000 mg sodium NNG/kg bw/day for 90 days. No treatment-related effects were observed on mortality, clinical signs, body weight gain, haematology, clinical chemistry, urinalysis, organ weights, gross pathology or histopathology. The NOEL was 2000 mg/kg bw/day.

Three groups of 30 Sprague Dawley rats/sex/dose level were intubated with 0 (vehicle control), 3000 or 6000 mg/kg bw for 91 days. Histopathology was limited to 0 and 6000 mg/kg bw/day groups except for liver, kidney and heart. There was a dose-related increase in mortality, (8, 11, 20 and 6, 9, 21 deaths in males and females at 0, 3000 and 6000 mg/kg bw/day, respectively), incidence of diarrhoea and blood around the nose and mouth. Food intake was reduced at both dose levels. Male body weight gain was reduced at 3000 and 6000 mg/kg bw/day. Haematology, clinical chemistry, urinalysis, gross, and histopathology did not show any significant biological changes. Increased relative testes weights were noted at 3000 and 6000 mg/kg bw/day, but since brain to body weight ratios and absolute body weights were reduced, the severe weight reduction may account for these observations. No NOEL was determined.

xvi) Long Term Toxicity

Hamster - Oral

Four groups of 70 Syrian Golden Hamsters/sex/dose level received 0, 3, 10 or 30 mg/kg bw/day for 390-392 days. Animals dying prior to 2 months were replaced and 5 animals/sex/dose level were added at 2 months. Mortality at 12 months was high in males, but was comparable between groups. An interim kill of 10 animals/sex/dose level was performed at 6 and 12 months. No biologically significant effects were reported with respect to toxic signs, ophthalmology, food intake, haematology or urinalysis. Fasting blood glucose was reduced in females at 17 months in the 30 mg/kg bw/day group. Relative kidney/body weights were increased in males at 10 mg/kg bw/day and in females at 30 mg/kg bw/day at 12 months. Similar but non-statistically significant increases were seen at 6 months and at termination. Histopathology (limited to 0 and 30 mg/kg bw/day groups at 6 and 12 months on 10 hamsters/sex/dose level) indicated an increased incidence of bilateral haemorrhage of adrenal glands in females (3/9 in controls versus 6/10), and increased splenic amyloidosis (2/10 in controls versus 8/10). Glomerular mesangial hyalinization (kidney) was also increased in females (4/10 in control versus 9/10). Absence of histopathology at low and mid dose levels precludes the estimate of a NOEL, however the compound was not found to be oncogenic at the top dose tested, 30 mg/kg bw/day.

xvii) Teratogenicity

Rabbit

This IBT study originally determined to be invalid was re-examined and deemed to be usable as "supplementary data". It was originally invalidated because no evidence of internal examination of pups was available. Relevant data are as follows: Three groups of 17 artificially inseminated New Zealand White rabbits were administered 0 (vehicle control), 10 or 30 mg/kg bw/day on days 6-18 of gestation by capsule. Three females at 30 mg/kg bw/day died, the original report indicating cause of death to be respiratory infection. The new data indicate toxicity of the test material may also be involved (food intake reduction). Incidence of resorptions was increased and 24-hour post natal survival was slightly decreased at 30 mg/kg bw/day.

Absorption, Distribution, Excretion and Metabolism

Single doses (1 mg/rat) and multiple doses (5.93 mg/rat/day for 5 days) resulted in rapid excretion within 24 hours (ca 90%). In males, urinary excretion accounted for approximately 80% of single dose administration, compared to 75% in females. Fecal elimination was 10% in females compared to 3% in males. In multiple administration, urinary excretion was 43-61% in males compared to 39-60% in females. Fecal elimination was 25-43% in males and 14-40% in females. Retained compound at 5 days post-dosing (0.02-0.2% of dose) was mainly unchanged NNG.

xviii) Mutagenicity

An Ames test using *Salmonella typhimurium* strains TA 1535, 1537, 1538, 98 and 100 exposed to dose levels of 0.2, 2, 20 or 100 :g/plate was negative.

xix) Toxicology Summary

Technical Glyphosate and Roundup^{R}/Vision^{R}

In acute studies, technical glyphosate and the Roundup^{R}/Vision^{R} formulation were found to be virtually non-toxic via the oral, dermal, intraperitoneal and inhalation routes of exposure. The technical was observed to be non-irritating to skin while the formulation was found to be a moderate skin irritant. The technical and the formulation were observed to be minimally irritating to the eyes.

Repeated short-term dietary administration of technical glyphosate at high dose levels resulted primarily in body weight reduction in mice, no effect on rats, and increased incidence lymphoid nodules of the epididymis in dogs. The dog was judged to be the most sensitive species tested; the NOAEL was 100 mg/kg bw/day in the 1-year dog dietary study.

In the short-term dermal studies in rabbits, the NOEL for technical glyphosate was observed to be in excess of 5000 mg/kg bw/day; for Roundup^{R} the NOAEL for systemic toxicity was observed to be in excess of 114 mg/kg bw/day (highest dose tested). Skin irritation was noted in all test groups but cleared up by termination of the study.

In a short-term inhalation study in rats the NOEL for Roundup^{R} was observed to be in excess of 0.36 mg/L of air, the highest dose tested.

The long-term mouse dietary study showed evidence of body weight reduction and transient leucocyte count reduction, there was no evidence of tumour induction. The NOEL was 714 mg/kg bw/day.

The repeat long-term rat dietary study showed no evidence of tumour induction at 20,000 ppm. The NOAEL was concluded to be 362 mg/kg bw/day (8000 ppm) for minimal gastric mucosal changes in females noted at this dose level. At 20,000 ppm, female weight gains were reduced while decreased urinary pH and increased incidence of cataractogenic and testicular effects (typical of ageing rats) were noted in males, and an increased incidence of stomach mucosal changes (due to irritation) was recorded in both sexes.

In rats, the NOELs for glyphosate were found to be 1000 mg/kg bw/day for maternal toxicity, teratology and fetotoxicity; the next highest dose was 3500 mg/kg bw/day. In rabbits, the NOEL was concluded to be 75 mg/kg bw/day based on maternal toxicity at the mid and high dose levels (175 and 350 mg/kg bw/day) and fetotoxicity at 350 mg/kg bw/day.

In a repeat reproduction study in rats, the NOEL was determined to be 100 mg/kg bw/day based on clinical signs of toxicity and decreased parental and pup body weight at the next highest dose (500 mg/kg bw/day). There was no evidence of adverse effects on reproductive performance at the highest dose tested, 1500 mg/kg bw/day. Glyphosate was negative in a dominant lethal assay at 2000 mg/kg bw/day, the highest dose tested.

Glyphosate was not observed to have any mutagenic potential in the battery of mutagenicity tests conducted. Roundup® was found to be a weak genotoxin in a single assay for sister chromatid exchange.

<u>AMPA and NNG</u>

AMPA and NNG were not acutely toxic by the oral route, the only route of administration tested

For short-term NNG toxicity, the mouse was found to be the most sensitive species tested; a NOEL of 150 mg/kg bw/day was based on spleen weight change and histopathology findings. For AMPA, a NOEL was estimated to be 400 mg/kg bw/day.

A NOEL in a hamster long-term study could not be established for NNG due to study limitations; the compound was not found to be oncogenic at the top dose tested, 30 mg/kg bw/day.

NNG was not found to be mutagenic in a single Ames test using S. typhimurium.

The data bases for the soil metabolite, AMPA and the contaminant NNG are incomplete but there is sufficient evidence that following acute or short-term administration, these compounds are not more toxic than the glyphosate acid. NNG contamination in the product Roundup^R/Vision^R is not detectable.

9.4 Food Exposure

a) Acceptable Daily Intake (ADI)

An ADI of 0.75 mg/kg bw/day has been estimated based on the lowest NOEL of 75 mg/kg bw/day for maternal toxicity in a rabbit teratology study and use of a 100 fold safety factor. In this study, glyphosate did not demonstrate any teratogenic potential.

b) Food Residue Exposure

i) Label

For quackgrass control and crop desiccation. Apply Roundup^R prior to harvest of crops in a single application at a rate equivalent to 0.89 kg glyphosate acid equivalent per hectare at the time when the moisture content of grain is less than or equal to 30% (14 days before harvest).

c) Plant Metabolism

Glyphosate plant metabolism has been extensively studied in various crops including soybean, wheat, barley, peas, forage crops and several vegetables and fruit trees. When glyphosate was applied foliarly to plants at various growth stages, including forage crops at the time 7-14 days before normal harvest, little metabolism of the compound was found in treated plants and the parent compound was identified as the major, if not the only, component in terminal residues.

AMPA was identified as a soil metabolite of glyphosate formed as a result of microbial action. Under field conditions, AMPA in soil may be taken up by plants at very low levels. Residue data indicate that about 1-2% of total glyphosate residues found in crops from the proposed preharvest use may be attributed to AMPA. However, when multiple applications were applied, such as the proposed use on soybeans in the U.S., up to 40% of the total terminal residues in soybean grain were identified as AMPA. These high levels of AMPA residues may occur as a result of the following conditions:

i) accumulation in the soil and translocation into crop plants;

ii) microbial action on the leaf surface prior to absorption in the plants;

iii) as a result of plant metabolism.

d) Analytical Methodology

Analytical methods capable of determining the residues of the parent compound and its metabolite AMPA in crops, processed products (such as flour, beer and oil etc.), animal products, water and soil are available.

e) Residues

i) Crop Residues

Residue data generated using these analytical methods have shown that when crops are treated in accordance with the proposed label directions (single application at the rate of 0.89 kg acid equivalent/ha and the time of 7 to 14 days before harvest) the following maximum residue limits (MRL) may be required:

Wheat[a]	5 ppm
Barley	10 ppm
Wheat and barley milling fractions, excluding flour	15 ppm
Soybeans	6 ppm
Soybean oil	<0.1 ppm[b]
Peas	5 ppm
Lentils	4 ppm
Rapeseed (canola)	---[c]
Rapeseed (canola) oil	<0.1 ppm[d]
Flax[e]	1.0 ppm

<u>Note</u>: Residues such as those noted above are not considered to pose a health hazard to consumers.

[a] Including flour.
[b] This level will not be listed but may be covered by the proposed 6 ppm MRL on soybeans.
[c] No MRL for rapeseed needed because the whole seed is not consumed as such in significant quantities as a food; residues up to 5 ppm in whole seed may result from the proposed use.
[d] This level will be covered under general regulation B.15.002(1).
[e] Including flax oil.

Residue data submitted for beans and mustard are inadequate to support the proposed use.

No data were provided to support the multiple use of glyphosate on a crop in one crop year, i.e. preplant plus preharvest, etc.

Based on the residue data available, low levels of AMPA (up to 1%-2% of the terminal glyphosate residues) were occasionally detected in treated crops. These AMPA residues should not be of concern because of the comments in the toxicology section which indicate that AMPA is not more toxic than the glyphosate acid. There is a possibility that residues of AMPA may exceed 0.1 ppm in treated crops and therefore the MRLs established for glyphosate should include residues of the metabolite AMPA.

ii) Animal Residues

Residues of 5 - 15 ppm in cereal and oil seed grain, grain fractions and meal may result from the proposed uses. Feeding of these treated products to livestock is not expected to cause significant residues (<0.05 ppm) in meat, milk or fat of meat.

Proposed uses on forage crops however appear to result in residues up to 50 ppm which may cause significant residue levels in livestock kidneys. Although MRLs may be needed to cover residues in meat byproducts (kidney) from the use of glyphosate on forage crops, insufficient Canadian residue data were provided to evaluate this proposed use, and therefore the proposed use on forage crops can not be evaluated at this time.

f) Dietary Risk Assessment

It is estimated that the maximum theoretical daily intake (TDI) of residues from all presently registered uses (which result in residues of less than 0.1 ppm), plus proposed preharvest uses, assuming maximum residue levels at all times, would not exceed 0.0224 mg/kg bw/day including the intake from beer consumed by total adult population; not exceed 0.0232 mg/kg bw/day including the intake from (541 g/capita/day) beer users only. These calculated TDI's are about 3.0% of the estimated ADI of 0.75 mg/kg bw/day.

g) Drinking Water Exposure and Risk Assessment

Although analytical methodology exists for the determination of glyphosate in water down to part per billion levels, an acceptable routine quantitative technique is not available and therefore no monitoring studies have been carried out in Canada on drinking water supplies. Since glyphosate is strongly adsorbed to soils, it is not thought to have much potential for leaching into groundwater supplies. It has been detected after forestry applications in which spraying took place near or over water. This could lead to contamination of downstream drinking water supplies, as it is moderately persistent in water.

Intake of glyphosate residues from drinking water is expected to be negligible in comparison to the ADI, but quantitative estimation of theoretical daily intake from this source is not possible at this time due to lack of data. The proposed new use of glyphosate is not expected to increase risks due to exposure from drinking water.

9.5 Occupational Exposure and Risk Assessment

a) Exposure Assessment

Groundboom equipment application on wheat, barley, canola, field beans, forage legumes and grasses, peas and lentils:

> The potential for worker exposure for the requested uses (as noted above) is not likely to be greater than that of currently registered uses since only a change in timing of application is involved. Furthermore, the rate of application is equal to or lower than current label rates.

To address occupational exposure for mixer/loaders and applicators using groundboom equipment on the aforementioned crops, an exposure study was previously submitted by the registrant. Although the study was reviewed and accepted, it is old and does not meet present-day standards with respect to study design and is limited by an inadequate number of replicates; a short, atypical work day and poor field recovery data.

Aerial application on wheat, barley, canola and lentils:

> Although there is currently no submission for the aerial application of Roundup^{R}, an attempt was made to assess the occupational

exposure for aerial use of Roundup[R] on the aforementioned crops.

In a surrogate study (USDA Forestry Service 1988 and references cited within) submitted by the registrant, exposure studies done with 2,4-D by various researchers were cited and the absorbed dose for mixer/loaders during aerial operation was estimated. The usefulness of these studies to estimate exposure to mixer/loaders using Roundup[R] under Canadian use scenarios is limited for the following reasons:

i) in most of the studies, biological monitoring was undertaken to estimate dose. These data cannot be used to estimate dose of glyphosate as the pharmacokinetics of the two products in humans have not been demonstrated to be similar;

ii) in studies where dermal deposition was monitored, inadequate methods were used;

iii) exposure for a typical workday was not monitored.

In a second study (Centre de Toxicologie du Quebec 1988), biological monitoring of Canadian forestry workers handling glyphosate was reported. This study also cannot be used to estimate an internal dose of glyphosate following occupational exposure since urine collection was not adequate for this purpose.

Owing to the above limitations, exposure could not be estimated for individuals using Roundup[R] for aerial application.

b) Risk Assessment

The risk associated with occupational exposure is not expected to be increased from that of currently existing uses of Roundup[R] as only the timing of application has been changed.

REFERENCES

Centre de Toxicologie du Quebec (1988). Étude de l'exposition professionnelle des travailleurs forestiers éxposes au glyphosate.

EPA Summaries - Guidance for the Reregistration of Pesticide Products Containing Glyphosate as the Active Ingredient. June 1986.

United States Department of Agriculture (1988). Managing Competing and Unwanted Vegetation. Final Environmental Impact Statement, Appendices D and H.

Vigusson, N.V. and E.R. Vyse (1980). Mutation Research 79 (1), 53-57.

Wester, R.C. et al. (1991). Glyphosate Skin Binding, Absorption, Residual Tissue Distribution and Skin Decontamination. Fundamental and Applied Toxicology 16, 725-732.

10. **ENVIRONMENTAL ASPECTS: ENVIRONMENT CANADA INPUT**

10.1 Summary

Environment Canada's review of glyphosate, is with reference to the proposed preharvest use of Roundup[R], by aerial and ground applications.

Glyphosate is not susceptible to chemical hydrolysis or to phototransformation and is not likely to volatilize. Transformation of the herbicide in terrestrial or aquatic systems is mainly through biotransformation. Laboratory studies conducted at 25°C indicate that there is rapid transformation of glyphosate in aerobic soil or aerobic aquatic systems but that glyphosate is persistent in anaerobic systems. Field data on dissipation in soil from agricultural areas in Canada are currently unavailable and are required. U.S. field data indicate that glyphosate dissipates rapidly in regions with warm climates but less so in areas with cool climates. Despite high solubility in water, glyphosate has strong adsorption to soils and is thus not mobile. U.S. field data indicate that leaching in soils is minimal.

Glyphosate is not expected to pose an acute and chronic hazard to birds and mammals. It is relatively nontoxic to soil microorganisms, earthworms, bees and ***Daphnia magna*** and at the proposed application rate the impact would be limited. The major transformation product AMPA is practically nontoxic to ***Daphnia magna***.

In regard to the preharvest use of glyphosate for weed control and for crop desiccation, it is necessary to obtain Canadian field information on the fate of glyphosate and AMPA in soil when applied according to the proposed use directions. This is important as U.S. field data have revealed that dissipation of glyphosate is slow in cool climates. The information is relevant for both ground and aerial applications of the herbicide.

As glyphosate is a nonselective herbicide, there is concern about the potential impact on nontarget terrestrial and aquatic vegetation from spray drift from aerial and ground applications of Roundup[R]. However, Monsanto Canada has recently indicated that the proposed preharvest use of glyphosate will be by ground application

only and that aerial application has been deleted from the proposed preharvest use pattern. Nevertheless more information on the effect of low doses of Roundup[R] is needed in order to assess thoroughly the impacts (damage and recovery to non-target plants) of this herbicide on wildlife habitats in the vicinity of sprayed fields. The area to be sprayed for weed control and crop desiccation is potentially very extensive since it involves wheat, barley, canola, flax, lentils, peas, soybeans, forages (grass and broad-leaved species).

10.2 Environmental Chemistry and Fate

a) Physicochemical Characteristics

i) Water Solubility:

Solubility of glyphosate (acid) in water was high (15700 mg/L (1.57%) at 25°C. The isopropylamine salt of glyphosate is much more soluble in water than glyphosate acid.

ii) Vapour Pressure:

The vapour pressure of glyphosate determined by the gas saturation method was negligible (<1.0 x 10^{-5} Pa (<7.5 x 10^{-8} mm Hg) at 25°C) and indicated that the herbicide would be non-volatile. Henry's Law Constant (<1.669 x 10^{-12} atm. m^3. mol^{-1}.) showed that in view of the low vapour pressure and high water solubility, glyphosate is not likely to volatilize from water or moist surfaces.

iii) Octanol-Water Partition Coefficient:

Octanol-water partition coefficient (K_{ow}) of glyphosate was reported to be low (0.0006 and 0.0017) and indicates limited potential for bioconcentration.

iv) Dissociation Constant:

The pKa values were determined to be <2, 2.6, 5.6 and 10.6. Glyphosate is amphoteric (capable of reacting chemically either as an acid or as a base) and exists predominantly in zwitterionic form (dipolar ion), and so will behave like an ionic salt.

b) Transformation

i) Hydrolysis:

Chemical hydrolysis is not expected to be a major mode of degradation of glyphosate in the environment as laboratory data indicated that glyphosate was stable in sterile, buffered solutions of pH 3, 6 and 9 at temperatures of 5 and 35°C, in the dark for 32 days.

ii) Phototransformation:

Transformation of [^{14}C]-labelled glyphosate on sandy loam soil when exposed to natural sunlight for 31 days, was insignificant. Analysis of soil samples showed that half-life values (by extrapolation) were 90.2 and 96.3 days for light irradiated and dark control samples, respectively.

Results of a study with aqueous solutions indicated that phototransformation of glyphosate in water by natural sunlight was not a significant process. When sterile aqueous solutions of [^{14}C]-glyphosate were exposed to natural sunlight for up to 31 days, half-life by extrapolation was calculated to be 413 and 555 days for light irradiated and dark control samples, respectively. The stability of glyphosate to sunlight is as expected as absorption spectrum data indicated that absorption of U.V. radiation by glyphosate was at a wavelength less than the relevant energy spectrum of natural sunlight (>290 nm).

iii) Biotransformation:

Results from a laboratory aerobic soil study conducted at 25°C showed that glyphosate in sandy loam and silt loam soils was non-persistent as DT50 (50% decline time) was 2 days. Other laboratory aerobic soil studies (conducted at 30°C, 32°C and at an unspecified room temperature) showed that glyphosate was non-persistent in silt loam (DT50 1 week) and moderately persistent in silty clay loam (DT50 3.5 to 5 weeks). Transformation of glyphosate was mainly through microbial action and resulted in the major transformation products aminomethylphosphonic acid (AMPA) and carbon dioxide.

In a laboratory aerobic aquatic (water/sediment) system at 25°C, glyphosate was not persistent (DT50 14.4 days). Most of the applied glyphosate had partitioned from water into sediment. The transformation route of glyphosate was similar to that observed in aerobic soil.

Results from a laboratory anaerobic aquatic (water/sediment) study at 25°C, indicated that glyphosate was persistent (DT50 208 days). By the end of the test (365 days), the parent compound accounted for 20% of the applied amount and demonstrated that rate of transformation of glyphosate under anaerobic conditions was slow. Most of applied glyphosate partitioned from water into sediment.

c) Mobility (Laboratory Data)

i) Adsorption/desorption:

Laboratory studies on soil adsorption/desorption of glyphosate showed that adsorption of glyphosate to soils was strong and that desorption from soils was minimal. Values of K_{oc} were high (2660 - 12930) in the soils tested and indicated low mobility of glyphosate in soils and consequently a low potential to leach.

ii) Soil Thin Layer Chromatography:

Laboratory soil thin layer chromatography studies have indicated that the leaching potential of glyphosate is low. According to the results, glyphosate in the soils tested (sandy loam, silt loam and silty clay loam) would be classified as immobile (Helling's mobility class 2).

iii) Soil Column Leaching Study:

Results from soil column leaching studies with soils treated with radiolabelled glyphosate and aged for a month, showed that leaching of the major transformation product AMPA was minimal. AMPA in leachate was <1% of applied radioactivity.

d) Field Dissipation

i) Field Soil Dissipation Studies:

Data from Canadian field soil dissipation studies conducted in major areas of proposed use were not available for review. The applicant has indicated that it will initiate these studies in 1991 in Alberta, Manitoba and Ontario.

Data from field soil dissipation studies conducted in the United States indicated that glyphosate (Roundup[R]) at 2.24, 4.48 and 8.97 kg a.i./ha, was non-persistent in Texas and North Carolina (DT50 2 to 16 days) but persistent in Minnesota (DT50 122 to 174 days). When glyphosate was applied late in the season (September/October) as at the Minnesota site and at another site in Colorado, dissipation of the herbicide was slow (DT90 210 to 300 days) and residues of glyphosate were carried over to the next season. The soil types at the different locations included sandy loam, sandy clay loam, silt loam and loam.

Results from the U.S. field studies also indicated that when Roundup^R was applied at 2.24 and 4.48 kg a.i./ha, in most cases residues of the main transformation product AMPA declined to non-detectable levels (<0.05 mg/kg) within one year of treatment.

Buildup of residues of glyphosate or AMPA in soil was minimal following multiple applications over several years, according to monitoring studies in orchards and vineyards in three U.S. states next to the Canadian border. Results from other U.S. field studies that involved four applications of Roundup^R per year, also indicated that accumulation of glyphosate was limited.

Analysis of soil cores in the U.S. field studies indicated that glyphosate and AMPA had negligible leaching potential in the soils tested. In soil cores 0 - 15 and 15 - 30 cm deep, residues of glyphosate and AMPA remained mainly in the top 0 - 15 cm soil profile (detection limits 0.05 mg/kg for both compounds).

Results from field soil run-off studies indicated that rainfall events after 24 hours of treatment, would probably not cause any appreciable movement of solubilised glyphosate in runoff water, especially at the proposed application rate. Glyphosate at a relatively high application rate, e.g. 8.97 kg a.i./ha, can be moved into runoff water, if there is rain within 24 hours of treatment.

10.3 Environmental Toxicology

a) Wild Birds

Wild birds are most likely to be exposed to glyphosate by direct overspray (birds foraging in cropland) or spray drift, or by consumption of sprayed vegetation or consumption of contaminated prey. The area to be sprayed for weed control and crop dessication in August is potentially very extensive since it involves wheat, barley, canola, flax, lentils, peas, soybeans, forages (grass and broad-leaved species).

The application of Roundup[R] at recommended label rates is not expected to pose an acute risk to birds ingesting glyphosate residues. The quail acute LD50 of technical glyphosate is greater than 3851 mg/kg and no reproductive effects were seen either in mallards or quails at dietary concentrations of 1,000 ppm. Surface exposure to chicken eggs did not cause any adverse effect.

b) Wild Mammals

Wild mammals could be exposed to glyphosate through direct overspray or by ingesting plants in sprayed fields, adjacent fencerows and wetlands or woodlots that have been contaminated by spray drift before the plants exposed to glyphosate

showed any visible effects. Some mammals could be exposed by ingestion of invertebrates or small herbivores. However since glyphosate does not bioaccumulate toxicity is not likely to be enhanced through the food web.

Glyphosate is practically non-toxic to mammals. The acute oral LD50 for glyphosate in rats is >5000 mg-ai/kg body weight. The acute oral LD50 in rats for the primary metabolite, aminimethylphosphonic (AMPA) acid is in the same order. Mice were fed with 50,000 ppm of glyphosate in their diet for 90 days without suffering any serious health effects.

c) Amphibians and Reptiles

No data were available to evaluate the risk to amphibians and reptiles from the use of glyphosate. These organisms could be exposed by direct dermal exposure from spray drift or by ingestion of contaminated invertebrates.

d) Soil Microbial Systems

Laboratory studies have indicated that glyphosate has limited impact on soil microorganisms, based on observations of soil respiration and soil nitrification.

e) Terrestrial Invertebrates

Results from contact and oral toxicity tests indicated that glyphosate (technical and formulated) is relatively nontoxic to bees (LD_{50} >100 ug a.i./bee). A laboratory study in which earthworms (*Allolobophora caliginosa*) were exposed to glyphosate at concentrations of up to 100 mg/kg in a New Zealand soil, showed no mortality or any significant adverse effect on the growth rate of the earthworms.

f) Aquatic Invertebrates

Data on the acute toxicity of technical glyphosate to *Daphnia magna* indicated that technical glyphosate was practically nontoxic (48-h LC_{50} 780 mg/L). Chronic toxicity of technical glyphosate was also low (no observed effect level 50 mg/L), as determined in a 21-day chronic toxicity study, based on survival, growth and reproduction of *Daphnia magna*. Tests showed that Roundup[R] formulation had a higher level of acute toxicity than technical glyphosate (48-h LC_{50} 5.3 mg of product/L) with a NOEL close to 1.9 mg product/L. At the proposed application rate of 0.89 kg a.e./ha, residues of glyphosate that may result from drift, are not expected to be a major hazard to *Daphnia*. Data provided by the applicant on the acute toxicity of AMPA to *Daphnia magna* indicated that it was practically nontoxic. The 48-h LC_{50} was 690 mg/L and the 48-h no observed effect concentration was 320 mg/L.

g) Wildlife Habitat Considerations

Wildlife living in the vicinity of cultivated fields could be affected by a shortage of food invertebrates due to a reduction of macrophytes on which these organisms subsist, or reduction of cover through damage and destruction of plants.

Crops to be included in the new label extension will cover a total area of 30 million hectares. Wheat, barley, canola, lentils and flax are extensively grown in the prairie provinces where most wildlife habitats (e.g. potholes) and croplands coexist in close proximity. There is also some concern about damage to hedgerows, shelterbelts, woodlots, and other wetlands in Ontario where wheat, soybeans and forage crops are grown. Southwestern Ontario is also an area inhabited by several endangered and threatened species.

This new use of glyphosate for weed control prior to harvest may potentially be significant, especially in the wetter areas of Southwestern Ontario and Northern prairies; in Canada the growing season is short and frequently farmers may not have enough time in the spring to apply a herbicide that control large perennials such as thistles and quackgrass without subsequently affecting the crop. After harvest in the fall the weeds often are too small to effectively be controlled before winter comes. The property of glyphosate as a desiccant at a low dose is an added advantage that can only increase the probability of it being widely selected by farmers.

Glyphosate is a non-selective herbicide, effective in annuals as well as on deep rooted perennials such as thistle, quackgrass, cattails, etc. From the literature, it seems to be toxic to a large number of plants including 76 of the 78 world wide noxious weeds (Carlisle and Trevors, Water, air and Soil Pollution, 39).

The indirect impact to wildlife is a major concern with glyphosate, because of its potential effects on habitats and food sources through overspray and drift. Drift to non-target habitats is an issue related to aerial as well as to ground applications. With ground equipment alone it is estimated that drift deposition is 1-10% in the prairies. In the case of glyphosate application with high clearance ground equipment, boom height will be at the upper end or even higher than usually recommended; even with a buffer zone around wetlands, bodies of water and terrestrial habitats, drift level is expected to remain high.

In the light of the above issue, it is believed essential to identify the potential effects of low doses of glyphosate on non-target plants. The registrant has provided credible data on dose response curves for 4 terrestrial species from 2 families (study PCP # 13644). Alfalfa, oats and soybeans showed practically no effect at 10% maximum label rate (visual rating), while a moderate effect was detected on sorghum with some recovery at day 42. Another table was presented including 17 species from 5 families; however given that no documentation on methodology, growing conditions, location of the study, time and mode of application were provided, we cannot assess its validity.

Studies were provided on the effect of glyphosate on 4 algal species: *Selenastrum capricornutum, Navicula pelliculosa, Skeletonema costatum, Anabaena flos-aquae*. EC50s range from 0.64 to 24.9 mg/L. The estimated environmental concentration in a 15 cm column of water at the expected dose of 890 g/L is 0.59 mg/L; risk factors are generally low between 0.02 to 0.13. Only the marine diatom *Navicula pelliculosa* exhibits a higher risk factor reaching 0.92. From these studies, the hazard posed by glyphosate to algae is considered to be low.

A growth inhibition study was provided with *Lemna gibba*, testing the toxicity of glyphosate dissolved in water. The 14-day EC50 is 25.5 mg/L. With an estimated environmental concentration of 0.59 mg/L, the risk factor is low at 0.02 (.59/25.5). However, Lockhart *et al* (Hydrobiologia, vol. 188-189, 1989) demonstrated that when *Lemna minor* was exposed to glyphosate sprayed on the fronds, the toxicity was greatly enhanced as opposed to plant response when exposed to glyphosate dissolved in water; at 800 g-ai/ha sprayed on *Lemna*, growth was essentially zero. This may be due to the fact that the mode of entry of this herbicide into the plants is by contact with the leaves, and that glyphosate has little tendency to partition from water to plants as would be the case with a more hydrophobic compound. Clearly the study presented by the registrant is not a worst-case scenario, nor is it representative of fields situation where *Lemna* is more likely to be affected by drift or overspray. Lockhart *et al* (1989) cogently argue that spray deposit may pose a risk to emergent aquatic vegetation, especially since the herbicide deposited on the plants is not likely to be washed off as might be the case of floating leaves.

Because of the non-selectiveness and effectiveness of glyphosate, its area and potential extensiveness of use, it is believed that more information should be sought on the effect of low doses of glyphosate on important plant species that constitute wildlife habitats in the prairies and in Ontario.

Small plot studies or a field study should be provided which examine the impact of Roundup^R in these areas with emphasis on low rates, effects on plant communities (species richness and cover), the spectrum of activity observed and recovery.

Although glyphosate has been registered for agricultural use since 1976 and for forestry use since 1984, the above major new use will greatly extend the area of glyphosate application; in the light of what we now know on the ecology of the prairies and other wildlife habitats, it is considered crucial to document the indirect effect of glyphosate on wildlife habitats, in order to enable provision of appropriate mitigation measures for protection of wildlife.

11. EFFECTS ON FISH, FISH HABITAT AND FISHERY RESOURCES: **DEPARTMENT OF FISHERIES AND OCEANS INPUT**

11.1 Effects on Fish

Technical glyphosate is slightly to practically non-toxic to fish with LC_{50}s from 22-211 mg glyphosate/L. The formulated product, Roundup^R, however, is more toxic than technical glyphosate with LC_{50}s for fish in the range of 2.3-42.0 mg Roundup^R/L (see Tables below). Studies have shown that the toxicity of Roundup^R to fish is attributable to the surfactant, MON 0818, a polyethoxylated tallow amine, which comprises .15% (by weight) of the Roundup^R formulation. LC_{50}s of MON 0818 to fish range from 1.0-13 mg MON 0818/L. Based on 96-h LC_{50}

studies with Roundup^R, Monsanto reported no observed effect levels (NOEL) for rainbow trout of 6.4 mg/L and for bluegill sunfish a value of 2.2 mg/L.

	Acute toxicity 96-h LC_{50} (mg/L)		
	glyphosate	Roundup^R	MON 0818
rainbow trout	140	8.3	2.0
fathead minnows	97	2.3	1.0
channel catfish	130	13.0	13.0
bluegill sunfish	140	5.0	3.0

Folmar et al. 1979

	Acute toxicity 96-h LC_{50} (mg/L)	
	Roundup^R	MON 0818
sockeye fry	28.8	2.6
rainbow trout fry	25.5	3.2
coho fry	42.0	3.5

Servizi et al. 1987

	Acute toxicity 96-h LC_{50} (mg/L)		
	glyphosate	Roundup^R	MON 0818
Creek water (soft)			
coho	36	27	3.2
chinook	30	27	2.8
rainbow	22	15	2.5
Lake water (hard)			
coho	174	13	1.8
chinook	211	17	1.7
rainbow	197	14	1.7

Wan et al. 1989

Young rainbow trout fingerlings (1.0 g) and channel catfish swim-up fry were the most sensitive life stages of those species exposed to Roundup[R] by Folmar et al. (1979). The authors reported 96-h LC_{50}s of 1.3 and 3.3 mg Roundup[R]/L for rainbow trout fingerlings and channel catfish swim-up fry, respectively.

The results of Wan et al. (1989) indicated that the characteristics of the water used in the toxicity studies affected the acute toxicity of the various compounds to salmonids. Glyphosate was more toxic to salmonids in soft water, whereas MON 0818 and Roundup[R] were more toxic in hard water.

Fathead minnows were not affected by chronic (255 d) exposure to glyphosate at measured concentrations of up to 25.7 mg/L (Monsanto).

No sublethal physiological effects were observed in coho salmon exposed to Roundup[R] in fresh water at 0.029 to 2.78 mg glyphosate/L for 10 days prior to seawater challenge exposure (Mitchell et al. 1987). No abnormalities were observed in the fecundity and gonadal development of rainbow trout exposed for 12 h in artificial streams to either the isopropylamine salt of glyphosate (IPA) or Roundup[R] at nominal concentrations up to 2.0 mg/L (Folmar et al. 1979). In avoidance reaction studies, Folmar (1976) reported that rainbow trout did not avoid water containing IPA at nominal concentrations of up to 10 mg/L. Hildebrand et al. (1982) indicated that a concentration of Roundup[R] of .40 mg/L was required before rainbow trout would avoid the treated water. No avoidance was observed at 30 mg Roundup[R]/L.

Monsanto reported bioconcentration factors of <1 for rainbow trout, largemouth bass, channel catfish, and carp exposed to 10 mg glyphosate/L for 14 days. Following 35 days depuration the glyphosate residues in all species had decreased to #0.07 mg glyphosate/kg (detection limit = 0.05 mg/kg). No residues of aminomethylphosphonic acid (AMPA), a transformation product of glyphosate, were detected in the tissue (detection limit = 0.05 mg/kg). The heads and viscera of the fish contained higher glyphosate residues than the tissue. The highest residue detected was observed in carp (heads and viscera) at 3.96 mg glyphosate/kg, but by 35 d depuration the level had decreased to 0.05 mg/kg. Studies on channel catfish have shown that glyphosate is not readily metabolized by fish.

11.2 Effects on Fish Habitat

a) Aquatic Invertebrates

As observed with fish, aquatic invertebrates are more sensitive to Roundup[R] and MON 0818 than to glyphosate alone. For midge larvae (Chironomus plumosus), Folmar et al. (1979) reported a 48-h EC_{50} (immobilization) of 13 mg MON 0818/L (nominal concentration) compared to 18 mg/L for Roundup[R] and 55 mg/L when exposed to technical glyphosate. Similarily, Daphnia pulex has a 96-h LC_{50} of 25.5 mg/L when exposed to Roundup[R], but the value for MON 0818 is 2.0 mg/L (Servizi et al. 1987). For Daphnia magna exposed to Roundup[R] the 48-h EC_{50} ranges from 3.0 - 5.3 mg/L (Folmar et al. 1979 and Monsanto), whereas the 48-h LC_{50} for D. magna exposed to technical glyphosate is 780 mg/L (Monsanto). Monsanto reported a NOEL for D. magna of <1.9 mg/L for Roundup[R] and 50 mg/L for technical glyphosate.

Marine invertebrates were not very sensitive to technical glyphosate. Ninety-six hour LC_{50}s for grass shrimp and fiddler crabs of 281 and 934 mg glyphosate/L (nominal) were reported in studies submitted by Monsanto, as were NOELs of 210 and 650 mg/L, respectively. Atlantic oyster were more sensitive with a NOEL of 10 mg/L (nominal concentration) in reports submitted by Monsanto.

b) Algae

Algae demonstrate a wide range of susceptibility to Roundup[R]. Some cyanophytes were considerably more sensitive to glyphosate than green algae. Glyphosate inhibited growth of cultures of the cyanobacteria Aphanocapsa (strain 6308), Anabaena variabilis and Nostoc (strain MAC) by 50% at a concentration of 2 mg/L (Hutber et al. 1979). Growth was completely inhibited in these cultures at 10 mg glyphosate/L. Another strain of Aphanocapsa (strain 6714) was considerably more tolerant, requiring a concentration of 100 mg glyphosate/L to inhibit growth by 50%. When exposed to an unspecified formulation of glyphosate, the growth rates of Chlorella sorokiniana cultures were reduced 7% at 1 mg glyphosate/L, 58% at

3 mg/L, and 100% at ≥ 4 mg/L (Christy et al. 1981). The growth, in terms of cell density, of _Euglena gracilis_ cultures was significantly inhibited by 96 h exposure to glyphosate (formulation not stated) at concentrations of about 100 mg/L (Richardson et al. 1979). The chlorophyll content of the cultures was significantly reduced at about 5 mg glyphosate/L at some sampling times, but a concentration 200 mg glyphosate/L was required for significant (P=.05) reductions at all sampling times. Richardson also reported that photosynthesis, as indicated by oxygen evolution, was inhibited at concentrations of 1 mg/L when exposed to glyphosate for more than 20 minutes, but was stimulated at concentrations of 50 mg/L or greater. Goldsborough and Brown (1988) reported that Roundup^{R} at 0.89 mg glyphosate/L had no effect on the carbon fixation of periphytic algal communities colonizing artificial substrates from ponds and concluded that the EC_{50} was >8.9 mg glyphosate/L.

c) _Aquatic Macrophytes_

Lockhart et al. (1989) reported no reduction in growth of _Lemna minor_ fronds when exposed to Roundup^{R} at dissolved concentrations of 17 mg/L or less. They observed no growth at 169 mg/L. Lockhart also reported that when _Lemna minor_ cultures were exposed to Roundup^{R} spray at 800 g glyphosate/ha in a spray chamber, no growth occurred.

Fragrant water lillies (_Nymphaea odorata_) were killed by applications of glyphosate (formulation not known) applied by hand-held boom sprayer at rates of 0.6 kg glyphosate/ha or greater. One year after application, visually observed rates of effectiveness on mature plants was 98%, 93% and 100% for nominal application rates of 0.6, 1.1 and 2.2 kg glyphosate/ha, respectively (Welker & Riemer 1982).

No inhibitory effects on _Potamogeton pectinatus_ tuber sprouting and early growth were observed by Hartman and Martin (1985) when the plants were exposed to Roundup^{R} at nominal glyphosate concentrations of up to 10 mg/L.

11.3 Movement into and Transformation in Aquatic Environments

Although glyphosate is highly soluble in water (15,700 mg/L) and has a low Kow (6×10^{-4}), it has a high potential for adsorption (K_{OC} of 2640, Kenaga & Goring 1980) and is relatively immobile in soils [Rf values in the range 0.04 to 0.2 in sandy loam to clay loam soils (Sprankle et al. 1975)]. Feng and Thompson (1990) observed that more than 90% of the recovered glyphosate residues were in the top 15 cm of B.C. soils and remained available with DT_{50} (50% decline time) of 45-60 days.

Runoff of glyphosate from treated fields occurs, but it is limited (Edwards et al. 1980). Following the application of Roundup[R] at 1.12 kg glyphosate/ha to fields in 1973 and 1974, the maximum concentration in runoff water was 0.090 and 0.094 mg glyphosate/L, respectively. In 1973, runoff from 5 rain events transported 5.14 g glyphosate/ha from the field and in 1974, runoff from 3 rain events transported 6.52 g glyphosate/ha. The amount of glyphosate transported by runoff represented .0.6% of the glyphosate applied.

Under agricultural conditions, downwind drift can transport and deposit glyphosate off-site. Data from Yates et al. (1978) indicated that a 0.001 kg/ha exposure to glyphosate spraydrift from aerial application, recorded as deposition on Mylar sheets, could result in about 20% injury (visually assessed) to wheat plants and that such a deposit could occur at distances >250 m downwind of the application site. However, when Roundup[R] was applied by helicopter fitted with micro-foil boom or by ground operated boom sprayer fitted with low pressure deflector nozzles, deposit of 0.001 kg/ha was not likely to be exceeded beyond 20 m.

In an aquatic environment, glyphosate is not susceptible to hydrolysis or photolysis, but is susceptible to biotransformation. In aerobic water/sediment studies in which most of the glyphosate was recovered from the sediment, the glyphosate remained available for transformation as demonstrated by the formation of AMPA and carbon dioxide. In the water/sediment system, glyphosate had a DT_{50} of 7-10 days. AMPA reached a maximum residue level of 25% of the applied glyphosate and decreased to 23% by 30 d post-treatment (Monsanto). In aerobic studies without sediment the glyphosate DT_{50} ranged from 7-10 weeks. Under anaerobic water/sediment conditions glyphosate demonstrated a biphasic degradation curve. Initially a rapid decrease in glyphosate was observed in the system with a DT_{50} of 1-2 weeks. A second phase followed during which the glyphosate concentration remained fairly constant for several hundred days at .20% of the applied glyphosate. AMPA reached a maximum of 25% of the applied glyphosate and decreased to 18% by 365 d post-treatment (Monsanto).

The importance of sediment for the removal of glyphosate from the water column was demonstrated by Goldsborough and Beck (1989) with microcosms of natural water and water plus sediment which were exposed to operational oversprays of Roundup^R and incubated <u>in situ</u> for 30 days. Glyphosate concentrations in the water did not appreciably decline within the 30 day sample period when sediment was not present, but declined rapidly in the first few days in the water of microcosms containing sediment and remained steady to the end of the sampling. Glyphosate residues in the sediments were in the range <0.01 to 0.07 :g/g dry mass, increasing to days 8 to 20 and declining by day 30. Concentrations of AMPA did not exceed 20 :g/L.

A summary of the results of laboratory studies of the fate of the polyethoxylated tallow amine surfactant was submitted by Monsanto. The summary indicated that the surfactant was susceptible to transformation by microorganisms in soil and in natural water. The assessment of the fate of the surfactant in aquatic systems cannot be completed until the entire reports of the studies are submitted and reviewed.

11.4 <u>Analytical Detection Methods</u>

Miles et al. (1986) described methodology for the detection of glyphosate and AMPA in natural waters with minimal detectable quantities of 10 :g/L for glyphosate and 5 :g/L for AMPA. Payne et al. (1987) reported quantification limits of 0.5 :g/L for glyphosate and 0.15 :g/L for AMPA. Monsanto reported a method for the analysis of glyphosate and AMPA residues in fish tissue at a detection limit of 0.05 mg/kg.

No methodology was available for the analysis of MON 0818 in water at concentrations toxic to aquatic organisms.

11.5 Impact Assessment

The expected environmental concentration (EEC) of glyphosate in water is sufficiently below the toxicity of glyphosate to fish and aquatic invertebrates that direct acute toxicity is unlikely to occur. The EEC of glyphosate from a direct overspray of Roundup^R to water 0.15 m deep would be 1.2 mg glyphosate/L, based on the maximum preharvest application rate of 1.78 kg glyphosate ae/ha (5 L Roundup^R/ha). This concentration is substantially below the LC_{50}s for fish (which are typically in the range of 22-211 mg glyyphosate/L), below the EC_{50} for midge larvae (55 mg/L) and below the toxic concentrations for marine invertebrates (NOELs 10-650 mg/L).

Direct effects on fish and aquatic invertebrates due to chronic exposure to glyphosate also are unlikely since the EEC (1.2 mg glyphosate/L) is substantially less than the no effect levels for chronic exposure to fathead minnows (25.7 mg glyphosate/L) and for daphnids (50-96 mg glyphosate/L).

Fish are not likely to be sublethally affected by glyphosate since no significant adverse effects relative to fish development, avoidance, and seawater challenge would be expected at glyphosate concentrations equal to the EEC. Bioconcentration of glyphosate by fish should not be significant.

The toxicity of the Roundup^R formulation to aquatic fauna is of concern to Fisheries and Oceans. Unlike glyphosate which is practically non-toxic, the MON 0818 surfactant, which comprises .15% (by weight) of the Roundup^R formulation, is moderately to highly toxic to fish and to aquatic invertebrates (EC_{50}/LC_{50}s in the range of 1-2 mg MON 0818/L for the most sensitive species studied). As a component of the Roundup^R spray, the EEC of MON 0818 in 0.15 m water would be 0.6 mg MON 0818/L (based on the worst case scenario of the maximum preharvest application rate at 5 L Roundup^R/ha to forage legumes and grasses). With an EEC of 0.6 mg MON 0818/L compared to EC_{50}/LC_{50}s of 1-2 mg MON 0818/L, the margin of safety for aquatic fauna is limited. A direct overspray of fish habitat with Roundup[R] could result in significant effects to fish and/or to fish habitat. Concern is enhanced by the lack of data on the fate of MON 0818 in aquatic systems and by the lack of an analytical method for the quantification of MON 0818 in water at concentrations lower than the NOEL for the most sensitive non-target aquatic species.

Algal susceptibility to Roundup[R] is varied, with the cyanophytes being more sensitive to Roundup[R] than green algae. Even between strains of cyanophytes, susceptibility can vary with EC_{50}s for Roundup[R] ranging from 2-100 mg glyphosate/L. For periphytic algal communities the EC_{50} for Roundup[R] of >8.9 mg glyphosate/L is above the EEC of 1.2 mg glyphosate/L. Because of the wide range of toxic response, the effect of Roundup[R] on algal communities should be minimal and unlikely to affect fish habitat.

Exposure of riparian and emergent aquatic vegetation to direct overspray and to spray drift of Roundup[R] is also a concern. Studies have indicated that injury to plants could occur at deposit rates of 1 g glyphosate/ha and that such deposits can occur at >250 m downwind from aerial application sites. With a maximun application rate of 1.78 kg glyphosate/ha, off-target deposit of Roundup[R] must be reduced in order to avoid phytotoxic effects on non-target plants. Reducing off-target deposit also limits the amount of glyphosate which can enter aquatic systems and partition to sediment where it has a slow rate of dissipation under anaerobic conditions, and where it could be available to affect aquatic vegetation.

In order to protect fish and fish habitat during the preharvest use of Roundup[R], MON 0818 should be excluded from aquatic systems and the deposit of Roundup[R] onto riparian and emergent aquatic vegetation should be avoided. To reduce the probability of direct oversprays, and to reduce the amount of drift deposit onto fish habitat, Roundup[R] should be applied only by ground equipment and not by air. Additional protection of fish and fish habitat can be achieved by observing a 15 m buffer zone around the edge of fish habitat or waters draining into fish habitat.

11.6 Summary

The preharvest use of Roundup^{R} herbicide by ground application to flax and to other crops (wheat, barley, canola, lentils, peas, soybeans, forages) should not result in significant effects on fish and fish habitat provided that a 15 m buffer zone is observed. The preharvest use of Roundup^{R} by aerial application to wheat, barley, canola, lentils, peas, soybeans and forages may result in significant effects on fish and fish habitat.

REFERENCES

Christy, S.L., E.P. Karlander & J.V. Parochetti (1981). Effects of glyphosate on the growth rate of Chlorella. Weed Sci. 29: 5-7.

Edwards, W.M., G.B. Triplett & R.M. Kramer (1980). A watershed study of glyphosate transport in runoff. J. Environm. Quality 9: 661-665.

Feng, J. & D.G. Thompson (1990). Fate of glyphosate in a Canadian forest watershed. 2. Persistence in foliage and soils. Agric. Food Chem. 38: 1118-1125.

Folmar, L.C. (1976). Overt avoidance reaction of rainbow trout fry to nine herbicides. Bull. Environ. Contam. & Toxicol. 15: 509-514.

Folmar, L.C., H.O. Sanders & A.M. Julian (1979). Toxicity of the herbicide glyphosate and several of its formulations to fish and aquatic invertebrates. Arch. Environm. Contam. Toxicol. 8: 269-278.

Goldsborough, L.G. & D.J. Brown (1988). Effect of glyphosate (Roundup[R] formulation) on periphytic algal synthesis. Bull. Environ. Contam. Toxicol. 41: 253-260.

Goldsborough, L.G. & A. E. Beck (1989). Rapid dissipation of glyphosate in small forest ponds. Arch. Environ. Contam. Toxicol. 18: 537-544.

Hartman, W.A. & D.B. Martin (1985). Effects of four agricultural pesticides on Daphnia pulex, Lemna minor, and Potamogeton pectinatus. Bull. Environ. Contam. Toxicol. 35: 646-651.

Hildebrand, L.D., D.C. Sullivan & T.P. Sullivan (1982). Experimental studies of rainbow trout populations exposed to field applications of Roundup[R] herbicide. Arch. Environm. Contamin. Toxicol. 121: 93-98.

Hutber, G.N., L.J. Rogers & A.J. Smith (1979). Influence of pesticides on the growth of cyanobacteria. Zeits. fur Allge. Mikrob. 19: 397-402.

REFERENCES (continued)

Kenaga, E.E. & C.A.I. Goring (1980). Relationship between water solubility, soil sorption, octanol-water partitioning and bioconcentration of chemicals in biota. In Eaton, J.C., R. Parrish and A.C. Hendricks, eds. Aquatic Toxicology, ASTM STP 707, American Society for Testing and Materials.

Lockhart, W.L., B. N. Billeck & C. L. Baron (1989). Bioassays with a floating aquatic plant (Lemna minor) for effects of sprayed and dissolved glyphosate. Hydrobiologia 188/189: 353-359.

Miles, C.J., L.R. Wallace & H.A. Moye (1986). Determination of glyphosate herbicide and (aminomethyl)phosphonic acid in natural waters by liquid chromatography using pre-column fluorogenic labelling with 9-fluorenylmethyl chromate. J. Assoc. Off. Anal. Chem. 69: 458-461.

Mitchell, D.G., P. Chapman & T.J. Long (1987). Seawater challenge testing of coho salmon smolts following Roundup[R] herbicide exposure. Environm. Toxicol. Chem. 6: 875-878.

Monsanto Canada Inc., 350 - 441 Maclaren Avenue, Ottawa, Ontario K2P 2H3

Payne, N., J. Feng & P. Reynolds (1987). Off-target deposit measurement and buffer zones required around water for various aerial applications of glyphosate. FPM-X-80. Forest Pest Management Instit., Forestry Canada. Sault Ste. Marie.

Richardson, J.T., R.E. Frans & R.E. Talbert (1979). Reactions of Euglena gracilis to fluometuron, MSMA, metribuzin, and glyphosate. Weed Sci. 27: 619-624.

Servizi, J.A., R.W. Gordon & D.W. Martens (1987). Acute toxicity of Garlon 4 and Roundup[R] herbicides to salmon, Daphnia and trout. Bull. Environ. Contam. Toxicol. 39: 15-22.

Sprankle, P., W.F. Megitt & D. Penner (1975). Adsorption, mobility and microbial degradation of glyphosate in soil. Weed Sci. 35: 229-234.

REFERENCES (continued)

Wan, M.T., R.G. Watts & D.J Moul (1989). Effects of different dilution water types on the acute toxicity to juvenile pacific salmonids and rainbow trout of glyphosate and its formulated products. Bull. Environ. Contam. Toxicol. 43: 378-385.

Welker, W.V. & D.N. Riemer (1982). Fragrant waterlily (Nymphaea odorata) control with multiple applications of glyphosate. Weed Sci. 30: 145-146.

Yates, W.E., N.B. Akesson & D.E. Bayer (1978). Drift of glyphosate sprays applied with aerial and ground equipment. Weed Sci. 26: 597-604.

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