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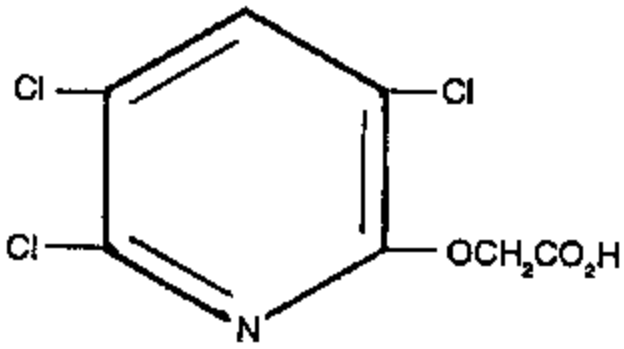
Pesticides Directorate

Direction des pesticides

Decision Document E91-02

TRICLOPYR



HERBICIDE

PRODUCT MANAGEMENT DIVISION SEPTEMBER 16, 1991

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TRICLOPYR HERBICIDE

FOREWORD

TRICLOPYR

As part of the ongoing efforts to provide a summary of the data received and outline the regulatory action on the active ingredient, triclopyr, a Decision Document has been prepared. This document reflects input from specialists within Agriculture Canada and key interdepartmental advisors. Based on the review of all available information and in consideration of its benefits, a regulatory decision has been made to grant registration for triclopyr, and the end-use products Garlon 4 Herbicide and Release Silvicultural Herbicide for ground application in industrial (non-cropland) and woodland sites respectively.

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TRICLOPYR HERBICIDE

1. SUMMARY

The purpose of this document is to provide a summary of the data reviewed and to outline the regulatory action on the active ingredient triclopyr.

Agriculture Canada, with the assistance of advisors from Environment Canada, Forestry Canada, Health and Welfare Canada and the Department of Fisheries and Oceans has completed a review of the available data supporting triclopyr. The data base is modern and sufficient for registration of the product for use by ground application equipment. However, further data are required to complete a full assessment of environmental impact and occupational exposure for aerial use.

An occupational exposure study conducted in Canada, using the stem-foliage method of brush control, indicates that with the judicious use of protective clothing and with adequately trained and supervised workers, an adequate margin of safety will be achieved.

Field studies indicate that there is little concern for persistence and leaching in soil. Hydrolysis, photolysis and microbial action all contribute to product breakdown. In water, the rate of transformation from the ester to acid can be slow under cool, low pH conditions. The ester form is more toxic to fish and aquatic invertebrates than the acid form. Additional information is therefore necessary to further delineate the impact on these species from direct overspray and drift which could result from aerial applications.

Acute toxicity to wild birds and mammals is low. Prolonged exposure to significant levels of the product by consumption of treated vegetation is unlikely, as residues will decline rather than remain constant. In addition, treated vegetation susceptible to triclopyr will not be palatable for several days following treatment. Tolerant species such as members of the grass family are able to metabolize triclopyr residues. However, additional data will soon be available on the residues in foliage, leaf litter and soil following aerial applications of Garlon 4.

Triclopyr is an effective herbicide for the control of various broadleaved weeds and woody plants on rights-of-way, industrial and forest/woodland sites. It is particularly useful for the control of hard-to-kill root suckering and basal sprouting woody species.

Based on a review of all available information and in consideration of its benefits in vegetation management programs, this herbicide has been granted a registration for use on rights-of-way, industrial sites and other non-crop land areas and woodland sites by ground application only. Aerial application may be considered when additional information on environmental impact and occupational exposure is available.

2. PESTICIDE NAME AND PROPERTIES

2.1 Pesticide Name

Common Name:	triclopyr
Chemical Name:	[(3,5,6-trichloro-2-pyridinyl)oxy]acetic acid
Trade Names:	Garlon 4 Herbicide andRelease Silvicultural Herbicide
CAS Registry No.:	55335-06-3

2.2 Physical and Chemical Properties

a) Triclopyr Acid

Empirical Formula:	$C_7H_4Cl_3NO_3$
Molecular Weight:	256.5
Physical Appearance:	white fluffy solid
Melting Point:	140-150°C
Vapor Pressure:	1.26×10^{-6} mm Hg at 25°C
	Ionization Constant (Pka) =
	2.68, 2.70 Octanol/Water
Partition	
Coefficient (K_{ow}):	0.205 at pH 7
Solubility:	g/100 g of solvent at 25°C:
acetone	98.9
acetonitrile	12.6
benzene	2.73
chloroform	2.73
n-hexane	0.041
n-octanol	30.7
xylene	2.79
water	430-440 ppm
Thermal Stability:	decomposition temperature 290°C
Hydrolysis Rate:	no significant hydrolysis occurs after nine months incubation of 3 ppm in buffered distilled water at pH's 5.1, 7.2 and 8.3 at 15°C, 25°C and 35°C.

b) Formulated Product

Product Name:	Garlon 4 Herbicide and Release Silvicultural Herbicide
Guarantee:	triclopyr 480 g/L present as butoxyethyl ester
Specific Gravity:	1.082 at 20°C
Flammability:	TOC flash point 82°C
Storage Stability:	Exceeds 2 years. Store above 2°C.

3. DEVELOPMENT AND USE HISTORY

Triclopyr is manufactured by the Dow Chemical Company in Midland, Michigan. The Canadian development program was conducted by Dow Chemical Canada Inc., the registrant for both the triclopyr butoxyethyl ester technical and the end-use products.

The Canadian field testing program with triclopyr was initiated in 1974. The original submission for registration of triclopyr was received in 1979; however both of the original long-term feeding studies, conducted during the early 1970's, were judged to be inadequate to allow a risk assessment to be conducted. Repeat studies were submitted in July 1987. Some environmental studies were received in November 1988 and March 1989. Research on environmental impacts is continuing, for the purpose of supporting aerial application of this herbicide.

Triclopyr is currently registered for use in the following countries:

United States	Industrial Vegetation Control Forestry Turf Range and Pasture
United Kingdom and France	Pasture Industrial Vegetation Control Forestry
Italy	Rice
Greece	Forestry
Egypt	Sugar Cane
E. Germany	Industrial Vegetation Control
Czechoslovakia	Forestry
Middle & East Africa	Rice & Brush
Costa Rica	Rice
Mexico	Pasture
Argentina	Pasture
Colombia	Pasture

Chile	Forestry Pasture
Brazil	Pasture
New Zealand	Pasture Industrial Vegetation Control
Australia	Industrial Vegetation Control

4. REGULATORY POSITION AND RATIONALE

Triclopyr is an auxin-type selective herbicide for control of many broadleaved weeds and woody species. In comparison to other auxin-type herbicides, it provides superior control of ash, oaks, maples and other root sprouting species. Most grasses are tolerant. It is an excellent herbicide for brush and broadleaved weed control on industrial sites and forest areas.

Triclopyr has a moderate acute toxicity to mammals. In chronic studies, a relatively low no observed effect level (NOEL) was demonstrated. However, use of protective equipment reduces exposure to an acceptable level. The studies do not indicate any carcinogenic potential.

A Canadian worker exposure study was conducted (1989) in which individuals mixed and loaded Garlon 4 and applied the dilute spray mixture as a stem-foliage treatment. The findings of this study indicated that adequate margins of safety can be achieved with judicious use of protective clothing, with training in proper application techniques of the stem-foliage treatment (i.e., "walk in - spray out" method) and with supervision to ensure label directions and proper application techniques are followed.

One worker in this study did not achieve an adequate margin of safety (i.e., received a high exposure) when calculated on the basis of a lifetime exposure. Although this individual was involved in activities similar to the other eight (i.e., mixing, loading, applying product) inexperience and lack of attention to proper spray techniques and to proper use of protective clothing, aimed at minimizing exposure, resulted in increased exposure.

With respect to environmental fate, triclopyr ester transforms rapidly to triclopyr acid via hydrolysis and photolysis. Triclopyr acid is further degraded by photolysis and microbial action. Although laboratory studies indicate triclopyr has the potential to be persistent and mobile in soil, field studies show that it is not excessively persistent and does not leach appreciably. In the aquatic environment, the rate of transformation of the ester to the acid via hydrolysis can be quite rapid under certain conditions. However, under conditions of low pH and cool temperature it can be slow, leaving photolysis as the most rapid degradation route. As the toxicity of the ester to fish and other aquatic species is of concern, transformation to the less toxic form (i.e., period of exposure to the ester) is an important consideration where direct oversprays of aquatic sites are possible, such as in the case of aerial applications. Additional data are necessary to characterize the effect on fish and other aquatic species under field conditions of commercial use of the product. Additional

Canadian studies with aerial application have recently been completed and submitted for review which will provide further information on field dissipation, both aquatic and soil, and impact on fish and aquatic invertebrates, to support the aerial application of Garlon 4/Release.

Additional information is required to better understand the potential impact if Garlon 4/Release enters water bodies by either direct application or by drift. Provincial setbacks, judicious observation of label precautions and the limitation respecting aerial application should mitigate against such an occurrence. Additional data have been provided which will further define the effects of direct application to water bodies and allow further consideration of aerial application.

Exposure to Garlon 4/Release is not expected to cause direct mortality of wild birds and mammals through acute toxicity. Prolonged or chronic exposure of toxic levels, through ingestion of contaminated food, is unlikely. Residues in the environment are not static but decline via various means identified in this document, including hydrolysis, photolysis and metabolism in both plants and soil.

Susceptible broadleaved species of weeds and brush would not remain palatable as brown-out and leaf fall occurs within 3-6 weeks after application.

Grasses which are browsed by a number of wildlife species are, in fact, known to metabolize triclopyr thus removing the potential for prolonged exposure via feeding. In addition, current information from a number of mammalian and avian studies including chronic and carcinogenicity, mutagenicity, teratogenicity and reproduction, indicate no cause for concern as levels which may cause an effect are relatively high. An aerial application study conducted in New Brunswick will provide additional information on residue levels in foliage and soil immediately after application, as well as the persistence in foliage, leaf litter and soil.

Based on the information available, Agriculture Canada has concluded that ground application of Garlon 4 for weed and brush control on rights-of-way and other non-crop land areas and of Release for similar uses in woodland sites, if used according to label directions, will not pose an unacceptable risk to the user or the environment. Registration has been granted for use on rights-of-way, industrial sites and other non-crop land areas and woodland sites by ground application only.

Aerial application and use on forest sites may be considered when additional information is available. This includes the final reports from field studies on impact on fish and on field dissipation from major forest areas as well as an aerial application exposure study to determine margins of safety for mixers, loaders and applicators.

5. BIOLOGICAL PROPERTIES

Triclopyr is absorbed by both plant leaves and roots. It is readily translocated through plants. It tends to accumulate in meristematic tissues and is not readily metabolized in susceptible plants. However, tolerant species such as cereals rapidly metabolize triclopyr.

Triclopyr induces characteristic auxin-type responses in broadleaved plants. Foliage applications have achieved maximum plant response when the treatment takes place soon after full leaf development and soil moisture is adequate for normal plant growth.

6. USE SUMMARY AND BENEFITS

6.1 Use Properties

Triclopyr herbicide has been field tested extensively in Canada over the past ten years, alone and in combination with other herbicides. Triclopyr as the ester formulation provides effective control of many woody plants and broadleaved weeds. The chemical has been proposed for use on industrial rights-of-way and in forest and woodland sites for site preparation and conifer release.

Triclopyr ester is effective as a foliage spray when plants are actively growing or it may be used in a dormant, basal bark or cut surface treatment for the control of woody plants.

Triclopyr herbicide is recommended for the control of unwanted woody plants and annual and perennial broadleaved weeds in non-crop areas (including rights-of-way, electrical power lines, communication lines, pipelines, roadsides and manufacturing and storage sites) and woodland sites by ground application.

Note: Species controlled, application methods, rates and timings of application provided in this section are those proposed for industrial and non-cropland use. Woodland site use patterns will differ - the reader is referred to the Release Silvicultural Herbicide label.

Among the woody plant species controlled at the lower rate are:

Alder	Dogwood	Poison Oak
Ash	Elderberry	Poplar
Aspen	Hawthorn	Sassafras
Basswood	Hickory	Sumac
Beech	Hop-hornbeam	Sycamore
Birch	Locust	Tamarack
Blackberry	Maples	Wild Rose
Buckthorn	Mulberry	Willow
Cottonwood		Witch Hazel

The following hard-to-control species may require treatment at the higher rate and may need to be retreated the following year, particularly if the original treatment was made at the lower rate:

Cherry	Honey Locust	Pines
Chokecherry	Red Maple	Raspberry
Elm	Oaks	

Among the annual and perennial broadleaved weeds controlled are:

Burdock	Field Bindweed	Smooth Bedstraw
Chicory	Lambs-quarter	Vetch
Curled Dock	Ragweed	Wild Lettuce
Dandelion	Smartweed	

6.2 Time and Rates of Application

Garlon 4 may be diluted in water and used as a foliage spray for the control of woody plants or herbaceous weeds. Applications are made when plant species are actively growing. For conifer release in woodland sites, application should be made in late summer, after conifers have hardened off and deciduous trees are in full leaf, but prior to autumn colouration.

Garlon 4, undiluted or mixed with various oils, may be used in treatments to control woody plants. The product penetrates the bark or cut surface and is translocated in the cambial layer.

a) General Directions for Controlling Woody Plants and Herbaceous Weeds Using Stem-Foliage Treatments

For best results, applications of Garlon 4 should be made when woody plants and weeds are actively growing. Do not treat woody plants which exceed 2.5 m in height. For woody plants exceeding this height, cut and spray regrowth or use basal bark, dormant stem or cut stump treatment. Use higher rates when hard-to-control species are present. If lower rates are used on hard-to-control species, resprouting may occur and retreatment may be necessary the following year.

Use higher rates for late summer application when plant growth rates are reduced.

For control of woody plants up to 2.5 m in height, use Garlon 4 at 4.0 L to 8.0 L in enough water to make 1000 L of spray mixture. Use the higher rate for late summer application when growth rates are reduced or when hard-to-control species are present. Spray brush to the point of runoff. Coverage should be thorough to wet all leaves, stems and root collars. To minimize spray drift, do not use pressures exceeding 1400 kPa at the spray nozzle. Direct the spray away from crops or desired non-target vegetation. Use of a drift control system is suggested to minimize spray drift.

Woody plants may also be controlled by using broadcast sprays of Garlon 4 at 4 to 8 L/ha diluted in a minimum of 200 L of spray solution. Make applications with equipment that will assure uniform coverage of the low spray volume applied. Do not use pressure exceeding 275 kPa at the spray nozzle. Apply any time during the growing season. Use the higher rates for late summer applications when growth rates are reduced or hard-to-control species are present.

For broadleaved weed control, use Garlon 4 at rates of 1 to 4 L per hectare in a minimum of 200 L of spray solution. Make applications with equipment that will assure uniform coverage of the low spray volume applied. Do not use pressure exceeding 275 kPa at the spray nozzle.

b) Woody Plant Control Using Basal Bark, Dormant Stem and Cut Surface Treatments

Woody plants may be controlled by applying Garlon 4 solution to the bark of deciduous tree species.

Use the higher rate when treating hard-to-control species or when applying during the late growing or dormant season. When using oil mixture sprays use oils such as diesel oil, fuel oil, kerosene or mineral oils.

i) Basal Bark Treatment: Use 1 to 3 L of Garlon 4 in enough diesel oil, No. 1 or No. 2 fuel oil or kerosene to make 100 L of spray mixture. Apply with knapsack sprayer or power spraying equipment using low pressures of 150 to 275 kPa. Spray the basal parts of brush and tree trunks to a height of 50 cm from the ground. Thorough wetting of the indicated area is necessary for good control. Spray to the drip point at the ground line. Old or rough bark requires more spray than smooth young bark. Apply at any time, including the winter months, except when snow or water prevent spraying to the ground line.

ii) Dormant Stem Treatment: Mix 500 mL to 1.5 L of Garlon 4 in enough oil to make 100 L of spray. Apply with knapsack or power spraying equipment using low pressures of 150 and 275 kPa. Treat any time when the brush is dormant and most of the foliage has dropped. Thoroughly wet the stems down to and including the root collar. For root suckering species such as sumac, sassafras and locust, also spray the ground under the plants to cover small root suckers which may not be visible above the soil surface. Brush of average density and 1.5 to 2 metres in height may take up to 1400 L of spray mixture per hectare.

iii) Thin Line Basal Bark Treatment: To control susceptible woody plants with stems less than 15 cm in diameter, apply undiluted Garlon 4 in a thin stream to all sides of the stems about 15 cm above the ground line. The stream should be directed horizontally to apply a narrow band of Garlon 4 around each stem or clump. From 2 to 15 mL of chemical will be required for treatment of single stems, and from 25 to 100 mL to treat clumps of stems. Use a sprayer capable of being calibrated to deliver the small amounts of Garlon 4 required. Use a nozzle orifice of size # 1 or # 1 1/2 to provide the thin stream required.

iv) Cut Stump Treatment: Make a mixture of Garlon 4 in diesel oil, No. 1 or No. 2 fuel oil or kerosene at a proportion of 1 part Garlon 4 to 30 parts oil and apply this mixture to the freshly cut stumps of susceptible brush. Be sure to thoroughly wet all cut surfaces as well as the remaining bark to the ground line. Care must be taken to ensure treatment of all cut stems in a clump of brush.

6.3 Use Benefits

The major market for Garlon 4 is for the control of woody plants in the areas of Canada where there is a predominance of deciduous hardwood species. The control of hard-to-kill species such as maple, oak and ash is particularly important. Vegetation managers are particularly interested in herbicides that will control these root suckering species.

There are many situations that require effective control of trees and brush clumps in rights-of-way and forest/woodland sites. Basal bark and dormant stem treatment techniques are useful in a number of these areas. These application methods are well suited for steep terrain situations that make it difficult to use large sprayers. And, because of their selective nature, they may be used in sensitive areas near susceptible crops and vegetation. They can also help reduce the brown-out commonly associated with other application methods. And basal bark and dormant stem treatments provide the users with application flexibility.

Garlon 4 readily penetrates the bark and it translocates through target trees and brush species. It is the only registered product in Canada that can be used as a thin-line basal bark application. This involves a pencil-point thin line of straight Garlon 4 applied to the basal parts of trees and brush. This product can be used at various times during the season using different application techniques.

6.4 Availability of Alternative Products

For foliage spraying of woody plants, several products have been used in industrial sites, such as 2,4-D, fosamine ammonium, 2,4-D + 2,4-DP, 2,4-D + dicamba, glyphosate and picloram plus 2,4-D. In forest/woodland sites, only 2,4-D, glyphosate and hexazinone are used. While the woody species show different degrees of susceptibility to the various herbicides, Garlon 4, as a leaf-stem foliage spray, controls most of the key deciduous hardwood species.

In areas where foliage brown-out is not acceptable, Garlon 4 can be utilized as a basal bark and dormant stem treatment technique.

7. TOXICOLOGY AND OCCUPATIONAL EXPOSURE: HEALTH AND WELFARE CANADA INPUT

7.1 Acute Toxicology

a) Acute Toxicity - Technical (triclopyr acid unless specified)

Triclopyr is moderately toxic to rats via oral dosing (male LD_{50} = 729 mg/kg, female LD_{50} = 630 mg/kg). It is not acutely toxic to rabbits by the dermal route (LD_{50}>2000 mg/kg). The technical product is a mild eye and dermal irritant and does not produce a sensitization response in guinea pigs. The inhalation toxicity (LC_{50}) of the butoxyethyl ester of triclopyr in rats exceeds 1.84 mg/L, the maximum attainable concentration.

b) Acute Toxicity - Formulation (Garlon 4)

Orally, Garlon 4 is of low toxicity to rats (male LD_{50} = 2460 mg/kg, female LD_{50} = 2140 mg/kg). In rabbits, the LD_{50} following dermal administration was >2000 mg/kg. The formulation is a non irritant to rabbit eyes but a slight irritant to rabbit skin and a sensitizer in guinea pigs. Additional information suggests that a contaminant in the

formulation, pyridone ester, may be responsible for the sensitization response. The inhalation toxicity (LC_{50}) of Garlon 4 in rats exceeds 0.82 mg/L, the maximum attainable concentration.

7.2 Short Term Toxicity

a) Short Term Toxicity-Technical

A 13-week dietary study in F344 rats demonstrated a NOEL of 5 mg/kg/day based on degenerative histological changes in the proximal tubules of the kidneys at doses of 20-250 mg/kg/day. Male rats appeared to be more sensitive to the toxic insult of triclopyr. Liver toxicity was also evident at doses of 250 mg/kg/day. A 2-week dietary study in F344 rats demonstrated renal changes (relative weights) at dose levels of 50-300 mg/kg/day in males only.

A 228-day dietary study in Beagle dogs demonstrated renal toxicity (proximal and distal convoluted tubule) and hepatoxicity at doses of 5-20 mg/kg/day. Effects included changes in clinical chemistry, urinalysis and histopathology.

A 183-day dietary study in dogs resulted in a NOEL of 0.5 mg/kg based on reduced phenolsulfone-phthalein clearance at 2.5 mg/kg. However, the response at this dose-level was not accompanied by other toxicological indicators (e.g., histopathology), and therefore the No Observable Adverse Effect Level (NOAEL), was set at 2.5 mg/kg/day.

b) Short Term Toxicity - Formulation

A NOEL of 54 mg (form.)/kg/day (females) and <54 mg (form.)/kg/day (males) was observed in a 21 day dermal study in rats (dosing was not continuous). However, these results must be interpreted with caution since the animals were unrestrained and had unoccluded sites of treatment, possibly leading to oral uptake of the test material.

7.3 Chronic Toxicity/Oncogenicity - Technical

a) Rat

A two year dietary study in Charles River CD rats performed by Industrial Bio-Test Laboratories was found to be valid by the IBT Task Force. Subsequent examination of this study revealed deficiencies, the most important being the lack of a full complement of tissues for histological examination. The study was deemed inadequate for assessing potential chronic toxicity or oncogenicity.

A two year dietary study in F344 rats was performed with dose levels of 0, 3, 12 and 36 mg/kg/day. The kidney was identified as a target organ. Although mortality, body weight gain and food consumption was not adversely affected by treatment, the NOEL for chronic toxicity in this study was 3 mg/kg bw/day based on renal toxicity.

Although a number of common tumour types were noted, the final assessment focused on the presence of several rare tumours in the treated animals including prostate adenomas (males), histiocytic sarcomas (females) and osteosarcomas (males). None of these tumours were observed in the concurrent study control nor in low dose groups. While the design and conduct of selected Dow and National Toxicology Program (NTP) historical studies do not permit direct comparison to the current study, the historical control data do nevertheless confirm the apparent rarity of these tumours. However, no statistical significance was achieved for these tumours using the primary group for comparison, the concurrent study controls. None of the observed numerical increases were preceded by a proliferative or hyperplastic response. In addition, no plausible biological connection between the noted tissue types could be postulated that would account for these responses. In summary, the rat long term study is best described as equivocal for tumorigenicity.

b) Mouse

A two-year dietary study in CDF1/COX mice was performed with dose levels of 0, 24, 80 and 240 ppm. This study was deemed inadequate for assessing potential chronic toxicity or oncogenicity in light of reporting deficiencies and the high incidence of urinary system disease in these animals.

A 22-month dietary study in SPF ICR:JCL mice confirmed the target organs to be the kidney and liver in mice. The high dose level of 1250 ppm showed clear effects on body weight, urinalysis (specific gravity and protein), clinical chemistry (total protein, albumin, blood urea nitrogen, alanine transaminase) and organ weights. Effects were also observed in the 250 ppm animals that included increased urinary protein (females at week 26), increased blood urea nitrogen (males at week 26) and weight gain reductions. Because most effects were observed early in the study (i.e., week 26) with little supportive clinical or histopathological evidence at termination, an adaptive response is suggested. The NOEL for chronic toxicity is 50 ppm (5 mg/kg/day). A slight numerical increase in mammary adenocarcinomas in the treated females was dismissed as treatment-related because the incidence was comparable to historical data and not statistically significant compared to concurrent control data.

7.4 Reproductive Toxicity - Technical

This study has certain limitations but overall was adequate to address reproductive toxicity. Triclopyr, administered in the diet, did not cause maternal toxicity or affect reproductive performance in rats at doses up to 30 mg/kg/day. However, a reduction in pup body weight gains was the basis for setting the NOEL at 3 mg/kg/day.

7.5 Teratogenicity - Technical

In a teratology study, doses of 0, 50, 100 and 200 mg/kg/day were administered by gavage to pregnant Sprague-Dawley rats on days 6-15 (inclusive) of gestation. Clinical signs of toxicity were noted in all treatment groups but weight gain and food consumption were reduced in the 100 and 200 mg/kg/day groups only. Embryo/fetotoxicity was observed at 200 mg/kg/day with a higher number of resorptions and pups with retarded ossifications. Two fetuses with major malformations were found in the 200 mg/kg/day group. One of these fetuses had cleft palate, brachycephaly and micromelia. Skeletal examination of this fetus revealed shortened nasals, maxillaries and mandibles and malformation of the pelvic girdle and long bones of all limbs. The second malformed fetus exhibited cleft palate, brachycephaly, kinky tail, imperforate anus, abnormal renal papillae and generalized edema.

A third fetus from the 200 mg/kg/day groups exhibited generalized edema. Historically, 3/6722 fetuses have exhibited cleft palate and brachycephaly whereas only 1/6722 fetuses have shown micromelia, impatent anus and abnormal urinary papillae. A multiple skeletal malformation similar to that seen in the high dose group has been observed in 2/4865 fetuses from historical data. Although the incidence of the reported malformations does not achieve statistical significance, the observation of 2 pups in the high dose group with historically rare multiple malformations together with the observed embryo/fetotoxicity at the same dose level is of concern. It is important to note that these findings are present only at dose levels which were also toxic to the mothers. A NOEL for maternal toxicity could not be established but for feto/embryo toxicity and teratogenicity 100 mg/kg/day appears to be a NOEL.

In an initial study with New Zealand White rabbits, pregnant females were intubated with 0, 25, 50 and 100 mg/kg/day on days 6-18 (inclusive) of gestation. Due to high mortality rates in all groups and the limited numbers of litters available for examination, the study was deemed unacceptable for an assessment of developmental toxicity.

In a repeat study, pregnant New Zealand White rabbits were administered 0, 10 and 25 mg/kg/day of triclopyr by gavage on days 6-18 (inclusive) of gestation. Mortality in all groups, reported to be related to enteric disorder, necessitated the combination of data from two separate studies 4 months apart. No evidence of differential responses to treatment between the experimental phases was apparent. The observed mortality was comparable in all dose groups when the entire period of gestation was considered. Administration of 25 mg/kg/day of triclopyr to rabbits did not demonstrate maternal toxicity, fetotoxicity or teratogenicity. In the absence of any treatment-related effects, it is questionable whether the rabbit dams were sufficiently challenged with the test material.

In a recently submitted range finding study in New Zealand White rabbits, pregnant females were intubated with 0, 25, 50, 100 and 200 mg/kg/day on days 6-18 (inclusive) of gestation. Dose levels of 100 and 200 mg/kg/day were maternally toxic to rabbit dams as evidenced by mortality, clinical signs, body weight loss and pathology.

In the most recent teratology study with New Zealand White rabbits, pregnant females were administered 0, 10, 25 and 75 mg/kg/day of triclopyr by gavage on days 6-18 (inclusive) of gestation. Maternal toxicity was observed at 75 mg/kg/day with the death of one dam. The necropsy findings in this animal were consistent with observations noted at toxic levels in the range-finding study. Thus the NOEL for maternal toxicity is 25 mg/kg/day. There were no signs of treatment-related fetotoxicity or teratogenicity at any dose level. The NOEL for teratogenicity and fetotoxicity is 75 mg/kg/day.

7.6 Mutagenicity - Technical

Triclopyr did not demonstrate mutagenic activity in the following assays: Ames test, in vitro and subacute in vivo host-mediated assay, acute and subacute in vivo cytogenetic study (rats), micronucleus test (mouse), dominant lethal assay (mouse), CHO/HGPRT forward mutation assay, unscheduled DNA synthesis assay (rat hepatocytes). A positive response was reported in a poorly documented rat dominant lethal assay.

7.7 Pharmacokinetics - Technical

Oral absorption and urinary excretion of technical triclopyr acid was studied in male human volunteers. The study was conducted in two phases, three weeks apart, to allow separate dosings of 0.1 and 0.5 mg/kg bodyweight to the same individuals. The systemic dose and excretion profile was monitored by repeated blood sampling and cumulative urine collections for 72 hours following dosing.

A two compartment pharmacokinetic model adequately described the time course of triclopyr in humans following oral dosing. Peak blood concentrations were rapidly achieved within 2-3 hours post dosing. Generally, the higher dose was absorbed at a slightly faster rate than the lower dose. The absorption half life for either dose was less than one hour.

About 80% of the administered dose was excreted in the urine as unchanged triclopyr over the 72 hour collection period. Most of the excretion (>95%) occurred during the first 24 hours after dosing. Less than 1% of the administered dose was present as the metabolite 3,5,6-trichloro-2-pyridinol.

Urinary metabolites consisted primarily of the parent acid with low levels of the pyridinol metabolite and/or conjugated derivative. Tissue concentrations were highest in the plasma, kidney, liver, adipose tissue and gall bladder (bile). Plasma concentration values indicated that the butoxyethyl ester of triclopyr is rapidly hydrolyzed to the acid in the gut (prior to or immediately after absorption) in the rat. A similar pattern of absorption, distribution, excretion and metabolism in rats receiving the acid or ester further supports the bioequivalency of these chemicals.

7.8 Dermal Absorption - Technical and Formulation

The review of the absorption studies in rabbits revealed a number of shortcomings. However, the data suggests that for high dermal doses, the rate of dermal penetration may be a factor in urinary excretion.

A dermal absorption study of the emulsifiable concentrate formulation (containing 482 g/L butoxyethyl ester form of triclopyr) was conducted on the forearms of human volunteers. The systemic dosage was monitored by repeated blood samples and by cumulative urine collections for 96 hours after application of 5 mg a.i./kg bodyweight (BW).

The half life for absorption through the skin was 16.8 $\pm$ 5.2 hours (range: 11 - 23 hours). Cumulative urinary excretion (corrected for incomplete excretion via the renal route) demonstrated about 2% (range: 0.88 - 3.11%) of a dermally applied dose of triclopyr is excreted during the first four days following application. Approximately 54% of the cumulative urinary excretion was excreted during the first 24 hours. Estimates of the absorbed dose (2%) underestimates the actual amount absorbed because two of four volunteers were still excreting significant amounts (182 and 183 ug) of triclopyr when urine collections ceased.

7.9 Toxicology Summary

The formulation (Garlon 4) is not acutely toxic but is a slight skin irritant and sensitizer.

Repeated administration of triclopyr at sufficiently high dose levels results primarily in renal toxicity. The data suggests that triclopyr exerts its effect on the organic anion transport mechanism in the kidney tubules and that clearance of the acid via this mechanism is a saturable process. A NOEL of 0.5 mg/kg/day was noted based on the most sensitive parameter measured in a dietary dog study, decreased renal clearance of phenolsulfonephthalein. However, the NOAEL for renal toxicity in the dog was 2.5 mg/kg/day.

The long-term rat study was interpreted as showing equivocal evidence for tumorigenicity. The long term mouse study was considered negative for carcinogenicity and there was an absence of mutagenic activity in all but one of the short-term assays. Overall, the strength of evidence does not support the consideration of carcinogenicity as an endpoint in risk assessment.

In rats, the NOEL for maternal toxicity was <50 mg/kg/day and for embryo/fetoxicity was 100 mg/kg/day. The malformations observed at 200 mg/kg/day could be a manifestation of teratogenic potential in the rat. Studies in the rabbit have not demonstrated teratogenic and fetotoxic effects at dose levels up to 75 mg/kg/day. The NOEL for maternal toxicity was 25 mg/kg/day.

No effect on reproductive performance was noted in rats receiving dietary doses up to 30 mg/kg/day but a reduction in pup body weight gain was the basis for a NOEL of 3 mg/kg/day.

7.10 Occupational Exposure

The registrant submitted an occupational exposure study of workers from a licensed pesticide application company contracted to treat powerline rights-of-way.

The study was conducted in two phases:

1) a dermal deposition and inhalation monitoring phase; and
2) a biological monitoring phase in which cumulative urine samples were collected during day of spraying and the following three days.

Twelve workers, 8 males, 4 females divided into 6 working crews of two, were monitored. Each work crew operated commercial, crew-cab, 4 x 4 trucks equipped with a standard polyethylene spray tank (800 or 1000 L capacity), a pump and a motor. A handgun/hose assembly coupled to the spray tank was used to spray vegetation. Prior to study start, application equipment and chemcial measuring units were calibrated.

The spray formulation was applied at maximum label rates. A latex based drift reducing agent was added to each spray tank batch. Each crew mixed, loaded and applied the herbicide, rinsed measuring devices and containers as they would during a normal work day. One worker applied the formulation by directing the spray away from self while walking through the brush. The other crew member drove the spray-tank vehicle seated in an enclosed cab. The members of each 2 person crew were to change tasks throughout the day so that all individuals included in the exposure assessment participated in all work routines. However, the study records did not allow determination of the amount of active ingredient handled per individual nor was it possible to determine who mixed, loaded or how long each individual drove the spray vehicle or applied the formulation. A typical work day ranged from 7.6-11 hours excluding travelling time to and from the work site.

As per label directions, all operators wore pre-laundered, cotton coveralls over personal garments which typically included a cotton t-shirt, sleeveless top or long-sleeved flannel shirt and denim jeans. Gauntlet-style neoprene rubber gloves were worn while handling, mixing and loading the concentrate. During spraying, most operators wore wrist-length heavy weight vinyl gloves with cloth inners while one continued to wear the gauntlets. Monogoggles were worn during handling and mixing/loading the concentrate. Some workers wore prescription safety glasses with side shields during spray applications. Although not required by the label, respirators (half-face) were worn by 4 workers during mixing/loading tasks. Most workers wore high, steel-toed rubber boots while two wore leather boots. All workers wore hard hats.

Dermal Deposition/Inhalation Monitoring - Results from the dermal deposition/inhalation monitoring were submitted as a draft report with summary tables only. Additional individual data has been requested to allow evaluation and validation of reported results. However, the summary data were used by the Health Protection Branch to derive estimates of systemic exposure from the dermal/inhalation routes.

Dermal deposition was determined from standard hand rinse techniques and monitoring patches located at conventional body areas on the outside and inside of protective clothing.

Inhalation exposure was determined by monitoring the personal breathing zone.

The systemic dosages derived from dermal (hands and body) deposition is shown on Table 1. Deposited doses were adjusted by a 2% dermal penetration factor based on results from the human study.

The estimated systemic dosage from the dermal route ranged from 1 - 30 ug/kg BW/day. The estimated systemic dosage from inhalation exposure ranged from 0.7 - 9 ug/kg BW/day (Table 1). For the majority of workers monitored (7/10), the systemic dosage derived from inhalation exposure was equal to or greater than that derived from dermal deposition. Accordingly, protective measures to reduce inhalation exposure would be important. The estimated total systemic dose (dermal and inhalation) ranged from 2 to 39 ug/kg BW/day.

Biological monitoring - Because human absorption studies (oral and dermal) demonstrated that triclopyr is not extensively metabolized and is primarily excreted in the urine and because appropriate biological monitoring provides a direct estimate of internal dose compared to the indirect dermal deposition technique, exposure estimates derived from the biological monitoring phase were used for risk assessment.

A pre-spray day urine was collected to ensure none of the applicators had previous exposure to triclopyr. Cumulative urines were collected on spray day and 3 days following spray day (total 4 days collection). Appropriate field recovery studies were conducted with spiked urines and all recovery values were close to 100% obviating the need to correct worker urinary measurements. Creatinine values were calculated to ensure urine collection compliance.

Due to problems with urine collection for one individual (substituted water for urine on day of spraying) and the fact that another worker did not participate in all work tasks and failed to provide a complete sample on the last collection day, results from these two workers were omitted from the exposure calculations.

The registrant had developed a pharmacokinetic model from oral and dermal human studies for predicting systemic dose following dermal exposure. However, the amount of triclopyr excreted on spray day from most workers was higher than that predicted by the model, and the registrant only reported systemic doses based on corrected cumulative urinary excretion values. From one worker (J), the registrant noted that modelled data predicted higher values than that measured. For conservative reasons the registrant and the Health Protection Branch used the higher systemic dose derived from the pharmacokinetic model.

Based on urinary excretion, the systemic dosage ranged from 0.51 - 146.6 ug/kg BW/day exposure (see Table 1). Values were corrected for the 20% of the systemic dose which is not excreted via urine. One worker excreted a significantly greater amount of triclopyr than fellow workers. The likelihood of contamination was discounted because excessive excretion of

tirclopyr was observed in at least five different urine samples throughout the collection period for this individual. The large exposure range between individuals most likely reflects differences in tasks performed and the varying amount of active ingredient handled during the typical work day. These biological estimates of exposure should be viewed with caution for the following reasons:

1. Most workers were still excreting active ingredient when urinary collection ceased. For 2 workers the excretion at the last collection was considerable (131 and 91 ug).

2. Urinary creatinine calculations indicate that several workers did not submit complete urine collection near the end of the study.

Taken together, these deficiencies would result in an underestimate of actual exposure. However, from information provided it is reasonable to assume that these exposure values approximate those attained by workers during a typical working day.

TABLE 1. Triclopyr: Estimated Systemic Dosage for Workers Following a Normal Working Day Treating Hydro Rights-of-Way

Worker	Estimated Systemic Exposure (ug/kg BW/day)			Urinary Excretion (ug/kg BW/day exposure)[a]
	dermal[b]	inhalation	total	
A	6	5	11	7.8
B	2	2	4	1.52
C	30	9	39	146.6
D	2	7	9	3.28
E	1	1	2	0.51
F	2	0.7	2.27	3.3
G	2	3	5	7.1
H	12	4.78	16.78	9.7
I	2	6	8	7.74
J	30	4	34	(modelled) 20.1[c]

a. corrected for incomplete excretion via the urinary route
b. corrected for 2% dermal absorption
c. systemic dose derived from pharmacokinetic modelling

Food Exposure - Triclopyr is not being considered for use on any food commodity at this point in time.

Risk Assessment - Triclopyr appears to exert its primary effect on the organic anion transport mechanism in the kidney tubules and clearance of the acid via this mechanism is a saturable process. Renal toxicity of triclopyr is a sensitive parameter for determining adverse effects upon repeated exposure. The 183 day dog study was considered the most relevant study for estimating the margin of safety (MOS) for workers who will experience repeated daily exposure during a full use season (spring to fall). The NOAEL for renal toxicity was set at 2.5 mg/kg/day.

The systemic dosage (from urinary monitoring) for 9/10 workers during right-of-way ground application is 0.02 mg/kg BW/day or less. Based on the NOAEL (2.5 mg/kg BW/day; dog study) for kidney effects, the estimated MOS for the majority of workers handling up to 10 kg active ingredient per day is greater than 125. The MOS was attained for workers who mostly wore maximum protection clothing including new coveralls over personal clothing, neoprene or vinyl gloves, rubber boots, and hard hat. Some workers also wore safety glasses during spraying and some wore respirators during mixing/loading.

One worker attained a very high exposure although the individual was involved in activities similar to others. For such workers an adequate margin of safety is not achieved during a typical work day despite maximum protection measures. Additional risk reduction measures such as training, supervision and medical checks should be required to ensure safety to those individuals.

A carcinogenic risk assessment was not performed although the rat study showed some evidence for tumorigencity. The overall weight-of-evidence was judged to be too weak to warrant the conduct of a formal cancer risk assessment.

There is also some evidence in the rat teratogenicity study for fetotoxic and teratogenic potential at high doses of triclopyr. However, these effects were observed only at maternally toxic levels far in excess of renal toxic dose levels used in the risk assessment. Dose levels which are considered to afford adequate safety for renal toxicity also provide adequate safety to the developing fetus (i.e., based on a NOEL of 100 mg/kg/day from the rat teratology study and the occupational exposure of 0.02 mg/kg/day, a MOS of 5000 for fetotoxicity and potential teratogenic effects would be achieved for most workers.

8. ENVIRONMENTAL ASPECTS: ENVIRONMENT CANADA INPUT

8.1 Summary

Laboratory studies have indicated that triclopyr (the active ingredient of Garlon 4) and its major transformation products have the potential to be persistent in soil, particularly under cool, dry conditions. Also, because of its chemical characteristics, triclopyr has the potential to be mobile in soil (specifically in soils of low organic content). However, a Canadian field study conducted in northern Ontario showed that triclopyr was not excessively persistent and did not leach appreciably in soil following application at proposed label rates for rights-of-way and forestry use. A full assessment of the environmental chemistry and fate of this compound under Canadian field conditions cannot be completed until additional field

dissipation studies in other areas of proposed major use in Canada are submitted for review. Additional data are also required to elucidate the aquatic environmental chemistry and fate of Garlon 4 under Canadian field conditions, particularly at low temperatures and pH's.

Exposure to Garlon 4 at proposed label rates for rights-of-way and forestry use is unlikely to cause direct mortality of wild birds and mammals through acute toxicity. Insufficient data exist to assess the possible effects of chronic residue ingestion through contaminated food. Possible areas of concern are the health and reproduction of small grazing or browsing species exposed to large residue levels in their food. No data were submitted to evaluate the effects on amphibians and reptiles. However, if they are as sensitive as fish, effects could be expected should a shallow water body receive direct overspray. Garlon 4 is not expected to be acutely toxic to honey bees, earthworms or soil microorganisms under conditions of operational use. Garlon 4 has the potential to be moderately toxic to aquatic invertebrates at low temperatures and pH's, and this should be examined in Canadian field studies. The algal growth inhibition study performed with Garlon 4 showed that this compound is likely to pose a hazard to the green algal species Selenastrum capricornutum. The algal study performed with triclopyr acid indicated that this degradation product is not very toxic to S. capricornutum. However since the butoxyethyl ester form will be present for several days in water, an adverse impact is likely to occur on algal species. No data were provided on aquatic vascular species, emergents or terrestrial non-target plants. Because aquatic and emergent plants serve as important food and habitat for wildlife and the risk to this habitat is undefined, Garlon 4 should not be applied near water bodies. Efforts should be made to acquire the data necessary to assess the possible impacts of Garlon 4 on vegetation associated with aquatic habitat.

8.2 Environmental Chemistry and Fate

a) Transformation

The triclopyr butoxyethyl ester hydrolyzes in water and soil to the active ingredient triclopyr. In various soils in the laboratory at 25°C and 75% of 1/3 bar moisture, the DT_{50} for triclopyr ester was found to be less than 4 hours (moisture content at 1/3 bar tension is equivalent to moisture content at field capacity). Hydrolysis of the ester in water is base-catalyzed, and under conditions of low pH and cool temperatures, can be slow (e.g., DT_{50} of 208 days at 15°C and pH 5). Photolysis seems to be the most rapid means of transformation of the ester in the aquatic environment (DT_{50} of 1.5-2.0 days).

Triclopyr is susceptible to photolysis and to transformation by microorganisms, however it resists hydrolysis. The rate of triclopyr transformation in soil is dependent upon the type of soil, the temperature, and soil moisture content. The DT_{50} of triclopyr in laboratory studies ranged from 9.6 days in high organic soil at 35°C and 100% of 1/3 bar moisture (field capacity) to 361 days in low-organic carbon soil at 15°C and 32% of 1/3 bar moisture. However, the DT_{50} was observed to be about 14 days for both sandy and clay soils at approximately 13°C in field plots located in northern Ontario.

The major transformation products of triclopyr in soil, in addition to carbon dioxide, are 3,5,6-trichloro-2-pyridinol and 3,5,6-trichloro-2-methoxypyridine. The DT_{50} of 3,5,6-trichloro 2-pyridinol was observed to be 8-279 days with a mean of 69 days in 15 soils from the U.S. incubated in the dark under aerobic conditions at 25**N**C and 75% of 1/3 bar moisture. In 12 of these soils the DT_{50} was less than 90 days. 3,5,6-trichloro-2 methoxypyridine was observed to have a DT_{50} of 35 to >300 days in three U.S. soils under laboratory conditions. Carbon dioxide was the major degradation product of both of these compounds.

Triclopyr was observed to have an aqueous DT_{50} of 5.4 hours under simulated midsummer conditions in the laboratory. The principal products of photolysis of triclopyr in aqueous solution are 3,5,6-trichloro-2-pyridinol and carbon dioxide. 3,5,6-trichloro-2-pyridinol was shown to photolyze several times more rapidly than triclopyr.

b) Mobility

Triclopyr has a high solubility in water and a low soil adsorption coefficient and therefore has the potential to be mobile in soil. Soil thin-layer chromatography studies have confirmed that triclopyr should be considered as a potentially mobile compound. In field studies conducted over a period of 336 days in northern Ontario, on average 97% of the recovered triclopyr was found within 15 cm of the soil surface at both sandy and clay soil sites. Less than 5% of the measured triclopyr residues were recovered from the 15-25 cm zone in sandy soil following a rainfall event. Additionally, residues of triclopyr in the quantifiable range (0.54 ug/kg) were never detected in soil downslope from plots treated with Garlon 4 at both sandy and clay soil sites. However, the plots sprayed in this study were quite small (2 x 20 m), making it improbable that residues would be detected in soil downslope because of the dilution factor.

A relatively small proportion of triclopyr adsorbed to bottom sediments following the application of Garlon 4 to a small northernOntario lake. Rapid photolysis of triclopyr in the water column and its low potential for adsorption probably explains the observed low adsorption to sediments.

8.3 Environmental Toxicology

a) Expected Terrestrial Exposure

It is expected that the main route of exposure of terrestrial wildlife to triclopyr will be through ingestion of contaminated foliage. Exposure to browsing or grazing species is therefore expected to be higher than for other species. No data were available to assess residue levels of triclopyr immediately after application to either rights-of-way or forested sites. However, such data are available from the experience gained with other herbicides. The following table summarizes the data reported for aqueous formulations of phenoxy herbicides used in forestry. It was felt that residue levels following

applications in oils might not be appropriate in this case. The data are expressed as ppm of residues (wet weight) for each kg of active ingredient per hectare. Each value is the mean value reported for a separate study or site. The amount of overstorey cover was not specified in most cases.

Plant Type	Aerial/Simulated Aerial	Ground
Grass	41 ppm, 65 ppm, 71 ppm 86 ppm, 92 ppm	11 ppm
Mixed grass/forb		60 ppm, 71 ppm
Raspberry/black-berry foliage	129 ppm	61 ppm
Birch leaves/ twigs	138 ppm	
Moss	30 ppm	
Raspberry/black-berry fruit	3.1 ppm	1.4 ppm, 2.7 ppm

It should be noted that grass residue levels may be higher where overstorey cover is sparse. A commonly cited tabulation of crop residue levels currently being used by the U.S. EPA in their hazard assessments gives a maximum grass value of 214 ppm for a 1 kg/ha application. The value given for leaves and leafy crops (112 ppm) is close to the values reported above for shrub and tree leaves. The value for small fruits is also similar at 5.4 ppm.

Under a worst-case situation from the above, browsing wildlife consuming birch leaves and twigs would be exposed to an initial residue concentration of 262 ppm and 524 ppm at the 4 L and 8 L rate of Garlon 4 formulation per hectare respectively. Grazing wildlife may be exposed to initial residue concentrations in grass ranging from 175-350 ppm for forested sites, presumably with some degree of overstorey (4 L and 8 L/ha application given a high of 92 ppm above) and initial residue concentrations ranging from 407-813 ppm in more open sites such as clearings or rights-of-way with little brush overstorey (4 L and 8 L/ha applications and a 214 ppm initial residue level for an application of 1 kg a.i./ha).

Insufficient information exists on residue dissipation to assess the length of exposure. Also, the rate of transformation of the ester to triclopyr on plant surfaces or the palatability of either compound to wildlife species has not been defined which further complicates any assessment of chronic exposure. However, we can predict that exposure will decline more rapidly for wildlife feeding on brush species susceptible to the herbicide because the standing crop of leaves at least should decline rapidly over time. Data reviewed by the U.S. Forestry Service indicate that residues in small fruit and berries may persist for weeks or even months. There are no data with which to assess the length of exposure to grass-eating species.

b) Wild Birds

The acute toxicities of triclopyr and Garlon 4 are presented in the table below:

Species	Compound	Adverse Effects
Mallard Duck	triclopyr	LD_{50} = 1698 mg/kg
	butyl ethyl ester	LD_{50} > 4640 mg/kg
	triclopyr	LC_{50} > 5620 ppm
	butyl ethyl ester	LC_{50} > 10,000 ppm
Bobwhite Quail	triclopyr	LC_{50} = 2935 ppm
	butyl ethyl ester	LC_{50} = 9026 ppm
Japanese Quail	triclopyr	LC_{50} = 3278 ppm

A one-generation reproduction study was conducted on 5 month-old Bobwhite Quail using 100, 200, and 500 mg/kg triclopyr in their diets. The birds were fed treated diets for 11 weeks prior to egg laying and during the 8 weeks of egg laying. Eggshell thickness was significantly ($p<O.Ol$) reduced and 27% fewer eggs were laid compared to the control at 200 mg/kg diet. These effects were not noted at 500 mg/kg diet however.

A one-generation reproduction study was conducted using 6-month old Mallard ducks. Their diet was treated with 100, 200 and 500 mg/kg of triclopyr. The birds were exposed to the treated diets 10 weeks prior to egg laying and for 10 weeks during egg laying. A significant ($p<0.02$) decrease in chick production was observed at both the 200 and 500 mg/kg levels.

Exposure to Garlon 4 is unlikely to cause mortality of wild birds as a result of acute toxicity. Effects from chronic exposure due to ingestion of contaminated vegetation may cause some effects on reproduction at predicted exposure levels.

c) Wild Mammals

Triclopyr is moderately toxic to small mammals when given orally. Results of acute oral toxicity studies using triclopyr and the formulated product, Garlon 4, are shown below:

Compound	Species	LD_{50} (mg/kg)
triclopyr	Rat - female	630
	- male	729
	Guinea pig - male	310
	Rabbit	550
Garlon 4	Rat - female	1318
	- male	1515

Triclopyr and Garlon 4 are of low acute dermal toxicity and are also relatively non-toxic via inhalation; the inhalation LC_{50} of triclopyr is greater than 1.84 mg/L.

No field studies have been conducted on small mammals. Small mammals could be exposed either directly to the spray or by eating contaminated vegetation. The oral ingestion route is thought to be the most important and certainly has the potential to result in a more chronic exposure situation. Toxicity data expressed in mg/kg body weight can be compared to environmental residue levels provided the daily feeding rate of the organism of concern is known. It has been estimated that laboratory rabbits weighing 2.0 kg consume 60 g of dry food/day. [This particular estimate is one that is currently used by the U.S. EPA for their hazard assessment and it has also been used by the U.S. Forestry Service in estimating exposure of wildlife to forestry pesticides.]

If one assumes that a wild rabbit or hare will be consuming grass which is 70% water (an average value for grass), the following rates of toxicant ingestion are obtained:

Expected Residue Level	(From Discussion Above)	Pesticide Ingestion
Forest site,	4 L/ha - 175 ppm	17.5 mg/kg body weight/day
	" 8 L/ha - 350 ppm	35.0 " "
'Open' site,	4 L/ha - 407 ppm	40.7 " "
	" 8 L/ha - 813 ppm	81.3 " "

Given LD_{50} data provided above, we do not expect Garlon 4 to cause direct mortality of herbivorous mammals. Based on a summary of subchronic and reproductive studies provided by the U.S. Forestry Service [the studies on which these summaries were compiled were not reviewed by Environment Canada], some sublethal effects such as decreased body weight, reduced liver weights as well as reduced kidney excretion may occur if exposure is prolonged. Increased maternal mortality of pregnant rabbits was seen at doses as low as 25 mg/kg body weight/day administered between the 6th and 18th days of gestation and an impact on wild lagomorphs may therefore be the most likely impact of this herbicide. However, no teratogenic effects were seen from levels as high as 100 mg/kg/day.

d) Amphibians and Reptiles

No data were available to evaluate the risk to amphibians and reptiles from the use of Garlon 4. Triclopyr ester is highly toxic to fish at concentrations that could result from a direct overspray to a shallow water body. Toxicity to amphibians and reptiles would depend on their sensitivity relative to fish and the length of time exposed to the more toxic ester form. Triclopyr ester is transformed to triclopyr, the rate depending on pH, temperature and other factors discussed above.

e) Aquatic Organisms

The 24 and 48-hour LC_{50}s of triclopyr to Daphnia magna were reported as 203.3 and 132.9 mg/L respectively. The temperature was 25°C and the pH was 7.6 in these studies. Triclopyr ester was more toxic than triclopyr acid with a reported 48-hour LC_{50} value of 10.1 mg/L and an LC_{10} value of 3.95 mg/L. Temperature of the test was 17°C and pH was 7.9. In another study using the formulated product, Garlon 4, the 48-hour LC_{50} was 2.2 (1.2-3.3) mg/L. Temperature of this test was 20°C and pH was 8.0.

If Garlon 4 is directly applied to a water body 0.5 m in depth, the resulting environmental concentration in the water column would be 0.77 mg a.i./L. Risk to aquatic invertebrates will depend on the length of exposure to the ester form, which is more persistent at low temperature and pH. In alkaline water, Garlon 4 is not expected to be toxic to aquatic invertebrates.

f) Terrestrial Invertebrates

Triclopyr and the butoxyethyl ester derivative are non-toxic to bees, the contact LD_{50}'s being >100 ug/bee.

The growth of six species of soil microorganisms was not affected after exposure to 500 mg/kg triclopyr using an agar petri dish method.

In laboratory studies using artificial soil, the 7 and 14-day LC_{50}s of Garlon 4 to the earthworm Lumbricus terrestris were reported as 910 and 430 mg/kg respectively. The no observed effect level (NOEL) based on the mortalities and weight gain data observed in these studies was 200 mg/kg. These results indicate that Garlon 4 is not expected to be toxic to earthworms under conditions of normal operational use.

g) Wildlife Habitat Considerations

Two algal growth inhibition studies were submitted for review. Triclopyr acid does not appear to be very toxic to the green algae Selenastrum capricornutum. The EC_{50} estimated from the regression analysis was 42-45 mg/L. However the NOEL was 0. The estimated environmental concentration (EEC), is calculated as if a worst case scenario is assumed where the pesticide is directly applied to a small pond, and the pesticide remains in the water column. The concentration assumed is usually in 15 cm depth (0.5 ft by US EPA, in Urban & Cook 1986). The calculated EEC for triclopyr is 2.56 mg/L and the calculated hazard is .06 (2.56/42).

The second algal study was performed with Garlon 4. In water the ester form has a half-life of 1.5 to 2.0 days and longer if temperature and pH are low. The ester form appears to be much more toxic to fish and aquatic invertebrates, than it is to the green algae Selenastrum capricornutum. The EC_{50} calculated from the data provided is 6.0 mg/L (61.3 active ingredient). The EC_{50} hazard assessment was .69 (2.56/3.7) and 3.0 (2.56/.85) when calculated with the NOEL. Because the butoxyethyl ester will be present several days after application, it is likely that Garlon 4 will pose an unacceptable hazard to algae.

The two algal studies could not be thoroughly evaluated since no raw data were provided. The initial cell number was too high in both studies, starting at 20,000 while EPA recommends 3000; pH was generally too low especially at concentration 100 mg/L of triclopyr acid; no actual chemical concentrations were measured.

No data were submitted to evaluate the effect of Garlon 4 on aquatic vascular and upland vegetation. The need for data on the potential impacts on aquatic vascular plants is closely linked to the possibility that this product will move from the site of application although accidental overspray of small wetlands is also likely in the course of operational use. Use of this product in roadside ditches or other rights-of-way may likewise present a hazard to receiving wetlands if the compound moves away from sites of application.

In terrestrial habitats, the main consequences of using Garlon 4 in forests will be the removal of the shrub layer and this may influence the pattern of wildlife use of the area. Based on research carried out on other herbicides in forest environments, we can predict that the main impact will be on those species that depend on hardwood browse and that have limited home ranges. Impacts are likely to be more severe in the winter when hardwood browse is the main food consumed by a number of species. Examples of those species are Snowshoe Hares and Ruffed Grouse. Larger browsing species such as deer and moose may be affected locally depending on the size and placement of the spray blocks. The added effect of herbicide
treatment is probably small in comparison to the initial impact of clear-cutting. Most of the shifts in species composition will have taken place following the logging operations. Also, it has been argued that, on a national scale, there is an excess of hardwood browse as a result of back-logged areas that have not been replanted to softwood species.

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

9.1 Fish

Triclopyr butoxyethyl ester, the active ingredient in Garlon 4, hydrolyzes to the herbicidally-active product, triclopyr acid. Triclopyr ester and triclopyr acid exhibit different toxicities to fish.

Species	96-h LC_{50} (mg/L) Triclopyr Ester	Triclopyr Acid
Bluegill sunfish	0.87	148
Rainbow trout	0.74	117
Fathead minnow	2.2	---
Coho salmon	1.3	---

The 96 h LC_{50} for Garlon 3A (triethylamine salt of triclopyr acid as the active ingredient) for Rainbow trout is 240 mg/L.

McCall et al. (1988) have explained the difference in fish toxicity as being the result of different rates of uptake of the ester and acid. In the absence of any environmental dissipation of the ester, the authors estimated the bioconcentration factor at 400 for the ester as compared to 0.5 for the acid. The ester, therefore, is taken up rapidly by the fish; then it is metabolized to the acid which increases in concentration to toxic levels within the fish.

The toxicity of Garlon 4 and technical ester to Coho salmon are illustrated below:

96-h LC_{50} [mg/L (ester)] Coho Salmon

Toxicant	pH of Water	Alevins	Juveniles
Garlon 4	7.8	0.26	1.3
Technical ester	7.8	0.31	1.3
Garlon 4	6	0.18	0.86

The above results suggest that the components of the formulation do not alter the toxicity of the ester to fish. The toxicity to fish, however, may be dependent on the pH of the water.

Short term sublethal effects have been observed in Coho salmon fry exposed to Garlon 4 in flow-through tanks for 96 h. At concentrations of 0.03 and 0.10 mg/L (ester), fry became very sensitive to photoperiod changes as indicated by increases in activity. The fry became less active and more lethargic at concentrations of 0.32 and 0.42 mg/L. As well, at 0.42 mg/L the fry became highly stressed and oxygen uptake increased compared to controls; gill irritation was also noted by occurrences of gill flairing and coughing.

Bioaccumulation of triclopyr ester has been investigated in Coho salmon. The ester is absorbed rapidly by the fish, metabolized and residues eliminated. Based on total residues and the initial water concentration, the maximum concentration factor was 115. Following 54 hours of depuration in freshwater, the total residue level in fish was <1% of the maximum total residue level.

To address the influence of environmental factors on the persistence of the ester in water, field studies have been conducted at the University of British Columbia Research Forest and at Hearst, Ontario. At the UBC site, Garlon 4 was applied at the high rate of 8.6 kg ester/ha (2.3 times the maximum labelled rate) to a stream 30 cm deep. Preliminary reports were that the test fish became stressed and would be susceptible to predation in a real situation or carried downstream out of the system. Ten percent mortality of Rainbow trout was observed 24 h post-treatment. The preliminary report on fish mortality at Hearst (rate of Garlon 4 application was not given) indicated that there was no statistical difference in the high fish mortality observed in both the treatment and control sites. Final reports of these studies have not been received by the Department of Fisheries and Oceans.

9.2 Fish Habitat

The 48 h LC_{50} of Garlon 4 to Daphnia magna, an indicator of the potential impact of Garlon 4 on fish food, was determined as 2.2 mg/L (ester). The no-adverse-effect-level was <0.7 mg/L (ester) (pH 7.8-8.4). In comparison, the 48 h LC_{50} of the acid to D. magna was quoted as 132.9 mg/L.

In the UBC study, five percent mortality of caged mayflies and stoneflies was observed 24 h post-treatment.

The Department of Fisheries and Oceans has conducted a review of five-day toxicity tests of triclopyr acid and Garlon 4 to the green alga Selenastrum capricornutum. Because of deficiencies in the studies, the results are not definitive, however, they do provide an indication of the relative toxicity of the Garlon 4 and triclopyr acid to algae. As occurred with the fish and D. magna, the alga is more sensitive to the ester (as contained in Garlon 4) than to acid. From the available results, growth inhibition was calculated to be minimal (about 4%) when the alga was exposed to the acid at $\leq$7.8 mg/L nominal concentration. Similar levels of inhibition occurred at 0.9 mg/L (nominal concentration of the ester) following exposure to Garlon 4. Confirmation of these results are required. Differences in toxicity may be the result of varying rates of uptake as indicated by the K_{ow} of the acid (0.205) and the ester (12300).

No data on the impact of Garlon 4 on aquatic macrophytes have been submitted.

9.3 Movement Into and Transformation in Aquatic Environments

Garlon 4 is intended for ground and aerial application to control woody plants and broadleaf weeds in forest site preparation and conifer release programs. Contamination of surface waters can result from spray drift, runoff, or by direct deposit as the result of an overspray.

Laboratory studies have indicated that triclopyr ester, applied to soil, will undergo rapid transformation to the acid (e.g., >80% transformation of ester to acid within 6 h at 25°C and 75% 1/3 bar moisture). Triclopyr acid may be susceptible to runoff to aquatic systems because of its high solubility in water (435 mg/L) and its low soil sorption coefficient (K_{oc} = 27). Runoff of triclopyr as the ester is less probable because of its lower solubility in water (23 mg/L), its higher sorption coefficient (K_{oc} = 640-1780), and its rapid transformation to the acid.

Transformation of the triclopyr acid is slower under waterlogged conditions than under aerobic conditions.

	Half-Life of Applied Triclopyr Acid (Days)	
Soil	Aerobic Flask	Waterlogged Flask*
1] Loam, ph 6.6 % O.C. = 0.86	18	130
2] Silty Clay Loam pH 5.2, % O.C. = 2.10	8	42

* 60-75% of applied acid partitioned to the water

Ester transformation in water occurs primarily by photolysis to the acid with a half-life of 1.5-2 days. Ester hydrolysis is not significant with half-lives at 15°C of 208 d at pH 5 and 26 d at pH 7 (typical stream pH are: British Columbia - pH 6.4-7.0, Nova Scotia - pH 4.5-5.5, New Brunswick - pH 5.5-6.5). The triclopyr acid also resists hydrolysis (no change in concentration after 9 months at pH 5, 7, 8), but is susceptible to photolysis with a laboratory photolytic half-life of 5.4 h. The main transformation product of the acid is 3,5,6-trichloro-2-pyridinol which is also susceptible to photolysis.

9.4 Impact Assessment

The results of the toxicity studies demonstrate that the triclopyr ester is more toxic to aquatic flora and fauna than the triclopyr acid. Because of the rapid transformation of the ester to the acid in terrestrial habitat, the greatest risk to fishery resources is associated with the deposit of the ester into aquatic habitat by spray drift or direct overspray. Under a feasible, worst case scenario (Coho salmon rear commonly in areas with a water depth of 10 cm and minimal flow), an expected environmental concentration of triclopyr ester from a direct overspray [label maximum application rate of 8 litres of Garlon 4 per hectare (3.84 kg ai./ha)] would be 3.84 mg/L (ester) in a stream 10 cm deep. Based on laboratory studies, this concentration of ester would be sufficient to severely affect fish, aquatic invertebrates, and algae. These studies do not take into account environmental dissipation factors such as photolysis, hydrolysis, or dilution due to flow. Although important, the effect of these factors can be reduced by environmental conditions, such as heavy cloud or vegetation cover; low pH; or minimal flow, that affect the dissipation of the ester. The duration of exposure from the triclopyr ester may, therefore, be sufficient to affect fish and fish habitat.

The aerial application of Garlon 4 increases the possibility of the direct deposit of the triclopyr ester into aquatic systems with the result that the risk to fishery resources could be significant. Conclusions about the risk to fishery resources of the aerial application of Garlon 4 cannot be reached, however, until the final reports of the UBC and Hearst studies are received and reviewed. Ground application of Garlon 4 reduces the risk to fishery resources due to the lower likelihood of contaminating nearby aquatic systems. Provided that the necessary precautions to avoid drift of the herbicide into aquatic systems and/or its riparian vegetation are observed, the risk to fishery resources from the ground application of Garlon 4 on industrial rights-of-way would be minimal.

9.5 Reference

McCall, P.J.; Laskowski, D.A.; and Bidlack, H.D. (1988). Simulation of the Aquatic Fate of Triclopyr Butoxyethyl Ester and its Predicted Effects on Coho Salmon. Environ. Toxicol. Chem. 7: 517-527.