Proposed Re-evaluation Decision PRVD2010-17

Clopyralid

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Overview

Proposed Re-evaluation Decision for Clopyralid

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

An evaluation of available scientific information found that, under the proposed conditions of use, clopyralid products have value in the food and crop industry and do not present unacceptable risks to human health or the environment.

The PMRA's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health and the environment.

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

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

The information is available in two parts. This Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessment of clopyralid. A full copy of the Science Evaluation section is available upon request through Publications.

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

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

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

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration[2]. The Act also requires that products have value[3] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies hazard and risk assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive subpopulations in both humans (e.g. children) and organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA section of Health Canada's website at www.pmra-arla.gc.ca.

Before making a re-evaluation decision on clopyralid, the PMRA will consider all comments received from the public in response to this consultation document[4]. The PMRA will then publish a Re-evaluation Decision document[5] on clopyralid, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

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

What is Clopyralid?

Clopyralid is a selective systemic broadleaf weed herbicide. It is registered for post-emergence use on terrestrial food crops, terrestrial feed crops, industrial oilseed and fibre crops, forest and woodlands, ornamental outdoors, and industrial and domestic vegetation control for non-food sites. Clopyralid may be used alone to control broadleaf weeds or in co-formulation with MCPA or flumetsulam to control both broadleaf and grassy weeds. It is applied once or twice per year at a rate of 75 to 298.8 g a.i./ha by ground equipment only.

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2 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*

3 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

4 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*

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

Health Considerations

Can Approved Uses of Clopyralid Affect Human Health?

Clopyralid is unlikely to affect your health when used according to the label directions.

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

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

Clopyralid is of low toxicity by the oral, inhalation and dermal route in laboratory animals. It is severely irritating to the eyes, non-irritating to skin, and non-sensitising. Clopyralid did not cause cancer in animals and was not genotoxic. There was also no indication that clopyralid caused damage to the nervous system and there were no effects on reproduction. The first signs of toxicity in animals given daily doses of clopyralid over longer periods of time were effects on body weight, the stomach and the liver. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

When clopyralid was given to pregnant animals, effects on the developing fetus were observed at doses that were toxic to the mother. In particular, an increase in hydrocephaly in rabbit fetuses occurred at a maternally toxic dose. Consequently, extra protective measures were applied during the risk assessment to further reduce the allowable level of human exposure to clopyralid.

Residues in Water and Food

Dietary risks from food and water are not of concern.

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

Human exposure to clopyralid was estimated from residues in treated crops and drinking water, including the most highly exposed subpopulation (e.g., infants and children 1 to 2 years old).

This aggregate exposure (i.e., to clopyralid from food and drinking water) represents less than 6% of the acute reference dose and less than 13% of the chronic reference dose.

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

MRLs for clopyralid are currently specified for barley, blueberries, broccoli, cabbages, cauliflower, Chinese broccoli, Chinese mustard cabbages, kohlrabi, napa Chinese cabbages, oats, strawberries, wheat, cattle, goats, hogs, horses, poultry, sheep, eggs, and milk or processed foods derived from these foods. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. Details regarding MRLs for clopyralid can be found in the Science Evaluation section of this consultation document.

Non-Occupational Risks From Clopyralid

Clopyralid is not registered for use in residential areas, thus a residential risk assessment was not required.

Aggregate risk from exposure incurred as a patron of a "Pick Your Own" facility is not of concern.

Dermal exposure to clopyralid residues during a pick-your-own operation was considered to be negligible and not of concern, thus an aggregate dermal and oral pick your own risk assessment was not required.

Occupational Risks From Handling Clopyralid

Occupational risks are not of concern.

Risk estimates associated with mixing, loading and applying activities are not of concern and additional personal protective equipment (PPE) are not required beyond what is currently specified on the label.

Post-application risks are not of concern.

Risks to workers entering crops treated with clopyralid are not of concern. The minimum 12 hour restricted entry interval (REI) is proposed for all uses.

Environmental Considerations

What Happens When Clopyralid Is Introduced Into the Environment?

Clopyralid poses a potential risk to non-target terrestrial plants therefore additional risk reduction measures need to be observed.

When clopyralid is released into the environment some of it can be found in soil and surface water. Clopyralid in soil or water is not susceptible to hydrolysis or phototransformation. However, it breaks down through microbial transformation with carbon dioxide being the only major transformation product. Clopyralid is non-persistent to persistent in soil and water.

Clopyralid is very soluble in water and does not adsorb strongly to soils and therefore may leach into groundwater and enter surface water in run-off. Water monitoring has revealed clopyralid residues in groundwater as well as surface water. Clopyralid is not expected in the air because of its low volatility and has low potential for bioconcentration in biota.

Clopyralid, when used according to label directions, does not present a risk to earthworms, bees, beneficial arthropods and other insects, small mammals, birds and aquatic organisms. However, clopyralid may pose a risk to some non-target terrestrial plants. In order to minimize the potential exposure to plants, spray buffer zones will be required. The width of these spray buffer zones will be specified on the product label.

Value Considerations

What is the Value of Clopyralid?

Clopyralid contributes to weed management in a variety of crop and non-crop sites when used in accordance with the label directions.

Unlike other auxin-mimics, clopyralid can be applied to many broadleaf crops. It controls many troublesome perennial broadleaf weeds including Canada thistle, dandelion and perennial sowthistle. It can be co-formulated or tank mixed with many other herbicides to broaden weed control spectrum. Clopyralid is the only post-emergence broadleaf herbicide registered for use in Canada on cole crops (cabbage, cauliflower, broccoli, Brussels sprouts, rutabaga, Chinese cabbage, radish, kohlrabi and mustard cabbage). Furthermore, it is the only alternative post-emergence broadleaf herbicide to bentazon in highbush blueberry, and to 2,4-D in cranberry and strawberry (harvest year, renovation). Other non-selective post-emergence herbicides are registered for use on shelterbelts, however, clopyralid is the only selective post-emergence herbicide registered for this use. When used in rotation with active ingredients from other herbicide groups, clopyralid plays a role in mitigating resistance development in weeds.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions are required by law to be followed.

Although no risk of concern were identified, measures in addition to those already identified on existing clopyralid product labels, are required to further protect human health and the environment. The following additional key risk-reduction measures are being proposed.

Additional Key Risk-Reduction Measures

Human Health

- A restricted entry interval to protect workers entering treated sites
- Statements for personal protective equipment are updated and standardized between the product labels
- A statement clarifying that product is not to be used in greenhouses
- A statement to promote best management practices to minimize human exposure from spray drift or spray residues resulting from drift

Environment

- Additional advisory label statements and specification of buffer zones to protect non-target terrestrial plants
- Advisory label statements to indicate that the use of clopyralid may result in contamination of groundwater and surface water through leaching and runoff, respectively

What Additional Scientific Information is Being Requested?

Data Requirements (Section 12) Related to Chemistry

DACO 2.13.4 **Impurities of Human Health or Environmental Concern**
The applicant must provide analytical data from at least five recent batches of the products for hexachlorobenzene, pentachlorobenzene and tetrachlorobenzenes (three isomers) from a GLP-compliant or government-accredited laboratory. The analytical method(s) used must utilize the lowest practical limits of quantitation and be fully specified, either by reference to a standard method or by inclusion of a detailed description together with validation data.

Next Steps

Before making a re-evaluation decision on clopyralid, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision Document, which will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

At the time of the re-evaluation decision, registrants will be asked to submit information to confirm or refine the current risk assessment.

Other Information

At the time that the re-evaluation decision is made, the PMRA will publish an Evaluation Report on clopyralid in the context of this re-evaluation decision (based on the Science Evaluation section). In addition, the test data on which the decision is based will also be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

1.0 Introduction

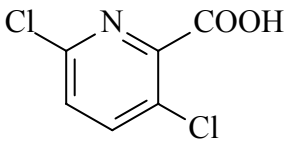
Clopyralid is a selective "auxin mimic" or "synthetic auxin" herbicide. It belongs to the carboxylic acid chemical family and is classified as a Group 4 herbicide. It mimics the plant growth hormone auxin, indole acetic acid (IAA), inducing characteristic auxin-type responses in susceptible broadleaved plants and resulting in uncontrolled or deregulated plant growth that leads to plant death.

Following the re-evaluation announcement for clopyralid, Dow AgroSciences Canada Inc., the registrant of the technical grade active ingredient (TGAI) and primary data provider in Canada, in coordination with BASF Canada Inc., the other registrant of clopyralid end-use products (EPs), indicated that it intended to provide continued support for all uses included on the label of Commercial Class EPs. There are no Domestic Class EPs containing clopyralid in Canada.

2.0 The Active Substance, Its Properties And Uses

2.1 The Technical Grade Active Ingredient, Its Properties and Uses

Identity of the Technical Grade Active Ingredient.

Common name	Clopyralid
Function	Herbicide
Chemical Family	Pyridinecarboxylic acid
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	3,6-dichloropyridine-2-carboxylic acid
2 Chemical Abstracts Service (CAS)	3,6-dichloro-2-pyridinecarboxylic acid
CAS Registry Number	1702-07-6
Molecular Formula	$C_6H_3Cl_2NO_2$
Structural Formula	
Molecular Weight	192.0

Registration Number	Purity of the Technical Grade Active Ingredient
18315	95% (92.2-99.0%)
25296	80.8% (70.7-86.0%)

Identity of relevant impurities of human health or environmental concern:

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are expected to be present in the product.

Hexachlorobenzene and pentachlorobenzene are present in the TGAI. The registrant for Lontrel T and Lontrel F provided 5 batch data for hexachlorobenzene (HCB) and pentachlorobenzene (QCB). The levels found in Lontrel T are: 0.34-3.1 ppm HCB and 0.16-1.7 ppm QCB and in Lontrel F: 0.04-2.05 ppm HCB and 0.01 ppm for QCB. Data for tetrachlorobenzenes, which can reasonably be expected to be present in these products, were not provided. Based on the manufacturing process used, other impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result*	Interpretation
Vapour pressure at 25°C	1.36 mPa*	Low to Intermediate volatility
Ultraviolet (UV)/visible spectrum	Minimal absorbance at λ >300 nm (absorbance maxima at 198, 224, 282 nm)	Unlikely to undergo direct phototransformation
Solubility in water at 20°C	pH — Solubility (g/L)* Dist Water — 7.85 5 — 118 7 — 143 9 — 157	Very soluble
n-Octanol/water partition coefficient (log Kow)	pH — Log K_{ow}* 5 — -1.81 7 — -2.63 9 — -2.55 1.07 (unionised, 25°C)	Unlikely to bioaccumulate in biota

Property	Result*	Interpretation
Dissociation constant (pKa)	pKa=2*	Dissociation in solution to form anion and acid

*From e-Pesticide Manual

2.2 Description of Registered Clopyralid Uses

Appendix I lists all clopyralid products that are registered under the authority of the *Pest Control Products Act*, specifically including two technical grade active ingredients (TGAI), two manufacturing concentrates (one contains clopyralid alone and the other contains clopyralid, 2,4-D acid and flumetsulam) and eleven Commercial Class products. Of the Commercial Class products, three contain clopyralid alone while the remaining eight are co-formulated with MCPA (six products) or flumetsulam (two products).

Appendix II lists all the uses for which clopyralid is presently registered. All uses were supported by the registrants at the time of initiation of re-evaluation and were, therefore, considered in the health and environmental risk assessments. Also presented is whether any of the uses were added through the Pest Management Regulatory Agency's User Requested Minor Use Label Expansion (URMULE) Program. While currently supported by the registrants, the data supporting these minor uses was originally generated by a user group as well as the registrant(s).

Uses of clopyralid belong to the following use site categories: terrestrial food crops, terrestrial feed crops, industrial oilseed and fibre crops, forest and woodlands, ornamental outdoors and industrial and domestic vegetation control for non-food sites.

3.0 Impact on Human and Animal Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels where no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species. The health effects noted here were observed in animals at dose levels at least 100-fold (often much higher) above levels to which humans are normally exposed through use of products containing this chemical. See Appendix III for the toxicological profile of clopyralid.

3.1 Toxicology Summary

Oral metabolism/excretion studies in the rat with radio-labelled clopyralid indicated rapid absorption and excretion. Urinary excretion was the primary route of elimination with 73-97% of the administered dose (AD) eliminated in urine within 24 hours of dosing. Seventy two hours following dosing, 74-98% of the AD was found in urine, 10-22% in cage washes, and 1-5% in faeces. Clopyralid was distributed widely in the tissues and tissue residues were low (<0.01% AD). There was no evidence of metabolism as only unchanged clopyralid was detected in the urine and most of the radioactivity in the faeces was also unchanged clopyralid.

In acute toxicity studies, clopyralid was of low toxicity by the oral and inhalation route in the rat and the dermal route in the rabbit. It was severely irritating to the rabbit eye, non-irritating to the rabbit skin, and non-sensitising in guinea pigs.

In a 21-day dermal rabbit study, there were no treatment-related systemic effects but there were signs of minimal dermal irritation. In 90-day studies in the rat and mouse, there were reductions in body weight gain and/or body weight, and an increase in relative liver weights. The mouse liver showed an increase in the size of the centrilobular hepatocytes and altered tinctorial properties. In the rat study, there were increases in the relative kidney weight and stomach lesions (slight irregularities and accentuations of the limiting ridge). Six-month and 1-year dog studies also showed an increase in relative liver weights with further increases in relative heart and kidney weights at the highest dose tested. The major findings in the 1-year dog study were a reduction in haematological parameters and vacuolation of adrenal cortical cells.

In the chronic studies in the mouse, there were no major toxic effects. There was a reduction in body weight, body weight gain and food efficiency. In the chronic studies in the rat, there were lesions in the gastric limiting ridge of the stomach (epithelial hyperplasia and thickening), as well as other stomach lesions (chronic active inflammation, increased incidence of mononuclear cell aggregates in the stomach mucosa). There were reductions in body weight, body weight gain and food consumption. There was also an increase in liver and kidney weights.

All of the *in vivo* and *in vitro* genotoxicity studies were negative. These included Ames reverse mutation tests, a CHO/HGPRT gene mutation assay, an *in vitro* chromosomal aberration assay with rat lymphocytes, an unscheduled DNA synthesis assay with primary rat hepatocytes, a dominant lethal assay in rats, an *in vivo* chromosome aberration assay in rats, *in vitro* and *in vivo* host mediated mutation assays with *Salmonella* and *Saccharomyces* strains, and a mouse bone marrow micronucleus test.

In a developmental toxicity study in the rat, maternal toxic effects included increased mortality, reduced body weight and body weight gain, and reduced food consumption. There were no significant developmental effects. In the rabbit, maternal toxic effects included increased mortality, reduced body weight and body weight gains, some clinical signs (laboured breathing, rales, shallow respiration, coughing), and histopathologic lesions of the gastric mucosa. The main developmental effects in the rabbit included a reduction in fetal body weight and an increase in hydrocephaly at the high dose. The increase in hydrocephaly, which occurred at a maternally toxic dose, was not statistically significant, but exceeded historical controls.

In a 2-generation reproduction study in the rat, effects on the offspring included reduced pup weights and increased pup liver weights. Parental toxicity effects included slight focal hyperkeratotic changes in the non-glandular mucosa of the stomach or small lesions in the forestomach in a few animals, reduced body weight and body weight gain, and reduced food consumption. There were no treatment-related effects on reproduction.

No specific neurotoxicity studies were conducted, however the parameters measured in the studies that were conducted did not indicate the presence of specific neurotoxic effects.

There were no dose-related increases in tumours in either mouse or rat chronic oncogenicity studies. Clopyralid was not considered to be oncogenic.

PCPA Hazard Consideration
For assessing risks from potential residues in food or from products used in or around homes or schools, the PCPA requires the application of an additional 10-fold factor to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children as well as potential pre- and post-natal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database, no additional studies are required at this time. Data available on clopyralid included a reproductive toxicity study in rats, a developmental toxicity study in rats and a developmental toxicity study in rabbits.

With respect to potential pre- and post-natal toxicity, sensitivity of the young was not noted in the reproductive study, nor were there significant developmental effects in the rat developmental toxicity study. In the developmental toxicity study in rabbits, an increase in hydrocephaly at the high dose occurred at a maternally toxic dose. The increase was not statistically significant, but it exceeded historical controls.

Overall, the database is adequate for characterizing pre- and post-natal toxicity. There is a concern for hydrocephaly findings in the rabbit fetus as this is a serious effect; however this concern was tempered by the presence of severe maternal toxicity at the same dose level. Therefore the PCPA factor was reduced to 3-fold for both acute and repeat exposure scenarios when using the rabbit developmental toxicity assay for risk assessments for populations including females 13-49. Other reference doses were sufficiently low so as to provide considerable inherent protection of all populations including females 13-49 and the PCPA factor in these cases was reduced to 1-fold. See Appendix IV for the toxicological endpoints for clopyralid.

3.2 Occupational and Non-Occupational Risk Assessment

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

3.2.1 Toxicology Endpoint Selection for Occupational Risk Assessment

3.2.1.1 Short-term and intermediate-term dermal and inhalation risk assessment

To estimate the risk from short-term and intermediate-term dermal and inhalation exposure, a NOAEL of 110 mg/kg bw/day for developmental toxicity from a developmental toxicity study in the rabbit (based on the occurrence of hydrocephaly at 250 mg/kg bw/day) was considered. Although this study used an oral route of exposure, the existing 21-day dermal study did not assess developmental endpoints. Standard uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability were applied. As the worker population could include pregnant females, it was necessary to ensure adequate protection of the fetus who may be exposed via their mother. In light of concerns regarding pre-natal toxicity (as outlined in the PCPA section), an additional 3-fold factor was applied to this endpoint to protect for a sensitive subpopulation (namely women 13-49 years of age). A target MOE of 300 was established.

3.2.1.2 Dermal Absorption

In the absence of a specific dermal absorption study, dermal absorption was assumed to be equivalent to oral absorption (i.e. 100%).

3.2.2 Occupational Exposure and Risk Assessment

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

3.2.2.1 Mixer, Loader and Applicator Exposure and Risk Assessment

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

- Mixing/loading emulsifiable concentrates
- Mixing/loading soluble granules
- Loading granules
- Groundboom application
- Right-of-way sprayer application
- Solid broadcast spreader application
- Mixing/loading/applying by backpack
- Mixing/loading/applying by low pressure handwand

Based on the number of applications, workers applying clopyralid would generally have a short- to intermediate term (1 day to several months) duration of exposure. The PMRA estimated handler exposure based on the following level of personal protection:

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

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

Occupational risk estimates associated with mixing, loading and applying clopyralid exceeded the target MOE at baseline PPE. Therefore, risk to workers handling clopyralid was not of concern.

3.2.2.2 Post-application Worker Exposure and Risk Assessment

The post-application occupational risk assessment considered exposures to workers entering treated crops. Based on the clopyralid use pattern, there is potential for short- to intermediate-term (1 day to several months) post-application exposure to clopyralid residues for workers.

Dislodgeable foliar residue (DFR) values and activity specific transfer coefficients (TC) were used to estimate post-application exposure resulting from contact with treated crops at various times after application. DFR data include the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant. A TC is a factor that relates worker exposure to transferrable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples, scouting late season corn) and reflect standard agricultural work clothing worn by adult workers. Post-application exposure activities include scouting and irrigating.

For workers entering a treated site, restricted entry intervals (REIs) are calculated to determine the minimum length of time required to reach target MOEs. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE (i.e. > 300 for short to intermediate -term dermal exposure scenarios for clopyralid).

Four DFR studies conducted on conifers, sugar beets, cereal grain and corn were submitted to the PMRA. In these studies, peak DFR values ranged from 14-22% of the application rate with half-lives ranging from 0.2 to 3.6 days. These data were considered along with standard transfer coefficients to derive estimates of post-application exposure and appropriate restricted entry intervals.

All post-application scenarios had MOEs that were above the target MOE on the day of application and therefore are not of concern. Mitigation beyond the minimum 12 hour REI is not required.

3.2.3 Non-Occupational Exposure and Risk Assessment

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

3.2.3.1 Residential Exposure and Risk Assessment

Clopyralid is not registered for use in residential areas, therefore a residential risk assessment was not required.

3.2.3.2 Post-Application Non-Occupational Exposure and Risk Assessment

"Pick Your Own" (PYO) farms are those that allow the public to harvest their own fruits and vegetables. As PYO fruit and vegetable operations become more and more prevalent, the PMRA recognizes the need for a means of assessing exposure to pesticides during hand-harvesting by members of the public. For the purpose of this risk assessment, "Pick Your Own" facilities are considered commercial farming operations that allow public access for harvesting in large-scale fields or orchards treated with commercially labelled clopyralid products.

Clopyralid is a selective herbicide used to control broadleaf weeds. Since any residues contacting the foliage of broadleaved crops, such as berries, may damage the crop, application is usually directed towards broadleaved weeds between the rows and not on the growing crop. In addition clopyralid is also applied early in the season (with long preharvest intervals (PHI) of 30 days – 10 months), and has a short half-life (0.2 - 3.6 days), so any potential residues that may be on foliage would be negligible by harvest. Therefore dermal exposure to clopyralid residues during a pick-your-own operation was considered to be negligible.

3.3 Dietary Risk Assessment

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

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

Residue estimates used in the dietary risk assessment (DRA) may be conservatively based on the maximum residue limits (MRL) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program (PDP).

Clopyralid acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.14), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

The dietary risk assessment considered exposure from domestic and imported foods and drinking water. Residue estimates for plant and animal commodities were based on MRLs and/or U.S tolerance levels. Default processing factors and 100% crops treated were assumed.

For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendix VI and VII.

3.3.1 Determination of Acute Reference Dose (ARfD)

Females aged 13-49:

To estimate acute dietary risk (1 day) for females aged 13-49, a NOAEL of 110 mg/kg bw/day for developmental toxicity from a developmental toxicity study in the rabbit (based on the occurrence of hydrocephaly at 250 mg/kg bw/day) was considered. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability are used. A PCPA factor of 3-fold was applied to account for the serious effect in the presence of significant maternal toxicity yielding a composite assessment factor of 300.

$$\textbf{ARfD} = \frac{\textbf{110 mg/kg bw/day}}{\textbf{300}} = \textbf{0.37 mg/kg bw}$$

General Population (excluding females aged 13-49):

To estimate acute dietary risk (1 day) for the general population, a NOAEL of 75 mg/kg bw/day for maternal toxicity from a developmental toxicity study in the rat (based on decreased maternal body weight gain and food consumption during gestation days 6-9 at 250 mg/kg bw/day) was considered. Since the decreased maternal body weight and food consumption is observed during an acute exposure scenario (i.e. gestation days 6-9), this effect was considered relevant to derive the ARfD. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability are used. The PCPA factor was reduced to 1-fold based on the completeness and quality of the database, and given that prenatal concerns were addressed by establishing a separate ARfD for females aged 13-49.

ARfD = 75 mg/kg bw/day = 0.75 mg/kg bw
100

3.3.2 Acute Dietary Exposure and Risk Assessment

Acute dietary risk is calculated considering the highest ingestion of clopyralid that would be likely on any one day, and using food consumption and food residue values. A statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of clopyralid residue that might be consumed in a day. A value representing the high end (95^{th} percentile) of this distribution is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is considered to be acceptable.

The acute potential daily intake accounted for < 5 % (95^{th} percentile) of the ARfD for all subpopulations and is, therefore, not of concern

3.3.3 Determination of Acceptable Daily Intake (ADI)

To estimate the risk from repeated exposure, the NOAEL of 15 mg/kg bw/day from a 2-year rat study (based on histopathological findings in the stomach: epithelial hyperplasia and thickening of the limiting ridge at 150 mg/kg bw/day) was considered. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability are used. The PCPA reduced to 1-fold in this instance since the NOAEL is sufficiently low that it is inherently protective of prenatal toxicity endpoints observed in the database. A composite assessment factor of 100 was considered protective for all populations including females aged 13-49 years.

ADI = 15 mg/kg bw/day = 0.15 mg/kg bw/day
100

3.3.4 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated by using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is acceptable.

The chronic potential daily intake accounted for < 11% of the ADI for all subpopulations and is, therefore, not of concern.

3.4 Exposure From Drinking Water

3.4.1 Concentrations in Drinking Water

Environmental concentrations (EECs) of clopyralid in potential drinking water sources (groundwater and surface water) were estimated using computer simulation models. An overview of how the EECs are estimated is provided in the PMRA's Science Policy Notice SPN2004-01, Estimating the Water Component of a Dietary Exposure Assessment. EECs of clopyralid in groundwater were calculated using the Leaching Estimation and Chemistry Model (LEACHM) to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using LEACHM are based on the flux, or movement, of pesticide into shallow groundwater with time. EECs of clopyralid in surface water were calculated using the Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS), which simulate pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in two types of vulnerable drinking water sources, a small reservoir and a prairie dugout.

A level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The level 1 EEC estimate is expected to allow for future use expansion into other crops at current application rates.

EECs of clopyralid in potential drinking water sources from modelling are summarized in the table below.

Groundwater EEC (µg a.i./L)		**Surface Water EEC (µg a.i./L)**			
		Reservoir		**Dugout**	
Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Daily[3]	Yearly[4]
133	133	24	5.0	80	73

Notes:

1 90th percentile of daily average concentrations
2 90th percentile of yearly average concentrations
3 90th percentile of yearly peak concentrations
4 90th percentile of yearly average concentrations

Available Canadian water monitoring data for clopyralid were sparse and obtained mainly from Alberta, Saskatchewan, Quebec and a few locations in Ontario. The data was collected in the early 2000's and was provided mainly by Environment Canada and the Provincial Governments. Given the sparseness of the monitoring data and its limitations as described in Appendix IX, clopyralid exposure could potentially be higher in some areas than indicated by the monitoring data thus, modelling results represent a reasonable high-end exposure estimate.

3.4.2 Food and Drinking Water Exposure and Risk Assessment

The drinking water EEC of 133 ug a.i/L was used in the acute and chronic food and drinking water assessment. This value was the highest daily and yearly EEC determined by the level 1 drinking water modelling assessment.

Risk from clopyralid through food and drinking water was below 6% of ARfD and 13% of the ADI for all subpopulation groups. Therefore, the PMRA concludes that clopyralid residues in drinking water, when considered along with dietary exposure, are not of concern.

3.5 Aggregate Risk Assessment

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

As clopyralid is not registered for residential and non-occupational uses, the aggregate risk assessment considered exposure from food and drinking only. Aggregate risk from all relevant sources is not considered a health concern (refer to Section 3.3 and Section 3.4).

A PYO aggregrate dermal and dietary risk assessment was not conducted as dermal exposure to clopyralid residues during a pick-your-own operation was considered to be negligible.

3.6 Incident Reports

Starting April 26, 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Incidents are classified into six major categories including effects on humans, effects on domestic animals and packaging failure. Incidents are further classified by severity, in the case of humans for instance, from minor effects such as skin rash, headache, etc. to major effects such as reproductive or developmental effects, life-threatening conditions or death.

The PMRA will examine incident reports and, where there are reasonable grounds to suggest that the health and environmental risks of the pesticide are no longer acceptable, appropriate measures will be taken, ranging from minor label changes to discontinuation of the product.

There were seven incident reports submitted to the PMRA for clopyralid as of September 21, 2009. These included four environmental incidents, one packaging failure, one incident involving a domestic animal and one incident involving a human. In the latter incident, classified as major, an operator experienced a rapid heart rate and general weakness after working on a malfunctioning sprayer containing a blend of Prestige Herbicide as well as another non-Dow AgroSciences pesticide. It was concluded that the symptoms reported by the patient were inconsistent with those associated with incidental exposure to the diluted herbicide.

For the years 1992-2007, the California Department of Pesticide Regulation reported one incidence of illness resulting from exposure to clopyralid. Clopyralid plus triflusulfuron-methyl was accidentally sprayed onto the applicator's face and body from a spray tank missing a valve. A subsequent rash and conjunctivitis was considered probably related to the pesticide exposure.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Terrestrial Environment
Clopyralid is non-volatile under field conditions based on its vapour pressure of 1.36 mPa at 25ºC. The octanol/water partition coefficient (log K_{ow}) is -2.63 at pH 7 which indicates that clopyralid has a low potential for bioaccumulation in biota. Clopyralid is not susceptible to phototransformation. Biotransformation is the main route of transformation for clopyralid in soil under aerobic conditions and the only major (> 10%) transformation product is carbon dioxide. In the laboratory, under aerobic conditions, clopyralid is non-persistent to persistent in soil depending on environmental conditions that maximize microbial population and activity but is stable in soil under anaerobic conditions. Field dissipation studies in Canada have shown clopyralid to be non-persistent to slightly persistent in soil (DT_{50} values of 12 - 32 days). Clopyralid has a very high mobility in soil as its K_{oc} values are low (0.03-28.57 mL/g), has a high potential to leach to groundwater (GUS in the range of 4.1 – 9.1) and can contaminate surface water through runoff. Environmental fate data for clopyralid are summarized in Table 1 of Appendix VIII.

Aquatic Environment
Clopyralid is very soluble in water (143 g/L at 20ºC). The Henry's Law constant (1.80×10^{-11} (Pa m^3 mol^{-1}) at 25°C), and 1/H value of 1.46×10^{-08} (1/H) at 20°C, indicate that clopyralid is non-volatile from moist soil and water. Clopyralid is stable to hydrolysis at environmentally relevant pH's (pH 5 to pH 9) and is not susceptible to phototransformation in water. Biotransformation is the major route of transformation under aerobic conditions. In the laboratory, clopyralid partitions slowly to the sediment phase and is moderately persistent in the water phase (DT_{50} in the range of 128 and 167 days) and persistent in the whole water/sediment system (DT_{50} in the range of 582 and 963 days). Under laboratory anaerobic conditions, no significant transformation occurs in either water or sediment. In contrast to the laboratory studies, clopyralid was found to be non-persistent under field aquatic conditions (DT_{50} 4.7 – 8.5 days). Studies on bioconcentration in fish indicated a low potential for bioconcentration in organisms.

Environmental fate data for clopyralid are summarized in Table 1 of Appendix VIII.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EEC) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using

standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible. Data derived from monitoring studies may also be used in refining a risk assessment (Appendix IX).

4.2.1 Risks to Terrestrial Organisms

Risk assessment of clopyralid to terrestrial organisms was based upon an evaluation of toxicity data to earthworms, bees, small mammals, birds and plants. A summary of terrestrial toxicity data is presented in Table 2 of Appendix VIII.

For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with clopyralid. For multiple applications the cumulative application rates were calculated taking into consideration the dissipation half-life of clopyralid in soil from the aerobic soil biotransformation study (80.4) and on foliage (35 and 10 days for the screening and refined risk assessments, respectively).

Terrestrial Invertebrates

The risk assessment indicated that the level of concern (LOC) for earthworms, bees and ground dwelling beneficial arthropods was not exceeded for any of the application rates. Other beneficial arthropods present on-field were at risk as the LOC was exceeded for almost all the application rates (with the exception of lowbush blue berry, field corn hybrid and canary seed). However, the off-field exposure indicated that the level of concern was not exceeded for any of the application rates. Table 3 of Appendix VIII summarizes the results of the screening level risk assessment to earthworms, bees and other beneficial arthropods from clopyralid.

Terrestrial Plants
The risk to non-target terrestrial plants is presented in Table 2 of Appendix VIII. The level of concern is exceeded by a factor of 53 for non-target plants at the site of application following a single application at 298.9 g ai/ha to flax. There was also risk from clopyralid to plants at other application rates (LOCs in the range of 18 to 53). Refinement of the assessment of the use on apple (210.5 g ai/ha) reduced the RQ from 51 to 38.

In addition, the risk from spray drift off the treated site was assessed taking into consideration the spray drift deposition of spray quality of ASAE medium for ground boom (6%), at 1 m downwind from the site of application. The LOC was still exceeded for all application rates by factors in the range of 1.1 to 3.2 (Table 3, Appendix VIII).

Birds
The result of the screening level risk assessment for birds is presented in Table 4 of Appendix VIII. The assessment showed that the risk to birds is negligible even at the highest application rate of 298.9 g a.i./ha, when applied to flax by ground boom. The acute oral, acute dietary and chronic LOCs were not exceeded for any of the generic body weights or feeding guilds of birds feeding in the treated sites.

Small Wild Mammals
The result of the screening level risk assessment for mammals is presented in Table 4 of Appendix VIII. The assessment showed that the risk to wild mammals is negligible even at the highest application rate of 298.9 g a.i./ha, when applied to flax by ground boom. The acute oral, acute dietary and chronic LOCs were not exceeded for any of the generic body weights or feeding guilds of mammals feeding in the treated sites.

4.2.2 Risks to Aquatic Organisms

A risk assessment of clopyralid to a range of aquatic organisms was based upon evaluation of toxicity data (Table 2, Appendix VIII) for invertebrates, fish and aquatic plants.

Table 5 of Appendix VIII summarizes the results of the screening level risk assessment of clopyralid to aquatic organisms. The acute or chronic level of concern is not exceeded for any of the freshwater species using these conservative EECs. The acute and chronic level of concern for amphibians was not exceeded following the same EECs. Aquatic organisms would, therefore, be at negligible risk from residues of clopyralid in aquatic systems following all applications in Canada. This included risk from exposure resulting from spray drift or runoff.

4.2.3 Incident Reports

Environmental incident reports are obtained from two main sources, the Canadian pesticide incident reporting system (including both mandatory reporting from the registrant and voluntary reporting from the public and other government departments) and the US EPA Ecological Incident Information System (EIIS). There are currently no incident reports from Canada on clopyralid. In the United States, there were 209 crop damage incidents linked to clopyralid that were reported in the EPA Ecological Incident Information System (EIIS). A total of 150

incidents occurred from registered use on corn through direct treatment and drift; 26 incidents in soybean through drift, direct treatment and carryover; and several carryover incidents in potatoes, lettuce, sorghum, chick pea, lentil, tomatoes, peas and beans. The certainty of all incidents resulting as a result of clopyralid was listed as “possible or probable”. Only 3 incidents were listed as “highly probable”. There have also been reported cases of crop damage from persistence of clopyralid in compost and manure made from lawn clippings, straw and leaves.

In 2002, the US EPA banned the use of clopyralid on lawns and turf and the state of California cancelled the residential uses of clopyralid.

5.0 Value

5.1 Commercial Class Products

All clopyralid uses are supported by the registrants. There are no risk concerns for any of the registered uses. Consequently, no alternatives to the use of clopyralid were listed in the appendices in order to aid public comment.

5.2 Domestic Class Products

There are no Domestic Class products containing clopyralid in Canada.

5.3 Value of Clopyralid

Clopyralid contributes to weed management in a variety of crop and non-crop sites when used in accordance with the label directions. Unlike other auxin-mimics, clopyralid can be applied to many broadleaf crops. It controls many troublesome perennial broadleaf weeds including Canada thistle, dandelion and perennial sowthistle. It can be co-formulated or tank mixed with many other herbicides to broaden weed control spectrum. Clopyralid is the only post-emergence broadleaf herbicide registered for use in Canada on cole crops (cabbage, cauliflower, broccoli, Brussels sprouts, rutabaga, Chinese cabbage, radish, kohlrabi and mustard cabbage). Furthermore, it is the only alternative post-emergence broadleaf herbicide to bentazon in highbush blueberry, and to 2,4-D in cranberry and strawberry (harvest year, renovation). Other non-selective post-emergence herbicides are registered for use on shelterbelts, however, clopyralid is the only selective post-emergence herbicide registered for this use. When used in rotation with active ingredients from other herbicide groups, clopyralid plays a role in mitigating resistance development in weeds.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, those that meet

all four criteria outlined in the policy, i.e. persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*.

During the review process, clopyralid and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[6] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Clopyralid does not meet Track 1 criteria, and is not considered a Track 1 substance. See Table 6 of Appendix VIII for comparison with Track 1 criteria.

- Clopyralid does not form any transformation products that meet all Track 1 criteria.

- Analysis of batch samples of technical grade clopyralid previously submitted to the PMRA revealed the presence of hexachlorobenzene (HCB) and pentachlorobenzene (QCB) in the TGAI. The levels found in Lontrel T are: 0.34-3.1 ppm HCB and 0.16-1.7 ppm QCB and in Lontrel F: 0.04-2.05 ppm HCB and 0.01 ppm for QCB. Data for tetrachlorobenzenes, which can reasonably be expected to be present in these products, were not provided. chlorinated benzenes have been identified in the federal government's TSMP as Track 1 substances. Analyses of recent production batches of the technical grade of clopyralid using sensitive and readily available analytical methods are required from the registrant.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[7]. The list is used as described in the PMRA Notice of Intent NOI2005-01[8] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[9], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

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6 DIR99-03, The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances *Management Policy*

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

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

9 DIR2006-02, PMRA Formulants Policy.

- Technical grade clopyralid and the end-use products contain two impurities or micro-contaminants of health or environmental concern identified in the *Canada Gazette* as hexa-chlorobenzene and penta-chlorobenzene.

The end-use products of clopyralid do not contain any formulants of health or environmental concern as identified in the *Canada Gazette*. However, the end-use products do contain an aromatic petroleum distillate. Therefore, the label for the end-use products Prestige, Prevail and Spectrum will include the statement:

> This product contains aromatic petroleum distillates that are toxic to aquatic organisms.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for clopyralid was adequate to define the majority of toxic effects that may result from exposure to clopyralid. Clopyralid is not expected to be genotoxic or carcinogenic and is not considered to be a neurotoxicant. The first signs of toxicity in animals given daily doses of clopyralid over longer periods of time were effects on body weight, stomach and liver. An increased incidence of hydrocephaly has been observed in the fetus following exposure of the pregnant animal to clopyralid at maternally toxic doses. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

7.1.1 Occupational Risk

Risk estimates associated with mixing and loading and applying clopyralid are not of concern. Post-application risks to workers are not of concern and the minimum 12 hour restricted entry interval (REI) is proposed for all uses.

7.1.2 Dietary Risk from Food and Drinking Water

Acute and chronic risk estimates associated with exposure of clopyralid from food and drinking water are not of concern.

7.1.3 Residential Risk

Clopyralid is not registered for residential areas, so a residential risk assessment was not required.

Dermal exposure at pick-your-own facilities was considered to be negligible and therefore not of concern.

7.1.4 Aggregate Risk

As clopyralid is not registered for residential and non-occupational uses, the aggregate risk assessment considered exposure from food and drinking only which was not of concern. Refer to section 7.1.2.

7.2 Environmental Risk

The assessment of clopyralid indicates risk of adverse effects to non-target terrestrial plants. There is also a potential for clopyralid to leach to groundwater and to move to surface water through runoff. To reduce the effects of clopyralid in the environment, mitigation in the form of precautionary label statements and terrestrial spray buffer zones are required (Appendix X).

7.3 Value

From the value perspective, clopyralid is acceptable for continued registration.

8.0 Proposed Regulatory Decision

After a thorough re-evaluation of the herbicide, clopyralid, Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing continued registration for the sale and use of clopyralid and associated end-use products for uses supported by the technical registrant.

The uses of clopyralid products proposed for continuing registration are presented in Appendix I.

8.1 Proposed Regulatory Actions

8.1.1 Proposed Regulatory Action Related to Human Health

The PMRA has determined that the risks from dietary and drinking water, risks to workers during mixing, loading and application, and post-application activities are not of concern provided that the mitigation measures listed in this section are implemented.

8.1.1.1 Toxicological Information

The following warning statement should appear on the label of the technical product:

Danger: Eye Irritant

8.1.1.2 Proposed Mitigation for Occupational Handlers

Although risks of concern were not identified, the following mitigation measures are proposed for inclusion on the labels of all products containing clopyralid:

- Workers must wear long pants, long sleeved shirt, and chemical resistant gloves. Goggles or a face shield are required during mixing and loading. Gloves are not required to be worn during groundboom application, but are required for mixing/loading, clean-up and repair.
- REI of 12 hours for all crops.
- Not for use in greenhouses.

8.1.1.3 Proposed Mitigation for Bystanders

There may be potential for exposure to bystanders from drift following pesticide application to agricultural areas. In the interest of promoting best management practices and to minimize human exposure from spray drift or from spray residues resulting from drift, the following label statement is proposed:

> Apply only when the potential for drift to areas of human habitation or areas of human activity; such as houses, cottages, schools and recreational areas, is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

8.1.1.4 Residue Definition for Risk Assessment and Enforcement

The current residue definition established in plants and animals is the parent clopyralid. Based on available metabolism data, no revisions to the residue definition are required.

8.1.1.5 Maximum Residue Limits for Clopyralid in Food

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to update Canadian maximum residue limits and to remove MRLs that are no longer supported. The PMRA recognizes, however, that interested parties may want to retain an MRL in the absence of a Canadian registration to allow legal importation of treated commodities into Canada. The PMRA requires similar chemistry and toxicology data for such import MRLs as those required to support Canadian food use registrations. In addition, the Agency requires residue data that are representative of use conditions in exporting countries, in the same manner that representative residue data are required to support domestic use of the pesticide. These requirements are necessary so that the PMRA may determine whether the requested MRLs are needed and to ensure they would not result in unacceptable health risks.

After the revocation of an MRL or where no specific MRL for a pest control product has been established in the *Pest Control Products Act*, subsection B.15.002(1) of the *Food and Drug Act* applies. This requires that residues do not exceed 0.1 ppm and has been considered a general MRL for enforcement purposes. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document: *DIS2006-01 Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. Health Canada issued a note: *Progress on Minimizing Reliance on the 0.1 Parts per Million as a General Maximum Residue Limit for Food Pesticide Residue* (December 2009), as an update to the DIS2006-01 document.

As indicated in Table 8.1.1.5, the *Pest Control Products Act* specifies MRLs for clopyralid residues in barley, blueberries, broccoli, cabbages, cauliflower, Chinese broccoli, Chinese mustard cabbages, kohlrabi, napa Chinese cabbages, oats, strawberries, wheat, cattle, goats, hogs, horses, poultry, sheep, eggs, and milk. Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specified MRL (i.e. apples, canola, corn (field), cranberries, and sugar beets) must not exceed the general MRL of 0.1 ppm.

With the exception of sugar beets, residue data were available to indicate the existing MRLs should not be exceeded if clopyralid is used according to good agricultural practice (GAP), as described by the current product labels. However, in most cases the existing residue data are dated, and do not fully satisfy the requirements as described in Regulatory Directive DIR98-02, *Residue Chemistry Guidelines*.

Parties interested in supporting a clopyralid MRL should contact the PMRA during the comment period of this document to discuss the submission of appropriate data.

Table 8.1.1.5 Clopyralid MRLs for Commodities Approved for Treatment in Canada and for Import Commodities with Specified MRLs

Commodity	MRL (ppm)
Apple	0.1*
Barley	2
Barley, milling fractions, excluding flour	7
Blueberries	0.1
Broccoli	1
Cabbage	1
Canola	0.1*
Cauliflower	1
Chinese Broccoli	1
Chinese Mustard Cabbage	1
Corn (field)	0.1*
Cranberries	0.1*
Eggs	0.05
Fat of cattle	0.05
Fat of goats	0.05
Fat of hogs	0.05
Fat of horses	0.05
Fat of poultry	0.05
Fat of sheep	0.05
Flax	0.2
Kidney of cattle	0.36
Kidney of goats	0.36

Commodity	MRL (ppm)
Kidney of hogs	0.05
Kidney of horses	0.36
Kidney of poultry	0.2
Kidney of sheep	0.36
Kohlrabi	1
Meat byproducts of cattle	0.05
Meat byproducts of goats	0.05
Meat byproducts of hogs	0.05
Meat byproducts of horses	0.05
Meat byproducts of poultry	0.05
Meat byproducts of sheep	0.05
Meat of cattle	0.05
Meat of goats	0.05
Meat of hogs	0.05
Meat of horses	0.05
Meat of poultry	0.05
Meat of sheep	0.05
Milk	0.01
Napa Chinese cabbages	1
Oats milling fractions, excluding flour	7
Oats	2
Strawberries	1
Sugar beets	0.1*
Wheat	2
Wheat milling fractions, excluding flour	7

* By virtue of subsection B.15.002(1) of the Food and Drug Regulations, the maximum residue limit of foods for which MRLs have not specifically been established is 0.1 ppm.

For supplemental MRL information regarding the international situation and trade implications, refer to Appendix XI.

8.1.2 Proposed Regulatory Action Related to Environment

In order to minimize the potential exposure to plants, spray buffer zones are required. The width of these spray buffer zones must be specified on the product label (Appendix X).

8.1.3 Proposed Regulatory Action Related to Value

No regulatory action is proposed from the standpoint of value.

8.2 Additional Data Requirements

8.2.1 Data Requirements Related to Chemistry

DACO 2.13.4 **Impurities of Human Health or Environmental Concern**

The applicant must provide analytical data from at least five recent batches of the products for hexachlorobenzene, pentachlorobenzene and tetrachlorobenzenes (three isomers) from a GLP-compliant or government-accredited laboratory. The analytical method(s) used must utilize the lowest practical limits of quantitation and be fully specified, either by reference to a standard method or by inclusion of a detailed description together with validation data.

8.2.2 Data Requirements Related to Health

No additional data required.

8.2.3 Data Requirements Related to Environmental Risks

No additional data required.

List of Abbreviations

ai	active ingredient
AD	administered dose
ADI	acceptable daily intake
ae	acid equivalent
ARfD	acute reference dose
ATPD	area treated per day
bw	body weight
bwg	body-weight gain
CFIA	Canadian Food inspection Agency
d	day(s)
DA	dermal absorption
DFR	dislodgeable foliar residue
EC	emulsifiable concentrate,
EEC	environmental concentration
EPA	Environmental Protection Agency
EU	European Union
F_0	parental animals
F_1	1st generation offspring
F_2	2nd generation offspring
FDR	Food and Drugs Regulations
FOB	functional observational battery
g	gram
GAP	good agricultural practice
Ha	hectares
HED	Health Evaluation Division
hr	hour
kg	kilogram
L	litre
LC_{50}	lethal concentration 50%
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LEACHM	leaching estimation and chemistry model
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOQ	limit of quantitation
MAS	maximum average score (at 24, 48 and 72 h)
mg	milligram
MIS	maximum irritation score
mL	millilitre
MMAD	mass median aerodynamic diameter
MOE	margin of exposure
MOR	magnitude of residue
MRL	maximum residue limit
MRM	multi-residue method
MTD	maximum tolerated dose

MTDB	maximum theoretical dietary burden
N/A	not applicable
NOAEL	no observed adverse effect level
NOEL	no observed effect level
^{o}C	degree Celsius
OECD	Organisation for Economic Co-operation and Development
PBI	plant back interval
PC	positive control
PDP	Pesticide Data Program
PPE	personal protective equipment
ppm	parts per million
PRZM/EXAMS	pesticide root zone model/exposure analysis modeling system
RD	residue definition
REI	restricted entry interval
SG	soluble granular
TC	transfer coefficient
TGAI	technical grade active ingredient
w/v	weight by volume
WSP	water soluble package

Appendix I Registered clopyralid products as of January 9, 2009. Discontinued products or products with a submission for discontinuation or products which the registrant wishes to discontinue are not included.

Registration Number	Marketing Type	Registrant Name	Product Name	Formulation Type	Guarantee[1]			
					DPI	MAE	DXA	FLM
23993	Commercial	BASF Canada Inc.	Flaxmax Herbicide	Emulsifiable Concentrate or Emulsion	50 g/L	280 g/L	-	-
25819			Flaxmax Herbicide (A Component of Flaxmax) Herbicide Tank Mix	Emulsifiable Concentrate or Emulsion	50 g/L	280 g/L	-	-
22764		Dow AgroSciences Canada Inc.	Curtail M Herbicide	Emulsifiable Concentrate or Emulsion	50 g/L	280 g/L	-	-
22878			Curtail F Herbicide	Emulsifiable Concentrate or Emulsion	50 g/L	280 g/L	-	-
23545			Lontrel 360 Herbicide	Solution	360 g/L	-	-	-
25464			Prestige B (A Component of Prestige Herbicide Tank Mix)	Emulsifiable Concentrate or Emulsion	50 g/L	280 g/L	-	-
27032			Spectrum B Emulsifiable Concentrate Herbicide (A Component of Spectrum HTM)	Solution	50 g/L	280g/L	-	-
27145			Fieldstar WDG Herbicide	Soluble Granules	50%	-	-	18.5%
27146			Fieldstar WDG WSP Herbicide	Soluble Granules	50%	-	-	18.5%
27306			Lontrel Dry Soluble Granular Herbicide	Granular	75%	-	-	-
28539			Eclipse II A Herbicide (a component of Eclipse II Herbicide Tan-Mix)	Solution	360 g/L	-	-	-
29032			Eclipse III A Herbicide (a component of Eclipse III Herbicide Tank-Mix)	Solution	360 g/L	-	-	-
18213	Manufacturing concentrate		Lontrel 35A Herbicide Concentrate	Solution	35%	-	-	-
25783			Striker Manufacturing Concentrate	Wettable Granules	25%	-	50%	9.3%
18315	Technical active ingredient		Lontrel T Technical Herbicide	Solid	95%	-	-	-
25296			Lontrel F Technical Herbicide	Paste	80.8%	-	-	-

1 DPI = clopyralid (present as acid or monoethanolamine salt or potassium salt); MAE = MCPA (present as 2-ethylhexyl ester); DXA = 2,4-D (present as acid); FLM = flumetsulam; - = not included. Note that the guarantee for liquid formulations are in g ae (acid equivalent)/L.

Appendix II Registered uses of clopyralid as of January 9, 2009. No aerial application is allowed for any registered uses.

Use Site Category	Site(s)	Weed(s)	Formulation Type	Maximum Application Rate (g a.e./ha)	Use Supported?[1]
13 = Terrestrial feed crops 14 = Terrestrial food crops	Wheat, including spring wheat and durum wheat	Broadleaf weeds as listed on the labels	Emusifiable Concentrate	100.0	Yes
			Solution	201.6	
	Barley, including spring barley		Emusifiable Concentrate	100.0	
			Solution	201.6	
	Oats		Emusifiable Concentrate	100.0	
			Solution	201.6	
7 = Industrial oilseed and fibre crops 13 = Terrestrial feed crops 14 = Terrestrial food crops	Flax		Emusifiable Concentrate	100.0	
			Solution	298.8	
	Canola		Solution	298.8	Yes (Minor use[2])
			Granules	200.3	
	Field corn (hybrid)		Soluble Granules	135.0	Yes
13 = Terrestrial feed crops	Seedling and/or established forage grasses grown for seed and/or forage [4,5]		Emusifiable Concentrate	100.0	
			Solution	298.8	
	Canaryseed		Emusifiable Concentrate	100.0	
	Rangeland and grass pasture[6]		Solution	298.8	
14 = Terrestrial food crops	Low bush blueberry			151.2	Yes, Minor use
	High bush blueberry			298.8	
	Strawberry (Renovation)			298.8	
	Sugarbeet			298.8	Yes
	Rutabaga			201.6	
	Cabbage, cauliflower, broccoli and kohlrabi (all transplanted), nappa cabbage (transplanted and seeded), Chinese radish, mustard cabbage and Chinese broccoli (all seeded)			201.6	Yes, Minor use
	Apple (bearing and non-bearing)			201.6	
	Cranberry			7.2 g a.e./L water	
	Summer fallow			298.8	Yes
4 = Forest and woodlands	Balsam Fir Christmas tree plantation			252.0	
4 = Forest and woodlands 27 = Ornamentals outdoor	Poplar and its hybrids			298.8	Yes, Minor use
4 = Forest and woodlands 16 = Industrial and domestic vegetation control for non-food sites	Shelterbelts (villas lilac, acute willow, Colorado spruce, white spruce, buffaloberry and chokecherry)			298.8	Yes
13 = Terrestrial feed crops 16 = Industrial and domestic vegetation control for non-food sites	Transline Industrial Vegetation Management System (non-crop uses)[7]			298.8	

Use Site Category	Site(s)	Weed(s)	Formulation Type	Maximum Application Rate (g a.e./ha)	Use Supported?[1]
16 = Industrial and domestic vegetation control for non-food sites	Non-crop farmland (around farm buildings, storage areas, fence rows)			298.8	Yes (Minor use[3])

1 Yes = Use is supported by the registrant. Minor use = Use was added as a User Requested Minor Use Label Expansion (URMULE).

2 The use on canola in Ontario is a minor use registration.

3 The use for the control of spotted and diffuse knapweed on non-crop farmland is a minor use registration.

4 Seedling and established grasses for seed production: Including weed control on creeping red fescue, intermediate wheat grass, crested wheat grass, meadow brome grass, smooth brome grass, timothy.

5 Seedling and established grasses for seed production and forage (western Canada only): Including weed control on Kentucky bluegrass, smooth bromegrass, reed canary grass, creeping red fescue, meadow fescue, tall fescue, meadow foxtail, orchard grass, altai wild ryegrass, Russian wild ryegrass, timothy, crested wheatgrass, intermediate wheatgrass, slender wheatgrass and streambank wheatgrass for forage and seed production and tall wheatgrass for forage only.

6 Rangeland and grass pasture: Including weed control on Kentucky bluegrass, smooth bromegrass, reed canary grass, creeping red fescue, meadow fescue, tall fescue, meadow foxtail, orchard grass, altai wild ryegrass, Russian wild ryegrass, timothy, crested wheatgrass, intermediate wheatgrass, slender wheatgrass, streambank wheatgrass and tall wheatgrass.

7 Transline Industrial Vegetation Management System (non-crop uses): Including weed control on rights-of-way (hydro, railroad, communication lines, pipelines) and associated stations, industrial manufacturing sites, storage sites, vacant lots and roadsides, military bases and low maintenance rough turf areas (grass areas where the dominant species are those listed in the Rangeland and Grass Pasture Section of this label, and where little or no maintenance is applied).

Appendix III Toxicology Profile for Clopyralid

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise specified.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	Results/Effects
Metabolism/Toxicokinetic Studies		
Absorption, distribution, excretion and metabolism of [^{14}C] - Clopyralid - Sprague-Dawley rats 3♂/2♀(blood) 3♂/3♀(urine, faeces, CO_2, tissues)	^{14}C-clopyralid: 10 mg/kg bw single oral dose radiochemical purity: >99%	Absorption: Rapidly and nearly completely absorbed (peak plasma concentration reached at 18 minutes). Distribution: Widely distributed. Low tissue levels (at 120 hr average conc.< 0.018% of administered dose (AD)/g, and in remaining carcasses, 0.025%AD/g). Metabolism: clopyralid only radioactive residue detected: 94-99% of radioactivity co-chromatographed with clopyralid Excretion: Rapidly excreted largely in the urine [92.2% AD excreted in urine by 120 hr (96.5% of this was excreted during the first 32 hr with half-life of 3.05 hr; remainder with half-life of 24.7 hr.)]. Faecal excretion was 2.69% AD, and expired air was 0.03% AD.
Absorption, distribution, excretion and metabolism of [^{14}C] - Clopyralid - Fischer-344 rats: A: 1/sex B,C,D,E: 5/sex	^{14}C-clopyralid (labelled in the 2,6-positions of the pyridine ring): 10 mg/kg bw in corn oil (oral dose) or saline (intravenous dose) A: (control) 1 mg/kg bw orally B: 5 mg/kg bw intravenously C: 5 mg/kg bw orally D: 5 mg/kg bw orally (15): 14 non-labelled (96% purity) followed by 1 labelled E: 150 mg/kg bw, orally radiochemical purity: >99%	Absorption: Rapidly and nearly completely absorbed (based on excretion rates). Distribution: Widely distributed. Low tissue levels [<0.01% of administered dose (AD)]. In individual tissues/organs (excluding carcass), residues were generally less than 0.002 mg/kg except in the stomach [up to 0.237/ 0.189 mg/kg (♂/♀) in high dose group]. Metabolism: Only unchanged clopyralid was detected in the urine, no metabolites; most of the radioactivity in the faeces was also unchanged clopyralid. Excretion: Rapidly excreted largely in the urine (during the first 24 hours: urine, 73.3-97.2% AD; faeces, 0.3-3.7% AD). At 72 hours: urine was 74.1-97.6% AD; cage washes were 10.47-21.83% AD; and faeces were 0.83-4.51% AD. -no apparent differences between treated groups or sexes; multiple applications did not change the tissue distribution or elimination pattern

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	Results/Effects
Acute Toxicity Studies		
Oral toxicity - Fischer 344 rats 5/sex	5000 mg/kg bw as a suspension in corn oil (Lontrel T) 95.4% purity	>5000 mg/kg bw **low toxicity**
Dermal toxicity - New Zealand White rabbits 5/sex	2000 mg/kg bw moistened with distilled water applied to shaved skin for 24 hr under occlusive wrapping (Lontrel T) 95.4% purity	>2000 mg/kg bw **low toxicity**
Inhalation toxicity - Fischer 344 rats 5/sex	1.0 mg/l (nose only; 4 hr exposure period, 14 day observation) (Lontrel T) 95.8% purity	LC_{50} >1 mg/L (highest attainable conc.) **low toxicity**
Eye irritation - New Zealand White rabbits 3/sex	0.1 g applied to the conjunctival sac of the right eye (Lontrel T) 95.4% purity	severely irritating symptoms persisted after 21 days **severely irritating**
Dermal irritation - New Zealand White rabbits 3/sex	0.5 g (moistened) applied under a 2.5 cm^2 gauze patch to fur -free skin for 4 hr (Lontrel T) 95.4% purity	**non-irritating**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	Results/Effects
Dermal sensitization (Buehler) - Hartley albino Guinea pig 10♂/group	Induction: 3 applications of 0.4 ml of 10% clopyralid in Dowanol DPM once a week for 6 hrs. Positive control: 10% solution of DER 331 epoxy resin in Dowanol DPM applied similarly to above Challenge (2 wks. After last induction): 10% clopyralid applied for 6 hrs (Lontrel T) 95.4% purity	no signs of erythema or edema with 10% clopyralid; **not sensitizing**
Dermal sensitization (Magnusson & Kligman Maximization test) - Dunkin-Hartley albino Guinea pigs 10/sex	Induction: 1st - 3 pairs of intradermal injections of 0.1 ml clopyralid (3% w/v in propylene glycol), FCA, and clopyralid (3%) in FCA 2nd - clopyralid (50%, w/v) in propylene glycol Challenge: 10% w/v clopyralid in propylene glycol; 3% w/v clopyralid in propylene glycol (Lontrel T) 97.9% purity	Challenge application of 10% w/v clopyralid in propylene glycol produced eschar formation (2 animals), and slight erythema (1 test, 1 control animal) **not sensitizing**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Subchronic Toxicity Studies			
21-day dermal toxicity - New Zealand White rabbits 1/sex/group (Probe study) 5/sex/group (Main study)	Probe Study: 500, 1000 mg/kg bw/day, 6hr/day, for 4 days Main Study: 0, 100, 500, 1000 mg/kg bw/day, 6hr/day, for 3 5-day periods (Lontrel T) 95.78% purity	**Systemic toxicity: >1000 mg/kg bw/day**	Systemic toxicity: none observed at the highest (limit) dose (1000 mg/kg bw/day) Dermal toxicity: non-irritating ≥500 mg/kg bw/day: slight erythema
90-day oral (feeding) study - $B_6C_3F_1$ mice 10/sex/group	0, 200, 750, 2000, 5000 mg/kg bw/day (Dowco 290) 97% purity	**2000 mg/kg bw/day**	≥2000 mg/kg bw/day: morphologic changes in the liver (↑size centrilobular hepatocytes, altered tinctorial properties)(♀) 5000 mg/kg bw/day: ↓bw ↑liver wt. (rel.), morphologic changes in the liver (↑size centrilobular hepatocytes, altered tinctorial properties)
28-day oral (feeding) study - CD rats 10/sex/group	0, 150, 500, 1500 mg/kg bw/day (Lontrel T) 95% purity	**150 mg/kg bw/day**	≥500 mg/kg bw/day: ↑urea nitrogen (♀), changes in electrolyte levels [↓Ca^{++} & Cl^- (♂); ↑Na^+ & K^+ (♀)], thickening of the forestomach limiting ridge (♀), histopathology showed minimal acanthosis and folding of non-glandular epithelium of the limiting ridge 1500 mg/kg bw/day: ↓bw gain, ↑RBC (♂), ↓ALT (♀), ↑kidney wt. (no macroscopic or histopathological change), thickening of the forestomach limiting ridge, histopathology showed minimal acanthosis and folding of non-glandular epithelium of the limiting ridge
90-day oral (feeding) study - Sprague-Dawley Spartan rats 15/sex/group	0, 5, 15, 50, 150 mg/kg bw/day (Dowco 290) 96.3% purity	**>150 mg/kg bw/day**	There were no toxicologically significant effects, and no histopathological changes.
90-day oral (feeding) study - Fischer-344 rats 15/sex/group	0, 300, 1500, 2500 mg/kg bw/day (Dowco 290) 96.4% purity	**1500/300 mg/kg bw/day (♂/♀)**	≥300 mg/kg bw/day: slight, but statistically significant ↑rel. liver and kidney wt.(♂) 1500 mg/kg bw/day:↓bw gain, ↓bw, ↓food consumption 2500 mg/kg bw/day:↓bw gain, ↓bw, ↓food consumption, ↑rel. liver and kidney wt., stomach lesions (slight irregularities and accentuation of the limiting ridge, microscopically consisting of increased thickness of the gastric mucosa)

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
6 month oral (feeding) study - Beagle dogs 4/sex/group	0, 15, 50, 150 mg/kg bw/day (Dowco 290) purity not stated	**>150 mg/kg bw/day**	no treatment related toxicological effects
6 month oral (feeding) study - Beagle dogs 4/sex/group	0, 15, 50, 150 mg/kg bw/day (Dowco 290) purity not stated	**>150 mg/kg bw/day**	150 mg/kg bw/day: ↑liver weight (♀ - rel.)
1 year oral (feeding) study - Beagle dogs 6/sex/group	0, 100, 320, 1000 mg/kg bw/day (achieved dose: 0, 99/99, 301/319, 983/977 mg/kg bw/day) (Dowco 290) 95.8% purity	**100 mg/kg bw/day**	100 mg/kg bw/day: ↓globulin (♀), ↓total protein (♀), ≥320 mg/kg bw/day: ↓RBC, ↓Hgb, ↓Hct, ↓albumin (♀), ↓total protein (♀), ↓BUN (♀), ↑liver weight (♂), ↑ focal vacuolation of adrenal cortical cells (♀: slight - mild)(♀ - findings occurred unilaterally in most control and low-dose dogs, and bilaterally in most mid- and high-dose dogs) 1000 mg/kg bw/day: ↓albumin, ↓globulin (♂), ↓total protein, ↑liver wt. ↑kidney wt. (rel. - ♂), ↑heart wt. (rel. - ♀)
Chronic Toxicity/Oncogenicity Studies			
18-month oncogenicity feeding study - Charles River strain Swiss albino mice 30 ♀&15 ♂ /group* *After 13 wks., ♂'s and ♀'s from the same dose group were mated and offspring distributed into same dose groups for 18 months (50-60/sex/group)	0, 35, 100, 350 ppm (0, 5.25, 15, 52.5 mg/kg bw/day) (Dowco 290) purity not stated		no toxicologically significant effects (i.e., there were no changes in behaviour, clinical appearance or bw of either parents or offspring, no changes in any of the tissues evaluated gross pathologically or microscopically) not oncogenic supplementary
2-year chronic toxicity/ oncogenicity feeding study - $B_6C_3F_1$ mice 70/sex/group (10/sex/group at 6 and 12 month interim sacrifices)	0, 100, 500, 2000 mg/kg bw/day (Dowco 290) 96.7% purity	**500 mg/kg bw/day/>2000 mg/kg bw/day (♂/♀)**	2000 mg/kg bw/day: ↓bw, ↓bw gain, ↓food efficiency **not oncogenic**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
2-year chronic toxicity/ oncogenicity feeding study - Sprague-Dawley rats 40/sex/group (80 ♂'s & 79 ♀'s were used as untreated controls)	0, 5, 15, 50, 150 mg/kg bw/day (Dowco 290) 92.8% purity		150 mg/kg bw/day:↓bw (♀) In two supplementary histopathological investigations no toxicologically significant treatment-related histopathological effects were found. **not oncogenic** **supplementary**
2-year chronic toxicity/ oncogenicity feeding study - Fischer-344 rats 70/sex/group (10/sex/group killed at 6 & 12 months; 50/sex/dose up to 24 months)	0, 15, 150, 1500 mg/kg bw/day (Dowco 290) 96.7% purity	**15 mg/kg bw/day**	≥150 mg/kg bw/day: ↓food consumption, stomach lesions [thickening of the epithelium of the anterior surface of the limiting ridge, hyperplasia 1500 mg/kg bw/day: ↓food consumption ↓bw, ↓bw gain, ↑liver & kidney wts. stomach lesions [↑prominence of the gastric limiting ridge, thickening of the epithelium of the anterior surface of the limiting ridge (↑cells in the stratum spinosum) and hyperplasia (↑cellular activity in the stratum basale), chronic active inflammation, ↑incidence mononuclear cell aggregates in the stomach mucosa] **not oncogenic**
Reproductive and Developmental Toxicity Studies			
2-generation reproduction study (with supplementary histopathology study) - Fischer-344 rats 30/sex/group	0, 150, 500, 1500 mg/kg bw/day (Dowco 290) 96.7% purity	**Parental/ Offspring toxicity: 500 mg/kg bw/day** **Reproductive toxicity: >1500 mg/kg bw/day)**	Parental: 500 mg/kg bw/day: ↓bw [F_0 ♀ - during pre-mating and lactation] 1500 mg/kg bw/day: slight hyperkeratotic changes in the nonglandular mucosa of the stomach (♂), small lesions in the forestomach (mucosal invaginations in the gastric wall)(♂), ↓bw (F_0 - pre-mating; F_0 ♀ - lactation; F_1), ↓bw gain (F_0 ♂ - pre-mating; F_0 ♀ - pre-mating; F_1 ♂ - overall), ↓food consumption (F_0 ♂ - for much of pre-mating interval; F_0 ♀ & F_1 ♂ - a few wks of the pre-mating interval) Offspring: ↓pup weight (F_{1a} /F_{1b} ♂), ↑pup liver weights (rel. - F_{1a} ♂&♀/F_{1b} ♂) Reproductive: no treatment-related effects

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Developmental toxicity study - Fischer 344 rats Phase I - 29-35 mated ♀'s/group Phase II - 25 mated ♀'s/group	Phase I - 0, 15, 75, 250 mg/kg bw/day in cottonseed oil (4 ml/kg bw) by gavage on gestation days 6-15, inclusive Phase II - 0, 250 mg/kg bw/day in cottonseed oil (2 ml/kg bw) by gavage on gestation days 6-15, inclusive (Dowco 290) 97.0% purity	**Maternal: 75 mg/kg bw/day** **Developmental: >250 mg/kg bw/day**	Phase I Maternal: ≥75 mg/kg bw/day: ↓liver wt. (absol.) 250 mg/kg bw/day: mortality (1 death on GD 11 - this animal exhibited moistening of the hair of the perineal region, slightly ↓thymus size, & gastrointestinal tract devoid of feed or fecal matter), ↓bw, ↓bw gain, ↓food consumption, Developmental: 250 mg/kg bw/day: no differences between control and treated in the live fetuses/dam, post-implantation losses or fetal sex ratios. No reduction in fetal weight. No single malformation occurred at a statistically or biologically significant greater incidence in the treated groups and the incidence of total major malformations was also not significantly increased for any of the treated groups Phase II Maternal: 250 mg/kg bw/day: mortality (2 deaths on GD 10 - both animals exhibited substantial weight loss, & exudative material from the nares), ↓liver wt. (absol.), ↓bw, ↓bw gain, ↓food consumption Developmental: 250 mg/kg bw/day: no significant effects (as phase I)
Developmental toxicity study - New Zealand White rabbits 26-34 presumed pregnant rabbits/group	0, 50, 110, 250 mg/kg bw/day in corn oil (2 ml/kg bw) by gavage on gestation days 7-19, inclusive 96.1-96.4% purity	**Maternal and Developmental: 110 mg/kg bw/day**	Maternal: 250 mg/kg bw/day: clinical signs (laboured breathing, rales, shallow respiration, coughing), mortality (8 treatment related deaths vs none at lower doses), ↓bw, ↓bw gain, histopathologic lesions of the gastric mucosa [multifocal erosions, focal ulcer, multifocal necrosis with inflammation, multifocal acute inflammation, multifocal hyperplasia, fibrosis of the lamina propria & mucosal autolysis] Developmental: 250 mg/kg bw/day: ↓fetal bw, hydrocephaly (3/15 litters contained fetuses–total of 8–with hydrocephaly vs 0/19 in controls, not statistically sig., but greater than historical control: 0-2 fetuses and litters)
Genotoxicity Studies			
Dominant lethal assay - Sprague-Dawley CD rats 10 ♂/group	0, 4, 40, 400 mg/kg bw (one dose /day for 5 days) by gavage in corn oil, then mated to 2♀/wk for 7 wk (Dowco 290) purity not stated	**negative**	

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
In vivo cytogenetic assay chromosome aberration - ♂ Sprague-Dawley rats acutely: 5/group/time interval (killed at 6, 24 and 48 h.) subacutely: 5/group	0, 4, 40, 400 mg/kg bw (either acutely, or one dose /day for 5 days) by gastric intubation in corn oil (Dowco 290) purity not stated	**negative**	
In vivo host mediated mutation assay - Charles River ICR ♂ mice (host) - *Salmonella* strains TA 1530, G-46, & *Saccharomyces* strain D-3 10 mice/group	*In vivo* test: 0, 4, 40, 400 mg/kg bw/day in corn oil to mice (by gavage) either acutely as a single dose, or one dose/day for 5 days, followed by intraperitoneal injection of organisms 100% technical grade	**negative**	
In vitro mutation assay - *Salmonella* strains TA 1530, G-46, & *Saccharomyces* strain D-3	*In vitro* test: discs containing 0.1 ml of 10%, 20%, or 50% saturated solutions in corn oil placed on inoculated plates 100% technical grade	**negative**	
In vitro unscheduled DNA synthesis assay - primary rat hepatocytes -2 studies	0, 5 x 10^{-5}, 1.56 x 10^{-4}, 5 x 10^{-4}, 1.56 x 10^{-3}, 5 x 10^{-3}, 1.56 x 10^{-2}, 5 x 10^{-2} M in Williams Media E (Lontrel T) 95.6% purity	**negative**	
Ames reverse mutation test - *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1528	0, 125, 250, 500, 1000 µg/plate ±S9 (3 plates/conc.) 95% purity	**negative**	

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Ames reverse mutation test - *Salmonella typhimurium* TA98, TA100, TA1535, TA1537	0, 50, 158, 500, 1580 and 5000 µg/plate ±S9 (3 plates/conc.) (Lontrel T) 95.4% purity		**negative**
CHO/HGPRT gene mutation assay -	(Expt.1.) 0, 250, 500, 750, 1000, and 1500 µg/ml (Expt 2.) 0, 125, 250, 500, 750, and 1000 µg/ml without S9 & 0, 1750, 2000, 2250, 2500, and 2750 µg/ml + S9 (Lontrel T) 95.4% purity		**negative**
In vitro chromosomal aberration assay - Crl:CD BR rat lymphocytes	(Expt.1.) 0, 43.6, 87.2, 174.4, 348.8, 697.5, 1395, and 2790 µg/ml ±S9 (Expt 2.) 0, 43.6, 87.2, 174.4, 348.8, 697.5, 1050, 1395, 2100, and 2790 µg/ml without S9 & 0, 174.4, 348.8, 697.5, 1395, and 2790 µg/ml + S9 96.9% purity		**negative**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Mouse bone marrow micronucleus test - CD-1(ICR) mice Groups of mice, 5/sex/treatment , were sacrificed at 24, 48 or 72 hr after treatment	0, 500, 1667, or 5000 mg/kg bw by gavage in corn oil 96.1% purity		**negative**

Appendix IV Toxicology Endpoints for Health Risk Assessment for Clopyralid

	RfD (mg/kg bw/day)	Study NOAEL (or LOAEL)	CAF or Target MOE and Rationale[1]
ARfD **general population**	0.75	NOAEL: 75 mg/kg bw Rat Developmental Toxicity (decreased maternal body weight gain and food consumption during gestation days 6-9 at 250 mg/kg bw/day)	100 PCPA = 1-fold
ARfD **females 13-49**	0.37	NOAEL: 110 mg/kg bw/day Rabbit Developmental Toxicity (hydrocephaly at 250 mg/kg bw/day)	300 PCPA = Additional 3-fold factor for serious effect in the presence of significant maternal toxicity
ADI **general population**	0.15	NOAEL: 15 mg/kg bw/day 2-year Rat Chronic Toxicity/ Oncogenicity (epithelial hyperplasia and thickening of the limiting ridge at 150 mg/kg bw/day)	100 PCPA = 1-fold
short and intermediate-term dermal[2] and inhalation[3]		NOAEL: 110 mg/kg bw/day Rabbit Developmental Toxicity (hydrocephaly at 250 mg/kg bw/day)	300 Additional 3-fold factor for serious effect in the presence of significant maternal toxicity

[1]CAF (Composite assessment factor) refers to the total of uncertainty and PCPA factors for dietary and residential risk assessments, MOE refers to target MOE for occupational assessments

[2]Since an oral NOAEL was selected, a dermal absorption factor of 100% (default value) is used in a route-to-route extrapolation.

[3]Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) is used in route-to-route extrapolation.

Appendix V Occupational Exposure Risk Estimates for Clopyralid

Table V.1 M/L/A Short to Intermediate-Term Commercial Applicator Exposure and Risk Assessment[a]

Scenario	Form	Application Equipment	Rate (kg ae/ha)	ATPD (ha)	Kg ae Handled per Day	Unit Exposure[b] (µg/kg ae)		Exposure (µg/kg/day)[c]		MOE[e]		
						Total		Daily		Dermal	Inhalation	Combd
						Dermal	Inhalation	Dermal	Inhalation	Target=300		
Label PPE: Long sleeved shirt, long pants, gloves (not required for groundboom application) open cab, open M/L												
All crops	EC, liquid	Groundboom	0.299	100	29.9	84.12	2.56	35.93	1.09	3061	100596	**2971**
		Groundboom (custom)		300	89.7	84.12	2.56	107.8	3.28	1020	33532	**990**
		Backpack	0.00299 kg ae/L	150 L	0.45	5445.85	62.1	34.89	0.4	3153	276463	**3117**
		Low pressure handwand			0.45	943.37	45.2	6.04	0.29	18199	379301	**17367**
		Right of way sprayer	0.299	50	14.9	923.68	6.6	197	1.41	558	78090	**554**
	SG, SG in WSP[f]	Groundboom	0.135	100	13.5	196.75	1.98	37.85	0.38	2906	288066	**2877**
		Groundboom (custom)		140	18.9	196.75	1.98	52.99	0.53	2076	205761	**2055**
	Gran	Solid broadcast spreader	0.2	80	16	34.98	3.8	8	0.87	13758	126645	**12410**
		Solid broadcast spreader (custom)		300	60	34.98	3.8	29.98	3.26	3669	33772	**3309**

Form = formulation; EC = emulsifiable concentrate; SG= soluble granular; WSP = water soluble package; Gran = granular; ATPD = area treated per day; MOE = margin of exposure; Comb = combined MOE; M/L = mixing/loading; A = application.

[a] The highest application rate and highest area treated per day for each formulation was combined with the potential application equipment that could be used on those crops registered for that formulation. For those crops where the rate was converted into a rate per litre, the lowest volume permitted on the labels (100 L/ha) from cereal grains was used. Volumes ranged from 100-300 L/ha for all crops. Granular formulation = canola; SG and SG in WSP = field corn; Liquid, EC formulation = balsam fir Christmas tree plantations, poplars and their hybrids, seedlings and established forage grasses grown for seed and/or forage, canary grass, rangeland and grass pasture, wheat, barley, oat, flax, canola, rutabaga, cabbage, cauliflower, broccoli, kohlrabi, nappa cabbage, Chinese radish, mustard cabbage, Chinese broccoli, apples, strawberries, cranberry, sugar beet, blueberry (low and high bush), summer fallow, shelterbelts, non-cropland

[b] A sum of unit exposure values from mixing and loading and application

[c] Where exposure (µg/kg/day) = (unit exposure x application rate x ATPD x dermal absorption)/70 kg bw. Dermal absorption was assumed to be equivalent to oral absorption (i.e. 100%).

[d] Dermal and inhalation MOEs are based on an oral NOAEL of 110 mg/kg bw/day, target is 300.

[e] Calculated using the following equation: Combined MOE = NOAEL/ (Dermal exposure + inhalation exposure)

[f] Exposure was calculated for SG only, not SG in WSP, since being packaged in a WSP would reduce exposure and target MOEs were met without it.

Table V.2 Dermal Post-Application Short-Term Exposure and Risk Assessment[a]

Activity	Transfer Coefficient (cm^2/hr)	DFR[b] (µg/cm^2)	Dermal Exposure[c] (µg/kg bw/day)	MOE[d] (Day 0)	REI (days)[e]
All crops [f]				**Target: 300**	
Hand harvesting in corn	Not required as applied as a pre-emergent application				
Hand harvest, irrigation, hand pruning in field crops	5000	0.598	342	322	**12 hours**
Hand harvesting in berries, scouting and irrigating in sugar beet	1500[g]	0.598	103	1073	**12 hours**
Scouting in seedlings, cereal grains, summerfallow	1500[h]	0.598	103	1073	**12 hours**
Handline irrigation	1,100[i]	0.598	75.18	1463	**12 hours**
Scouting in s non-cropland, shelterbelts, apples	500	0.598	34.2	3219	**12 hours**
Hand harvesting, hand pruning, scouting, thinning, hand weeding in cranberries	400	0.534[j]	24.41	4507	**12 hours**

DFR = dislodgeable foliar residue; TC = transfer coefficient; DA = dermal absorption; MOE = margin of exposure; REI = restricted entry interval.

[a] The highest exposure reentry activity for each crop was combined with the day 0 residues from the highest registered application rate from all formulations. Although up to two applications are permitted on the label for some crops (apples, cranberries, shelterbelts, non-cropland (spot treatment)), only 1 application was assumed as the interval between applications was 45 days or longer and residues will be minimal by the second application., based on submitted DFR studies Additionally crop height is not expected to change.

[b] DFR value was determined using default peak DFR value of 20% of the application rate.

[c] Exposure = DFR x TC x duration (8 hours) x DA (100%) / body weight (70 kg).

[d] Based on an oral NOAEL of 110 mg/kg bw/day and target MOE of 300.

[e] REI = Restricted Entry Interval.

[f] Field crops: rutabaga, cabbage, cauliflower, broccoli, kohirabi, nappa cabbage, Chinese radish, mustard cabbage, Chinese broccoli
Trees: balsam fir, x-mas tree plantations, poplars and their hybrids
Seedlings and summerfallow: seedlings and established forage grasses grown for seed and/or forage, canary grass, rangeland and grass pasture, summerfallow, shelterbelts
Cereal grains: wheat, barley, oat, flax, canola
Berries: strawberries, sugar beet, blueberry (low and high bush),

[g] TC for bushberries, caneberries and grapes

[h] TC value from scouting cereal grain, used as a surrogate for scouting seedlings, summerfallow

[i] TC value for Christmas trees, used as surrogate for poplars

[j] DFR is based on a rate which was determined based on information provided by Brian Mauza, Agricultural Scientist for Ocean Spray of Canada Ltd.

Appendix VI Dietary Exposure and Risk Estimates for Clopyralid

Table VI.1 Acute Food and Drinking Water Exposure Risk Estimates

Population Groups	Food Exposure[1]		Food and Drinking Water Exposure[1]	
	mg/kg bw	% ARfD[2]	mg/kg bw	% ARfD[2]
General Population[3]	NA	NA	NA	NA
All Infants (<1 year old)	0.03	4	0.04	6
Children 1-2 years old	0.03	4	0.04	5
Children 3-5 years old	0.03	4	0.03	4
Children 6-12 years old	0.02	3	0.02	3
Males 13-19 years old	0.01	2	0.02	2
Males 20-49 years old	0.01	1	0.02	2
Adults 50+ years old	0.01	1	0.01	2
Females 13-49 years old	0.01	3	0.01	4

NA=not applicable

1 95th percentile of exposure

2 ARfD (acute reference dose) for all population groups (except females aged 13-49 years) = 0.75 mg/kg bw
For females aged 13-49 years, ARfD = 0.47 mg/kg bw

3 The risk estimate could not be determined for the general population as separate ARfDs were selected for females aged 13-49 year and the other population groups.

Table VI.2 Chronic Food and Drinking Water Risk Estimates

Population Groups	Food Exposure		Food and Drinking Water Exposure	
	mg/kg bw/day	% ADI[1]	mg/kg bw/day	% ADI[1]
General Population	0.006	4	0.009	6
All Infants (<1 year old)	0.008	5	0.017	12
Children 1-2 years old	0.015	10	0.019	13
Children 3-5 years old	0.014	9	0.018	12
Children 6-12 years old	0.009	6	0.012	8
Youth 13-19 years old	0.005	4	0.007	5
Adults 20-49 years old	0.005	3	0.007	5
Adults 50+ years old	0.004	3	0.007	5
Females 13-49 years old	0.004	3	0.007	5

1 ADI (acceptable daily intake) for all populations = 0.15 mg/kg bw/day

Appendix VII Food Residue Chemistry Summary

1.1 Metabolism

The nature of the residue in plants and animals is understood. Based on available data, the residue definition is the parent, clopyralid. This is consistent with the established residue definition.

1.1.1 Plant Metabolism

Metabolism data were available for grass, corn, wheat, barley, and canola. The residue of concern in cereals, canola, and grass is the parent, clopyralid.

1.1.2 Livestock Metabolism

Metabolism studies for lactating goats and laying hens are available on file. The residue of concern in animals is the parent, clopyralid.

1.1.3 Residue Definition

The current residue definition (RD) established in plants and animals is the parent clopyralid. Based on the available metabolism data, RD revisions are not required.

The PMRA's current RD is consistent with the RD of the USEPA

1.2 Analytical Methods

Analytical methodology data on file are adequate. The Pesticide Analytical Method (PAM) Volume II lists enforcement methods for clopyralid residues in plant (Method ACR 75.6) and animal matrices (Method ACR 86.1). These methods have undergone inter-laboratory validation and are adequate for enforcement and residue data collection. Method ACR 79.5 (plant matrices) is also deemed acceptable as an enforcement analytical methodology by the USEPA. The sensitivity for these methods range from 0.05-0.10 ppm.

There are no data on file for multi-residue methods (MRMs). CFIA does not analyze for clopyralid with their current MRMs. The USDA Pesticide Data Program (PDP) has a validated MRM.

1.3 Food Residues

1.3.1 Storage Stability

Freezer storage stability data for plants are adequate. Data were available on file for safflower, soybeans, sugar beets, oats, and corn. Clopyralid is stable in safflower, soybeans, sugar beets, and oats for up to 4 years when stored at -20°C. The data for corn indicates that clopyralid remains stable for up to 1.5 years at -15°C.

There are no freezer storage stability studies on file for animal matrices. Feeding studies on file are out-dated and do not provide storage stability information. Although not up to the current standards of the Residue Chemistry Guidelines (Dir 98-02), the feed residue data overall indicates that clopyralid is unlikely to exceed current MRL levels in animals; thus storage stability data for animal matrices are not required.

1.3.2 Crop Residues

Magnitude of residue (MOR) data for plants are adequate. Although MOR data did not meet all the Residue Chemistry Guideline (Dir98-02) requirements, it indicates that clopyralid residues are unlikely to exceed MRLs in registered crops when used according to label directions. The only crops that may have residues potentially exceeding MRLs are sugar beets. Residues in sugar beets are covered by the general MRL under the Food and Drug Regulations (FDR), subsection B.15.002(1) at ≤ 0.1 ppm. MORdata indicated highest residues of 0.3 ppm in roots and tops, and 1 ppm in molasses. The U.S tolerances for sugar beets are 2 ppm for roots, 3 ppm for leaves, and 10 ppm for molasses. For the risk assessment, the tolerance levels were used to estimate residues in sugar beets as the general MRL (≤0.1 ppm) may be an underestimate.

1.3.3 Livestock Residues

Feeding studies were available for dairy cattle, calves, chickens, and swine. The estimated maximum theoretical dietary burden (MTDB) was determined to be 26 ppm for beef and dairy cattle, and 5 ppm for swine and poultry. Based on the feed residue data at or close to the MTDB, clopyralid residues are not expected to exceed the established MRLs in animals; 0.05 ppm for tissues except kidney, 0.01 ppm for milk, 0.05 ppm for eggs, 0.2 ppm for kidney of poultry, and 0.36 ppm for kidney of ruminants.

1.3.4 Confined Accumulation in Rotational Crops

An adequate confined crop rotational study was available on file. Total residues in rotational crops planted 10 months after application are not expected to exceed 0.01 ppm. Plant back interval (PBI) restrictions of 10 months or greater are specified for most labels to address phytotoxicity.

1.3.5 Processing

Processing data were available for apples, canola, and sugar beets. Residues in processed apple juice, white sugar (sugar beets), and canola oil are not expected to exceed the general MRL at 0.1 ppm. Residues in sugar beet molasses may reach levels of 1 ppm, which exceeds the general MRL. Thus, the U.S Tolerance level of 10 ppm was used to estimate residues for sugar beet molasses in the risk assessment.

Appendix VIII Impact on the Environment

Table 1 Fate and Behaviour in the Environment

Property	Test Substance	Value Transformation Products	Comments	Reference
Terrestrial Environment				
Abiotic transformation				
Hydrolysis	clopyralid	stable	will not contribute to the transformation of clopyralid in the environment	PMRA 1228826, PMRA 1228828
Phototransformation in soil		stable	will not contribute to the transformation of clopyralid in the environment	PMRA 1228826 PMRA 1228828
Phototransformation in air		Not available	Not required in view of low vapour pressure	
Biotransformation				
Biotransformation in airobic soil	clopyralid	DT_{50} = 11.9 - 293 d DT_{90} = 39.4 - 973 d	Non persistent to persistent[a]	PMRA 1228830, 1228831,1228832,1228834,1810628
Biotransformation in anairobic soil		DT_{50} = 564 – 3400 d DT_{90} = 1870 – 11300 d	persistent[a]	PMRA 1749104 PMRA 1228832
Mobility				
Adsorption / desorption in soil	clopyralid	K_{oc} 0.03 – 28.57 mL/g	Very highly mobile[b]	PMRA 1228838 PMRA 1219756 PMRA 1806251
Soil leaching		Detected in leachate to a maximum depth of 1.8 m and in soil profile to a maximum depth of 40 cm.	Very high potential to leaching	PMRA 1810625 PMRA 1228838 PMRA 1806251
Volatilization		Vapour pressure: 1.36 mPa HLC: (1/H) 1.80 x 10^{-11} (Pa m^3 mol^{-1})	Not volatile from water and moist surfaces.	PMRA 1806253
Field studies				
Field dissipation (bare plot)	clopyralid	DT_{50} = 11.8-32 d DT_{90} = 39.8 – 106 d	Clopyralid is classified as non persistent to slightly persistent on bare plots[a]	PMRA 1136184, 1137171, 1140983, 1158924
Aquatic Environment				
Abiotic transformation				
Hydrolysis	Clopyralid	Stable	not a principle route of transformation	PMRA 1228826 PMRA 1228828

Property	Test Substance	Value Transformation Products	Comments	Reference
Phototransformation in water	Clopyralid	Stable	principle route of transformation	PMRA 1228826 PMRA 1228828
Biotransformation				
Biotransformation in aerobic water systems	Clopyralid	DT_{50}: 128-167 d DT_{50}: 582-963 d (whole system)	moderately persistent in water systems and persistent in whole systems under aerobic conditions	PMRA 1806251
Biotransformation in anaerobic water systems	Clopyralid	DT_{50}: 700- 4570 d DT_{50}: 667-2390 d	persistent in aquatic systems under anaerobic conditions	PMRA 1749104 PMRA 1228832
Bioaccumulation				
Bioaccumulation	Clopyralid	BCF: < 1 (blue gill sunfish)	low potential for bioaccumulation	PMRA 1222502
Field studies				
Aquatic Field dissipation	Clopyralid	4.7 – 8.53 d	non-persistent in aquatic systems under field conditions	PMRA 118089 PMRA 1220480

[a]classified according to the classification of Goring et al (1975)
[b]classified according to the classification of McCall et al (1981)
[c] The Pesticide annual, 2000

Table 2 Toxicity to Non-Target Species

Organism	Study Type	Species	Test material	Endpoint	Value	Degree of Toxicity	References
Terrestrial Species							
Invertebrates	Acute	Earthworm (*Eisenia foetida)*	Clopyralid technical EF-1136 (Lontrel 100)	14-day LC_{50} 28-day NOEC	**>1000 mg a.i./kg substrate** 1.97 mg a.i./kg substrate (**1.50 mg a.i./kg**)	No effects up to 1.97 mg ai/kg substrate	PMRA 1220075
	Acute oral/ contact	Honey bee (*Apis mellifera*)	Clopyralid technical EF-1136 (Lontrel 100)	48-h LD_{50} 48-h LD_{50} Oral contact	**> 100 µg a.i./bee** [a] > 200 µg a.i./bee (**>152 µg a.i/bee**) > 98 µg a.i./bee (>75 µg a.i/bee)	Practically non- toxic	PMRA 1806252

Organism	Study Type	Species	Test material	Endpoint	Value	Degree of Toxicity	References
	Contact	Beneficial arthropods *Aphidius rhopalosiphi, Typhlodromus pyri, Chrysoperla carnea, Poecilus cupreus, Pardosa* spp and *Aleochara bilineata*	EF-1136	LR_{50}	> 200 g ai/ha. **(>152 g ai/ha)**		PMRA 1806252
Birds	Acute oral	mallard duck (*Anas platyrhynchos*)	Clopyralid technical	21-day LD_{50} NOEC	**1465 mg ai/kg** <398 mg ai/kg	Slightly toxic	PMRA# 1227441
		Bobwhite quail (*Colinus virginianus*)	Clopyralid technical	14-day LD_{50} NOEC	**>2000 mg ai/kg** 500 mg g	Practically non-toxic	PMRA 1806252
	Dietary	Bobwhite quail (*Colinus virginianus*)	Clopyralid technical	5-day LC_{50} NOEC	**> 4640 mg ai/kg diet** 5000 mg ai/kg	Non- toxic	PMRA# 1040132
		mallard duck (*Anas platyrhynchos*)	Clopyralid technical	5-day LC_{50} NOEC	**> 4640 mg ai/kg diet** 5000 mg ai/kg	Non- toxic	PMRA# 1040131
	Chronic (repro)	Mallard duck (*Anas platyrhynchos*)	Clopyralid technical	22- week NOEC	**>1000 mg a.i/kg diet**		PMRA# 1219752
Mammals	Acute oral	Rat	Clopyralid technical	LD_{50}	**>5000 mg a.i./kg bw**		HED
	Dietary	Rat	Clopyralid technical	90 day NOAIL	**150 mg a.i./kg bw/day**		HED
	Chronic (repro)	Rat	Clopyralid technical	2 generation NOAIL	**>1500 mg a.i./kg bw/day**		HED
Nontarget Plants	Post Emergence	*Avena sativa, Allium cepa, Cyperus esculentus, Brassica napus and Beta vulgaris*	EF-1136 (Lontrel 100) Clopyralid technical	EC_{50}	>120 g a.i./ha (>91.2 g ai/ha)		PMRA 1806252

Organism	Study Type	Species	Test material	Endpoint	Value	Degree of Toxicity	References
		Glycine max		EC_{25} EC_{50}	**7.4 g a.i./ha (5.6 g ai/ha)** 25.4 g ai/ha (19.3 g ai/ha)		
Freshwater Organisms							
Invertebrates	Acute	waterflea (*Daphnia magna*)	clopyralid technical Lontrel 100	48-h LC_{50} 48-h LC_{50}	**232 mg ai/L** 130 mg ai/L	Practically non-toxic	PMRA# 1228852
	Chronic	waterflea (*Daphnia magna*)	Clopyralid technical	21-d NOEC	**17mg ai/L**		PMRA 1806252
Fish	Acute	Rainbow trout *(Oncorhynchus mykiss)*	Clopyralid technical Lontrel 100	96-h LC_{50} 96-h LC_{50}	**>99.9 mg ai/L** 53 mg a.i./L	Practically non-toxic	PMRA 1806252
		Bluegill sunfish (*Lepomis macrochirus*)	Clopyralid technical	96-h LC_{50}	>102 mg ai/L	Practically non-toxic	PMRA 1806252
	Chronic	Fathead minnow *(Pimephales promelas*)	Clopyralid technical	34-d NOEC	**10.8 mg ai/L**		PMRA 1806252
Algae	Acute	Green algae (*Selenastrum capricornutum*)	Clopyralid technical Lontrel 200 Clopyralid technical	96-h EC_{50} (cell count and cell volume) 96-h EC_{50} (cell count and cell volume) 96-h EC_{50} (reduced growth rate and cell volume) NOEC	**6.9 & 7.3 mg ai/L** 11.2 & 12.4 mg ai/L 32.7 & 33.1 mg ai/L 24.8 mg a.i./L	Moderately toxic Slightly toxic	PMRA 120070 PMRA 120071 PMRA 1806252

Organism	Study Type	Species	Test material	Endpoint	Value	Degree of Toxicity	References
		Bluegreen algae *(Anabaena flos-aquae)*	Clopyralid technical	120-h EC50 NOEC	37.1 mg ai/L 24.2 mg ai/L	Slightly toxic	PMRA 1806252
Vascular plants	Dissolved – 14 d	*Lemna gibba*	Clopyralid technical	14-day EC_{50} NOEC	**89 mg ai/L** 12 mg ai/L		
Sediment dwelling organism	chronic	*Chironomus riparius*	Clopyralid technical	28-day EC_{50} NOEC	**>97 mg ai/L** 50 mg ai/L		
Amphibians[1]	Acute		Clopyralid technical	96-h LC50	**>99.9mg ai./L**		
	Chronic		Clopyralid technical	34-d NOEC	**10.8mg ai./L**		

[1] Endpoints from fish used as surrogate
[a] Atkins et al. (1981) for bees and US EPA classification for others, where applicable
Values in bold used in risk assessment

Table 3 Screening Level Risk Assessment On Terrestrial Non-Target Species Other Then Birds And Mammals

Organism	Exposure	Endpoint (mg ai/kg	Screening level EEC[1]	RQ [2]	LOC[3] Exceeded	EEC from spray drift	RQ	LOC Exceeded
Apple use (ground)								
Earthworm	14-d LC50	LC50 >500÷2	0.150393	<0.0003	No	N/A	N/A	N/A
Earthworm	28-d NOEC	>1.5	0.150393	<0.10	No	N/A	N/A	N/A
P. cupreus	Contact	LR_{50} 0.152	0.150	0.0009	No	N/A	N/A	N/A
Pardosa Sp.	Contact	LR_{50} 0.152	0.150	0.0009	No	N/A	N/A	N/A
A.bilineata	Contact	LR_{50} 0.152	0.150	0.0009	No	N/A	N/A	N/A
Apple (35 -day foliar half-life)								
Bees - oral	Acute	LD_{50} >112[4]	284.305	<0.003	No	N/A	N/A	N/A
Beneficial arthropods	Contact	LR_{50} >152	284.305	<1.9	Yes	17.06	<0.11	No
Non-target plants	Acute	EC_{25} 5.6	284.305	50.8	Yes	17.06	3.05	Yes
Apple (10 -day foliar half-life)								
Non-target plants	Acute	EC_{25} 5.6	210.515	37.6	Yes	12.63	2.3	Yes

Organism	Exposure	Endpoint (mg ai/kg	Screening level EEC[1]	RQ [2]	LOC[3] Exceeded	EEC from spray drift	RQ	LOC Exceeded
Flax (35 -day foliar half-life)								
Bees - oral	Acute	LD_{50} >112	298.9	<0.003	No	N/A	N/A	N/A
Beneficial arthropods	Contact	LR_{50} >152	298.9	<1.97	Yes	17.93	<0.12	No
Non-target plants	Acute	EC_{25} 5.6	298.9	53.4	Yes	17.93	3.2	Yes
Balsam Fir								
Bees - oral	Acute	LD_{50} >112	252	<0.002	No	N/A	N/A	N/A
Beneficial arthropods	Contact	LR_{50} >152	252	<1.7	Yes	15.12	<0.10	No
Non-target plants	Acute	EC_{25} 5.6	252	45	Yes	15.12	2.7	Yes
Wheat								
Bees - oral	Acute	LD_{50} >112	201.6	<0.002	No	N/A	N/A	N/A
Beneficial arthropods	Contact	LR_{50} >152	201.6	<1.3	Yes	12.096	<0.08	No
Non-target plants	Acute	EC_{25} 5.6	201.6	36	Yes	12.096	2.2	Yes
Lowbush blue berry								
Bees - oral	Acute	LD_{50} >112	151.2	<0.001	No	N/A	N/A	N/A
Beneficial arthropods	Contact	LR_{50} >152	151.2	<1.0	No	9.072	<0.06	No
Non-target plants	Acute	EC_{25} 5.6	151.2	27	Yes	9.072	1.6	Yes
Field corn Hybrid								
Bees - oral	Acute	LD_{50} >112	135	<0.001	No	N/A	N/A	N/A
Beneficial arthropods	Contact	LR_{50} >152	135	<0.89	No	8	<0.05	No
Non-target plants	Acute	EC_{25} 5.6	135	24.1	Yes	8	1.5	Yes
Canary seed								
Bees - oral	Acute	LD_{50} >112	100	<0.001	No	N/A	N/A	N/A
Beneficial arthropods	Contact	LR_{50} >152	100	<0.66	No	6	<0.04	No
Non-target plants	Acute	EC_{25} 5.6	100	17.9		6	1.1	Yes

[1)] Environmental Exposure Concentration (Soil: calculated based on a soil density of 1.5 g/cm^3, soil depth of 15 cm and the label rates taking into consideration dissipation between applications; Bee: maximum application rate (application rate x no. of applications).
[2)] Risk Quotient (RQ) = exposure/toxicity.
[3)] Level of Concern (LOC) = RQ = 1;a calculated RQ > 1 exceeds the LOC.
[4)] Toxicity in µg/bee converted to the equivalent kg a.i./ha using a conversion factor of 1.12 (Atkins et al., 1981).
Atkins EL; Kellum D; Atkins KW. 1981. Reducing pesticide hazards to honey bees: mortality prediction techniques and integrated management techniques. Univ Calif, Div Agric Sci, Leaflet 2883. 22 pp.
N/A not available

Table 4 Screening Level Risk Assessment On Birds And Mammals

Organism		Endpoint Value[1]	Feeding Guilds	Exposure[2]		RQ[3]	LOC exceeded
				EEC (mg ai/kg dry weight)	EDE[4] (mg ai/kg bw/day)		
Application Rate 298.9 g ai/ha							
Birds							
Bird: 20 g	Acute	146.5mg a.i./kg bw/day	Insectivore	59.06	15.06	0.10	No
			Granivore	14.77	3.77	0.03	No
			Frugivore	29.53	7.53	0.05	No
	Dietary	26.25mg a.i./kg bw/day	Insectivore	59.06	15.06	0.13	No
			Granivore	14.77	3.77	0.03	No
			Frugivore	29.53	7.53	0.06	No
	Reproduction	56.56mg a.i./kg bw/day	Insectivore	59.06	15.06	0.06	No
			Granivore	14.77	3.77	0.02	No
			Frugivore	29.53	7.53	0.03	No
Bird: 100 g	Acute	146.5mg a.i./kg bw/day	Insectivore	59.06	11.75	0.08	No
			Granivore	14.77	2.94	0.02	No
			Frugivore	29.53	5.88	0.04	No
	Dietary	26.25mg a.i./kg bw/day	Insectivore	59.06	11.75	0.10	No
			Granivore	14.77	2.94	0.02	No
			Frugivore	29.53	5.88	0.05	No
	Reproduction	56.56mg a.i./kg bw/day	Insectivore	59.06	11.75	0.05	No
			Granivore	14.77	2.94	0.01	No
			Frugivore	29.53	5.88	0.02	No
Bird: 1000 g	Acute	146.5 mg a.i./kg bw/day	Insectivore	59.06	3.43	0.02	No
			Granivore	14.77	0.86	0.006	No
			Frugivore	29.53	1.72	0.01	No
			Herbivore	397.84	23.11	0.16	No
	Dietary	26.2mg a.i./kg bw/day	Insectivore	59.06	3.43	0.13	No
			Granivore	14.77	0.86	0.03	No
			Frugivore	29.53	1.72	0.07	No
			Herbivore	397.84	23.11	0.88	No
	Reproduction	56.56mg a.i./kg bw/day	Insectivore	59.06	3.43	0.06	No
			Granivore	14.77	0.86	0.02	No
			Frugivore	29.53	1.72	0.03	No
			Herbivore	397.84	23.11	0.4	No

Mammals							
Mammal: 15 g	Acute	5000 mg a.i./kg bw/day	Insectivore	59.06	8.66	0.002	No
			Granivore	14.77	2.17	0.0004	No
			Frugivore	29.53	4.33	0.0009	No
	Dietary	150 mg a.i./kg bw/day	Insectivore	59.06	7.59	0.058	No
			Granivore	14.77	1.90	0.014	No
			Frugivore	29.53	4.33	0.029	No
	Reproduction	1500 mg a.i./kg bw/day	Insectivore	59.06	7.59	0.006	No
			Granivore	14.77	1.90	0.002	No
			Frugivore	29.53	4.33	0.003	No
Mammal: 35 g	Acute	5000 mg a.i./kg bw/day	Insectivore	59.06	7.59	0.0015	No
			Granivore	14.77	1.90	0.0004	No
			Frugivore	29.53	3.80	0.0008	No
			Herbivore	397.84	51.15	0.01	No
	Dietary	150 mg a.i./kg bw/day	Insectivore	59.06	7.59	0.05	No
			Granivore	14.77	1.90	0.013	No
			Frugivore	29.53	4.33	0.025	No
			Herbivore	397.84	51.15	0.34	No
	Reproduction	1500 mg a.i./kg bw/day	Insectivore	59.06	7.59	0.051	No
			Granivore	14.77	1.90	0.0013	No
			Frugivore	29.53	4.33	0.0025	No
			Herbivore	397.84	51.15	0.034	No
Mammal: 1000g	Acute	5000 mg a.i./kg bw/day	Insectivore	59.06	4.05	0.0008	No
			Granivore	14.77	1.0	0.0002	No
			Frugivore	29.53	2.03	0.0004	No
			Herbivore	397.84	27.33	0.055	No
	Dietary	150 mg a.i./kg bw/day	Insectivore	59.06	4.05	0.03	No
			Granivore	14.77	1.0	0.007	No
			Frugivore	29.53	2.03	0.0135	No
			Herbivore	397.84	27.33	0.18	No
	Reproduction	1500 mg a.i./kg bw/day	Insectivore	59.06	4.05	0.003	No
			Granivore	14.77	1.0	0.0007	No
			Frugivore	29.53	2.03	0.0014	No
			Herbivore	397.84	27.33	0.018	No

[1]) Endpoints were divided by an Uncertainty Factor to account for varying protection goals (i.e., protection at the community, population, or individual level)

[2]) EEC: For birds and mammals, the EEC takes into account the maximum seasonal cumulative rate on vegetation and is calculated using PMRA standard methods based on the Hoerger and Kenaga nomogram as modified by Fletcher (1994)

EDE = Estimated dietary exposure; calculated for each bird or mammal size based on the EEC on appropriate food item for each food guild (at the screening level, the most conservative EEC for each food guild was used). The EDE was calculated using the following formula: (FIR/BW) x EEC. For each body weight (BW), the food ingestion rate (FIR) was based on equations from Nagy (1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used; for mammals, the "all mammals" equation was used:

Passerine Equation (body weight ≤200 g): FIR (g dry weight/day) = 0.398(BW in g) $^{0.850}$
All Birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(BW in g) $^{0.651}$
All Mammals Equation: FIR (g dry weight/day) = 0.235(BW in g) 0.822
[3]) RQ = exposure/toxicity; RQs < 0.1 were not calculated to show all decimal points
[4]) Conversion from a concentration (EEC) to a dose (EDE): [EDE (mg ai/kg bw) = EEC (mg ai/kg diet)/BW (g) x FIR (g diet/day)]
Nagy, K.A. 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecological Monographs 57:111-128

Table 5 Risk Assessment to Aquatic Organisms

Organism	Exposure	Endpoint value[1]	Use Rate	EEC[2] (mg ai/L)	RQ	LOC exceeded
Freshwater Species						
waterflea (*Daphnia magna*)	Acute	48-h LC_{50} ÷ 2 (116 mg ai/L)	201.6 g a.i./ha x 2	0.05	0.0004	No
waterflea (*Daphnia magna*)	Chronic	21-d NOEC (17 mg ai/L)	201.6 g a.i./ha x 2	0.05	0.0029	No
Rainbow trout (*Oncorhynchus mykiss*)	Acute	96-h LC_{50} ÷ 10 (>9.99 mg ai /L)	201.6 g a.i./ha x 2	0.05	<0.005	No
Fathead minnow (*Pimphales promelas*)	Chronic	34-d NOEC (10.8 mg ai/L)	201.6 g a.i./ha x 2	0.05	0.005	No
Green algae (*Selenastrum capricornutum*)	Acute	96-h EC_{50} ÷ 2 (3.45 mg ai /L)	201.6 g a.i./ha x 2	0.05	0.003	No
Vascular plants (*Lemna gibba*)	Acute	14-d EC_{50} ÷ 2 (44.5 mg ai /L)	201.6 g a.i./ha x 2	0.05	0.001	No
Chironomid (*Chironomus riparius*)	Chronic	28-d LC_{50} (>97 mg ai /L)	201.6 g a.i./ha x 2	0.05	<0.0005	No
Amphibians[3]	Acute	96-h LC_{50} ÷ 10 (>9.99 mg ai /L)	201.6 g a.i./ha x 2	0.27	<0.026	No
Amphibians[3]	Chronic	21-d NOEC (10.8 mg ai /L)	201.6 g a.i./ha x 2	0.27	0.026	No

[1]) Endpoints were divided by an Uncertainty Factor to account for varying protection goals (i.e., protection at the community, population, or individual level)
[2]) EEC based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic organisms.
[3]) Endpoints from fish used as surrogate

Table 6 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value	Active Ingredient Endpoints	Transformation Products Endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes	-	-
Predominantly anthropogenic[2]	Yes	-	-

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints	Transformation Products Endpoints
Persistence[3]:	Soil	Half-life ≥ 182 days	Half-life = 32 d	
	Water	Half-life ≥ 182 days	Half-life = 167 d	
	Sediment	Half-life ≥ 365 days	Half-life = not available	
	Air	Half-life ≥ 2 days or evidence of long range transport	Volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (1.36 mPa) and Henry's Law Constant (1.80 x 10-^{11}Pa m^3 mol^{-1})	
Bioaccumulation[4]	Log K_{OW} ≥ 5		-2.63	
	BCF ≥ 5000		<1	
	BAF ≥ 5000		not available	
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.	No, does not meet TSMP Track 1 criteria.

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e., all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]Field data (e.g., BAFs) are preferred over laboratory data (e.g., BCFs) which, in turn, are preferred over chemical properties (e.g., log K_{OW}).

Appendix IX Monitoring Data

Water Monitoring Data

Summary of drinking water exposure estimates.

Acute and chronic exposure estimates for clopyralid in surface water for the purpose of environmental risk assessment are 1.23µg/L and 0.11µg/L, respectively, based on available monitoring data. The acute exposure estimate is the 95th percentile of the maximum detected concentrations from surface water monitoring studies. The chronic exposure estimate is the 95th percentile of the mean concentration for each study site, including non-detects which were assigned a value of half the limit of detection.

An important limitation of the monitoring data is that, in many cases, the data were not accompanied with clopyralid use information such as the application rate, time of application and meteorological conditions prior to sampling. Without this information, it is difficult to accurately interpret the data and conclude if non-detects were a result of non-transport or more simply a result of inappropriate timing of sampling. In addition, because the data are sparse and concentrations vary in time and space, the maximum concentration reported is unlikely to be the absolute maximum concentration that would be observed in Canada. Factors that may result in higher concentrations being detected include application at higher rates, precipitation and some areas/soils are simply more prone to leaching and/or run off. Sampling at intervals immediately following application would increase the likelihood that the maximum concentration would be detected. Thus, it is likely clopyralid was not used in some of the areas monitored, and that higher concentrations of clopyralid may occur in other areas not monitored.
Details of the available water monitoring data are available upon request.

Appendix X Label Amendments for Commercial Class Products Containing Clopyralid

COMMON NAME: Clopyralid

CHEMICAL NAME: 3,6-dichloro-2-pyridinecarboxylic acid

FORMULATION TYPES: Solution
Emulsifiable concentrate
Granular
Soluble Granular

USE-SITE CATEGORIES:

4	Forest and Woodlots
7	Industrial Oil Seed Crops and Fibre Crops
8	Livestock for Food
13	Terrestrial Feed Crops
14	Terrestrial Food Crops
16	Industrial and Domestic Vegetation Control for Non-Food Sites
27	Ornamentals Outdoor

GENERAL LIMITATIONS

SPECIFIC TO HEADER ON LABEL

The following warning statement should appear on the label of the technical product:

Danger: Eye Irritant

PRECAUTIONARY STATEMENTS

PROTECTIVE CLOTHING AND EQUIPMENT:

Workers must wear long pants, long sleeved shirt, and chemical resistant gloves. Goggles or a face shield are required during mixing and loading. Gloves are not required to be worn during groundboom application, but are required for mixing/loading, clean-up and repair.

RESTRICTED ENTRY INTERVAL:

Restricted entry interval (REI) of 12 hours for all crops.

DIRECTIONS OF USE

Not for use in greenhouses.

Apply only when the potential for drift to areas of human habitation or areas of human activity; such as houses, cottages, schools and recreational areas, is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

ENVIRONMENTAL HAZARDS:

TOXIC to non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE.

The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (e.g. sandy soil) and/or the depth to the water table is shallow.

To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to: heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g. soils that are compacted or fine textured such as clay).

Avoid application of this product when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

Add to DIRECTIONS FOR USE:

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground.

DO NOT apply by air.

Buffer Zones:

Uses of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

For application to rights-of-way, buffer zones for protection of sensitive terrestrial habitats are not required; however, the best available application strategies which minimize off-site drift, including meteorological conditions (e.g., wind direction, low wind speed) and spray equipment (e.g., coarse droplet sizes, minimizing height above canopy), should be used.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, woodlots, hedgerows, riparian areas and shrublands).

Method of application	Crop	Buffer Zones (metres) Required for the Protection of Terrestrial habitat:
Field sprayer*	Wheat, barley, oats, flax, canola, forage grasses, high-bush blueberry, low-bush blueberry, strawberry, sugar beet, rutabaga, cabbage, broccoli, cauliflower, field corn (hybrid), canary seed, balsam fir, Christmas tree plantations, shelterbelts, poplar and their hybrids, non-crop uses, rangeland and grass pasture	2**
	Apple	3

*For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy, the labelled buffer zone can be reduced by 30%.

**Buffer zones for the protection of terrestrial habitats are not required for use on rights-of-way including railroad ballast, rail and hydro rights-of-way, utility easements, roads, and training grounds and firing ranges on military bases.

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

Appendix XI Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices. There are clopyralid MRLs established in Canada and tolerances established in the U.S. There are no MRLs specified in the CODEX.

Under the North American Free Trade Agreement, Canada, the United States and Mexico are committed to resolving MRL discrepancies to the broadest extent possible. Harmonization will standardize the protection of human health across North America and promote the free trade of safe food products. Until harmonization is achieved, the Canadian MRLs and regulatory amendments presented in this document are necessary. The differences in MRLs/tolerances outlined above are not expected to impact businesses negatively or adversely affect international competitiveness of Canadian firms or to negatively affect any regions of Canada.

Table XI.1 Comparison between MRLs in Canada and in Other Jurisdictions

Commodity	Registered Canadian Use	MRL (ppm)[1]	U.S. Tolerance (ppm)[2]
Plant Crops			
Apple	✓		
Asparagus			1
Barley	✓	2	3 (grain)
Barley milling fractions, excluding flour	✓	7	12
Beet, garden, tops			3
Beet, garden, roots			4
Beet, sugar, molasses	✓		10
Beet, sugar, roots	✓		2
Beet, sugar, tops	✓		3
Blueberries	✓	0.1	
Brassica, head and stem, subgroup 5A	✓		2
Broccoli	✓	1	2
Cabbages	✓	1	2
Canola, meal	✓		6

Commodity	Registered Canadian Use	MRL (ppm)[1]	U.S. Tolerance (ppm)[2]
Canola, seed	✓		3
Cauliflower	✓	1	2
Chinese broccoli	✓	1	2
Chinese mustard cabbages	✓	1	2
Chinese radish	✓		
Corn, field, grain	✓		1
Corn, field, milled byproducts	✓		1.5
Corn, pop, grain			1
Corn, sweet, kernel plus cob with husks removed			1
Crambe, seed			3
Cranberry	✓		4
Flax	✓	0.2	6 (meal) 3 (seed)
Fruit, stone, group 12			0.5
Hop, dried cones			5
Kohlrabi	✓	1	2
Mustard greens			5
Mustard, seed			3
Napa Chinese Cabbages	✓	1	2
Oats	✓	2	3 (grain)
Oat milling factions, excluding flour	✓	7	12
Plum, prune, dried			1.5
Rapeseed, seed	✓		3
Rutabaga	✓		
Spinach			5
Strawberries	✓	1	1
Turnip, greens			4

Commodity	Registered Canadian Use	MRL (ppm)[1]	U.S. Tolerance (ppm)[2]
Turnip, roots			1
Wheat	✓	2	3 (grain)
Wheat milling fractions, excluding flour	✓	7	12
Animal Commodities			
Eggs		0.05	0.1
Fat of cattle, goats, horses, sheep		0.05	1
Fat of hogs		0.05	0.2
Fat of poultry		0.05	0.2
Kidney of cattle, goats, horse, sheep		0.36	3
Kidney of hogs		0.05	0.2
Kidney of poultry		0.2	0.2
Meat byproducts of cattle, goats, horses, sheep		0.05	36
Meat byproducts of hogs		0.05	0.2
Meat byproducts of poultry		0.05	0.2
Meat of cattle, goats, horses, sheep		0.05	1
Meat of hogs		0.05	0.2
Meat of poultry		0.05	0.2
Milk		0.01	0.2

[1] By virtue of subsection B.15.002(1) of the Food and Drug Regulations, the MRL of foods for which MRLs have not specifically been established is 0.1 ppm.

[2] As per Title 40 Part 180.261 of the United States Code of Federal Regulations. United States tolerances for livestock feed items (alfalfa, almond hulls, field pea vines and field pea hay) are not presented. See also http://www.access.gpo.gov/nara/cfr/waisidx_04/40cfr180_04.html

Table XI.2 Residue Definition in Canada and Other Jurisdictions

Jurisdiction	Residue Definition in Plants and Animals
Canada	clopyralid (3,6-dichloro-2-pyridinecarboxylic acid)
United States	clopyralid (3,6-dichloro-2-pyridinecarboxylic acid)

References

Chemistry

Studies/Information Submitted by Registrant

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PMRA 1797949 1993, DPI-DOA-7 Response to Special Data Call-In Notice for Product Chemistry Data Relating to Potential Formation of Hexachlorobenzene and Petachlorobenzene in Certain Pesticide Active Ingredients - September 2, 1992, DACO: 2.11

PMRA 1481488 2007, Control Product Specification Form, DACO: 0.1.6003

PMRA 1081603 2005, Statement of Product Specification Form, DACO: 0.1.6003

PMRA 1329023 2001, Clopyralid Batch Analysis, DACO: 2.13.3 CBI

PMRA 1329022 2002, Quality Control Data for Five Representative Batches of Lontrel F - Supplemental Information for Canada, DACO: 2.13.3 CBI

PMRA 1329024 2002, Clopyralid Batch Analysis (GC-MS Analysis for Determination of Hexachlorobenzene and Pentachlorobenzene., DACO: 2.13.4 CBI

Toxicology

Studies/Information Submitted by Registrant

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PMRA 1220825 1973, *In vitro* and subacute *in vivo* host-mediated assay for mutagenesis. Final report - Compound Dowco 290, DACO: 4.5.4

PMRA 1220864 1983, Dowco 290: Results of a 13-week dietary toxicity study in $B_6C_3F_1$ mice, DACO: 4.3.1

PMRA 1220869 & 1221059 & 1222492 1983, Dowco 290: Two generation dietary reproduction study in Fischer-344 rats, DACO: 4.5.1

PMRA 1220870 1976, Dowco 290 herbicide (3,6-dichloro- picolinic acid): Results of a six-month dietary feeding study in Beagle dogs (2508), DACO: 4.3.1

PMRA 1220871 1975, 180-day subacute toxicity study in dogs, DACO: 4.3.1

PMRA 1220903 1987, Acute oral toxicity study in Fischer 344 rats (K-038252-033A), DACO: 4.2.1

PMRA 1220904 1987, Acute dermal toxicity study in New Zealand White rabbits (K-038252-033D), DACO: 4.2.2

PMRA 1220906 1987, An acute aerosol inhalation study in Fischer 344 rats (K-038252-034), DACO: 4.2.3

PMRA 1220907 1987, Primary eye irritation study in New Zealand White rabbits (K-038252-033C), DACO: 4.2.4

PMRA 1220908 1987, Primary dermal irritation study in New Zealand White rabbits (K-038252-033B), DACO: 4.2.5

PMRA 1220909 1987, Dermal sensitization potential in the Hartley Albino Guinea pig (K-038252-033E), DACO: 4.2.6

PMRA 1220914 1986, Lontrel T Toxicity to rats by dietary admixture for 4 weeks (DWC 463/86108), DACO: 4.3.1

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PMRA 1914387 United States Environmental Protection Agency, 2001, Clopyralid; Pesticide Tolerance - Federal Register - Volume 66, Number 8, DACO: 12.5

PMRA 1914388 European Food Safety Authority, 2005, Conclusion Regarding the Peer Review of the Pesticide Risk Assessment of the Active Substance Clorpyralid, DACO: 12.5

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Dietary

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PMRA 1157114 1993, Summary of Clopyralid Applied Post-Emergent or Preplant Incorporated to Field Corn, DACO: 7.1

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PMRA 1158924 Soil dissipation study with Clopyralid (94dwe01;E4-07-102,E4-08-090,E4-08-091,E4-08-092,E4-090350,E4-09-351)(Lontrel/Lontrel 360), DACO: 8.3.2.3

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PMRA 1228831 1977, Effect of Temperature, Moisture and Concentration of the degradation rate of Dowco 290 in Soil incubated under Aerobic Conditions (GH-C996), DACO: 8.2.3.1

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