Evaluation Report for Category B, Subcategory 4.1 Application

Application Number: 2007-8790
Application: B.4.1 (Conversion to full registration without consultation)
Product: Marks Mecoprop-p Technical Acid
Registration Number: 27441
Active ingredients (a.i.): Mecoprop P-Isomer (present as acid) (MEP)
PMRA Document Number: 1902214

Background

During the re-evaluation of the active ingredient mecoprop (racemic: 50/50 R/S isomers), the PMRA had identified significant data gaps for racemic mecoprop that would have to be addressed in order to bring the supporting database up to modern standards (Re-evaluation Decision Document for Mecoprop, RRD2004-09). At the time, rather than generating the required data to support continuing registration, the registrants of technical racemic mecoprop had decided to discontinue sales of the racemic form of mecoprop and replace it with a specific isomer of mecoprop known as mecoprop-p.

Purpose of Application

The purpose of this application was to convert Marks Mecoprop-p Technical Acid (Registration Number 27441) to full registration. This application was assessed at the same time as conversion applications for Nufarm Mecoprop-p Technical Acid (Registration Number 27631) and A.H. Marks MCPP-p 600 Liquid Herbicide (Registration Number 28563).

Furthermore, there were approximately 60 associated end-use products assessed for conversion from conditional to full registration. The conversion of these applications was dependent on the conversion of the above three applications.

Chemistry Assessment

The chemistry requirements have been fulfilled.

Health Assessments

Toxicology Summary

The PMRA conducted a detailed review of the toxicological database for mecoprop-p. The database consists of an array of laboratory animal (*in vivo*) and cell culture (*in vitro*) toxicity studies currently required for health hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is acceptable, and the database is considered adequate to characterize the toxicity of this chemical.

Available acute, short-term, and long-term toxicity data comparing mecoprop-p, mecoprop racemate, mecoprop-p dimethylamine (DMA), and mecoprop-p ethylhexylester (EHE) showed no significant differences in toxicity potential. Systemic toxicity findings in laboratory animals were similar. *In vivo* and *in vitro* dissociation/degradation studies demonstrated that mecoprop-p DMA and mecoprop-p EHE were readily hydrolyzed to mecoprop-p. The degradation study findings supported the view that the toxicity effects observed in studies tested with mecoprop-p DMA and mecoprop-p EHE are mostly due to mecoprop-p. Therefore, toxicity data generated with mecoprop racemate, mecoprop-p DMA, and mecoprop-p EHE can be used to support the registration of mecoprop-p.

Laboratory studies demonstrated that the absorption of mecoprop-p was rapid and extensive following oral administration in the rat. Peak plasma concentrations were seen shortly after exposure. The compound was excreted rapidly in urine with most of the administered radioactivity (AR) collected in urine within 24 hours. Fecal elimination constituted about 4-12% of the AR. A total of >77% of the AR was eliminated within 24-48 hours. No radioactivity was detected in expired air. Tissue distribution of radioactivity was extensive, but the level declined rapidly. The total radioactivity remaining in tissues was low and there was no evidence of accumulation when the rats were killed at 168 hours after dosing. It was concluded that mecoprop-p was absorbed rapidly and extensively, and excreted rapidly in urine, either unchanged, as hydroxylated mecoprop-p, or in the form of one of up to seven minor metabolites. There were no notable gender differences in the metabolic profile of mecoprop-p in the rat.

In the rat, mecoprop-p is moderately to highly acutely toxic by the oral route, but is of low acute toxicity by the dermal and inhalation routes of exposure. Mecoprop-p is extremely irritating to the rabbit eye affecting the cornea, but is only slightly irritating to the rabbit skin. Mecoprop-p is not a skin sensitizer when tested in the guinea pig.

In short- and long-term dietary toxicity studies in mice, rats, and dogs, mecoprop-p induced systemic toxicity at high dose levels. Systemic toxicity invariably involved reduced food intake and lowered body weight and body-weight gains. The liver, kidneys, and the adrenals were the target organs. Liver effects were characterized by higher weights and cellular changes. Although the kidney weights were higher in mecoprop-p exposed rodents, there were no accompanying gross or histopathological changes. The effects in the adrenals were observed only at a high dose level in the rat, and the changes included discolouration and lipid accumulation.

After repeated dermal administration of mecoprop-p in the rabbit for 21 days, only minor local dermal effects were evident, and there was no systemic toxicity up to the limit dose.

In vivo/*in vitro* genotoxicity studies of mecoprop-p assessing gene mutation, chromosome aberration, and unscheduled DNA synthesis showed negative genotoxic findings. However, tests with mecoprop racemate in *in vitro* chromosome aberration and *in vivo* sister chromatid exchange in Chinese hamster bone marrow cells gave equivocal findings because some positive findings were observed at cytotoxic levels while others were not reproducible.

A two-year combined dietary toxicity and oncogenicity study on mecoprop (racemic mixture) in the rat is deficient because the dose levels tested were not high enough; the highest dose level tested did not produce any effects on mortality, clinical signs, ophthalmoscopy, haematology, clinical chemistry, urinalysis, or gross and histopathology. A second carcinogenicity study of mecoprop-p in the rat was later conducted. Sufficiently high dose levels were tested and the findings showed that mecoprop-p was not carcinogenic in the rat. Two studies were also conducted to assess the oncogenic potential of mecoprop-p in the mouse. In the first study, the highest dose level was terminated early at around one year and the mice at this level were killed without histopathological examination despite the presence of subcutaneous palpable masses in the majority of the high-dose mice. In the second study, a higher incidence of liver adenoma and carcinoma was recorded in the females. Combining the data from the two mouse oncogenicity studies demonstrated that mecoprop-p induced liver neoplasms in the female mouse but not in the male.

Reproductive toxicity data were generated for mecoprop racemate in the rat. There were no effects on the parental animal or on reproductive performance. There were no significant differences in birth, viability, and gestation indices. However, at the highest dose level, there was an increase in pup deaths and lower weight gains during lactation days zero to four. The effects occurred at a dose that did not induce maternal toxicity.

Teratology data on mecoprop racemate in rats, and mecoprop-p in the rat and rabbit did not demonstrate any evidence of teratogenicity. For the racemate, developmental toxicity (higher post-implantation loss, lower foetal weight and foetal crown/rump length) occurred at maternally toxic dose levels. For mecoprop-p, the highest dose level tested in the rabbit did not induce any maternal or developmental toxicity. It appeared that the maximum tolerable dose was not reached in the rabbit teratology study. However, data from other short- and long-term toxicity studies indicated that the highest dose level tested in the rabbit teratology study should be close to an effect level. Thus, the rabbit teratology study is considered adequate. In the rat, the highest dose level tested resulted in lower maternal body weight and increase minor skeletal variations in the pups.

Acute and short-term neurotoxicity data of mecoprop-p in the rat did not demonstrate any evidence of neurotoxicity. There were no triggers in the toxicological database to warrant a study to investigate developmental neurotoxicity.

In summary, mecoprop-p is moderately to highly toxic by the oral route. It is of low toxicity by the dermal and inhalation routes. Mecoprop-p is highly irritating to the eye, but is slightly to moderately irritating to the skin. Mecoprop-p is not a dermal sensitizer. Repeated exposures to mecoprop-p in laboratory animals cause liver, kidney, and adrenal changes, together with reduced body-weight gain at high dose levels. Mecoprop-p is not genotoxic, neurotoxic, or teratogenic. Oncogenicity data in the mouse indicated that mecoprop-p induced a higher incidence of liver tumours in the female. Reproductive toxicity study of the racemate in the rat showed that there was an increase in pup deaths at a dose level that did not cause maternal toxicity.

Results of the acute and repeat exposure tests conducted on laboratory animals with mecoprop-p technical, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Tables 1, 2, and 3 of Appendix I.

Incident Reports

Starting April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the report of incidents can be found on the PMRA website.

As of April 30, 2010, 49 incident reports involving humans (29) and domestic animals (20) were received by the PMRA. All incidents involved end-use products containing 2,4-D, dicamba, or 2,4-dichlorprop-P, and mecoprop-p as the active ingredients. In no cases were products containing mecoprop-p as the sole active ingredients involved. In most cases, exposure was dermal via accidental contact with the products or of lawns treated with weed control products and fertilizers; direct ingestion of the products was not confirmed or witnessed.

Causality has not been established for the effects noted in the incident reports for mecoprop-p exposure; the symptoms noted in the reports were non-specific and could be attributed to the exposure of a combination of chemicals. In all cases, the observed effects were of short duration.

In 2007, the EPA reviewed various databases such as the Office of Pesticides Program Incident Data System, Poison Control Center, California Department of Pesticide Regulation and the National Institute of Occupational Safety and Health's Sentinel Event Notification system for Occupational Risks and did not identify any human incidents involving mecoprop-p (EPA Reregistration Eligibility Decision (RED) for Mecoprop-p (MCPP), August 29, 2007).

PCPA Hazard Characterization

For assessing risks from potential residues in food or from products used in or around residential areas or schools, the *Pest Control Products Act* (PCPA) requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children and 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, extensive data are available for mecoprop-p and mecoprop racemate, including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in rats.

With respect to identified concerns relevant to the assessment of risk to infants and children, no fetotoxicity was identified in the rat and rabbit developmental toxicity studies at or below maternally toxic doses. Fetotoxic effects were observed in rats at high dose levels and included increased post-implantation loss and delayed maturation. These effects were only seen at dose levels causing decreased body weight and food consumption in the dams. In the rat reproductive toxicity study with the racemate, adverse offspring effects involving the increase in pup deaths during lactation days zero to four and lower pup weight gain were identified. The effects occurred at a maternally non-toxic dose and pup mortality was considered a serious endpoint. The effects were considered to have arisen from prolonged repeated exposure. Therefore, the PCPA factor has been retained at 10-fold for repeat exposure scenarios when using the rat reproductive toxicity assay to establish the point of departure. In acute exposure scenarios, the risk was considered well characterized and there was no pre- or post-natal toxicity that could be attributed to a single does. Accordingly, the PCPA factor was reduced to 1-fold.

Cancer Potency Factor

The carcinogenicity study of mecoprop-p in mice demonstrated a higher incidence of liver tumours in the female. The exact mode of action of carcinogenesis is not clearly determined. Therefore, linear low dose extrapolation (q_1*) is recommended for cancer risk assessment (q_1* = 1.59×10^{-3} (mg/kg bw/d)$^{-1}$).

Determination of Acute Reference Dose (ARfD)

General population:
The assessment of an acute reference dose for mecoprop-p for the general population is based on the NOAEL of 175 mg/kg bw established in the acute rat neurotoxicity study. At the LOAEL of 350 mg/kg bw, decreased body-weight gain and clinical signs were evident. Use of this study for ARfD determination is relevant because of the duration of exposure. The standard uncertainty factors (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) have been applied. As previously discussed, the PCPA factor has been reduced to 1-fold. The composite assessment factor (CAF) is 100. The ARfD proposed is calculated according to the following formula:

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{175 \text{ mg/kg bw}}{100} = 1.75 \text{ mg/kg bw}$$

The selected ARfD is also considered to be appropriate for the acute aggregate exposure and risk assessment for the general population.

Females aged 13-49:
To estimate acute dietary risk, the rat developmental toxicity study is selected for the appropriateness of exposure duration. At the LOAEL of 100 mg/kg bw/d, there were effects on the maternal animals affecting food intake and body-weight gains shortly after the initiation of

dosing. Pregnant animals appear to be more sensitive in terms of effects on body-weight gain. There was no indication of a similar sensitivity in the young. Based on the NOAEL of 50 mg/kg bw/d established in this study, and the CAF of 100-fold as discussed in the previous section (standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, and the reduced PCPA of 1-fold), the proposed ARfD is calculated according to the following formula:

$$\text{ARfD (Females 13-49)} = \frac{\text{50 mg/kg bw/d}}{100} = 0.5 \text{ mg/kg bw}$$

The selected ARfD is also considered to be appropriate for the acute aggregate exposure and risk assessment for females aged 13-49.

Determination of Acceptable Daily Intake (ADI)

All populations:
To estimate dietary risk from repeat exposure, the reproductive toxicity study of the mecoprop racemate in the rat is considered relevant for the duration of exposure as well as for the toxicity endpoints of concern. Offspring toxicity was demonstrated at the LOAEL 50 mg/kg bw/d. The effects included decreased body-weight gain and an increase in pup mortality during days one to four of the lactation period. The NOAEL for offspring toxicity established in this study is 10.3 mg/kg bw/d. For ADI determination, the standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed previously, the 10-fold PCPA factor has been retained. The CAF is therefore 1000. In the determination of the ADI for all populations, the identified concerns relevant to the assessment of risk to infants and children are taken into consideration.

The ADI proposed is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{\text{10.3 mg/kg bw/d}}{1000} = 0.01 \text{ mg/kg bw/d}$$

Maximum Residue Limit(s)
Residue data for mecoprop-p in cereal grains were submitted to support the conversion to full registration of this active on several end-use product labels. Residue data from field trials conducted in/on barley, corn and wheat were assessed in the framework of this application. In addition, a processing study in treated wheat was also assessed to determine the potential for concentration of residues of mecoprop-p into processed commodities.

Based on the maximum residues observed in crops treated according to label directions, maximum residue limits (MRLs) to cover residues of mecoprop-p in/on crops will be established as shown in Table 1. Residues in processed commodities not listed in Table 1 are covered under established MRLs for the raw agricultural commodities (RACs).

Table 1. Summary of Field Trial and Processing Data Used to Establish Maximum Residue Limit(s) (MRLs)

Commodity	Application Method/ Total Application Rate	PHI (days)	Residues		Experimental Processing Factor	Currently Established MRL	Recommended MRL
			Min	Max			
Barley grain	Postemergence foliar application/ 1050 g a.e./ha	53-79	All <0.02 ppm		No concentration observed	Under GMRL of 0.1 ppm	0.02 ppm (for all crops of Crop Group 15; Cereal grain)
Corn (K+CWHR)		61-79					
Corn grain		114-147					
Wheat grain		58-104					

Based on the dietary burden and residue data, MRLs of 0.01 ppm in milk, 0.02 ppm in eggs, fat and meat of cattle, goats, hogs, horses, poultry and sheep and 0.05 ppm in meat by-products of cattle, goats, hogs, horses, poultry and sheep to cover residues of mecoprop will be established.

Following the review of all available data, MRLs for crops and livestock are recommended to cover residues of mecoprop-p. Residues in these crop/livestock commodities at the established MRLs will not pose an unacceptable risk to any segment of the population, including infants, children, adults and seniors.

Occupational and Residential Risk Assessment

Toxicological Endpoints

Non-dietary oral ingestion:
For children who might be exposed to mecoprop-p in treated lawns for 1-7 days through incidental ingestion, the NOAEL of 175 mg/kg bw established in the acute rat neurotoxicity study is used. Lower body-weight gain was identified at the LOAEL of 350 mg/kg bw/d. The standard uncertainty factors (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) and the reduced PCPA factor of 1-fold as described previously provide a target margin of exposure (MOE) of 100.

Short-term dermal exposure:
Adequate 21-day dermal toxicity studies with mecoprop-p in the rat and rabbit are available. A NOAEL of 1000 mg/kg bw/d was established in both studies. Use of this endpoint is considered protective of all sub-populations, including nursing infants and unborn children of exposed female workers. The standard uncertainty factors (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) and the reduced PCPA factor of 1-fold as described previously provide a target MOE of 100.

Short-term inhalation exposure:
No short-term inhalation toxicity data are available. The appropriate endpoint for short-term inhalation exposure for all sub-populations is determined by the NOAEL of 50 mg/kg bw/d established in the rat developmental toxicity study. Lower body-weight gain was identified at the LOAEL of 100 mg/kg bw/d. The standard uncertainty factors (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) as described previously provide a target MOE of 100.

Intermediate- and long-term dermal and inhalation exposure:
To estimate dermal and inhalation risk from intermediate- and long-term repeat exposure, the reproductive toxicity study of the mecoprop racemate in the rat is considered relevant for the duration of exposure as well as for the toxicity endpoints of concern. Offspring toxicity was demonstrated at the LOAEL 50 mg/kg bw/d. The effects included decreased body-weight gain and increased pup mortality during days one to four of the lactation period. The NOAEL for offspring toxicity established in this study is 10.3 mg/kg bw/d. The standard uncertainty factors (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) have been applied. The worker population could include females of child-bearing age (13-49 years old). For this reason, an additional factor of 10-fold has been applied to protect nursing infants and unborn children of exposed female workers. This additional factor was applied in consideration of the seriousness of the endpoint (i.e. pup mortality) in the absence of maternal toxicity. The target MOE is 1000.

Environmental Assessment

Fate and Behaviour in the Environment
Table 2 summarizes the fate and behaviour of mecoprop-p in the terrestrial environment.

Mecoprop-p has a water solubility >250 g/L at pH 7.0 and pH 10 indicating it is very soluble in soil water under environmental conditions. Mecoprop-p is not expected to bioaccumulate in terrestrial biota as the log K_{ow} is 0.48. The measured vapour pressure of mecoprop-p at 20°C (3.0×10^{-5} mm Hg) indicates it has low volatility and the calculated Henry's law constant of $1/H = 2.4 \times 10^{6}$ indicates mecoprop-p is not expected to volatilize from moist soil surfaces. The dissociation constant (pK_a) of 3.68 indicates mecoprop-p will exist as an anion at environmentally relevant pHs and, therefore, is expected to be mobile in soil under environmental conditions. Mecoprop-p does not absorb light at wavelengths greater than 300 nm and thus, is not expected to undergo direct phototransformation in the terrestrial environment.

Hydrolysis is not an important route of transformation as mecoprop-p is stable in water at pH 5, pH 7 and pH 9 after 31.3 days. On soil, phototransformation is not an important route of transformation as the first-order half-life of mecoprop-p is 32 days under artificial light. In aerobic soil, the DT_{50} of mecoprop-p is 6.1-11.7 days which indicates that mecoprop-p is non-persistent in aerobic soil. The major transformation product in the aerobic soil studies is CO_2 (>25% of applied radioactivity) with 4-chloro-2-methylphenol as a minor transient transformation product (<3%). Other minor transformation products were also observed, but never exceeded 3% of the applied radioactivity and were never identified. Biotransformation in anaerobic soils is not a route of transformation of mecoprop-p and it is persistent under these conditions.

Under laboratory conditions, mecoprop-p has medium to high mobility in soil on the basis of the adsorption K_{oc} values of 135-167. Under field conditions, mecoprop-p is non-persistent as the DT_{50} values are 2.3-4.3 days. Residues of mecoprop-p were detected to the 61.5-76.9 cm soil depth (after the second application) which indicated that residues are mobile in the soil profile.

Table 2 Fate and behaviour of mecoprop-p (MCPP-P) in the terrestrial environment.

Property	Test substance	Value / Observation	Comments
Physical and Chemical Properties			
Vapour pressure at 20°C	MCPP-P	3.0×10^{-5} mm Hg	Low volatility
Henry's law constant at 20°C	MCPP-P	$1/H = 2.4 \times 10^{6}$ $K = 1.0 \times 10^{-8}$ atm · m^3/ mole	Not expected to volatilize from moist soil
Ultraviolet (UV) / visible spectrum	MCPP-P	No absorption at wavelengths >300 nm	Not expected to undergo direct phototransform in the terrestrial environment
Solubility in water at 20°C (g/L)	MCPP-P	pH 4: 6.65 pH 7: >250 pH 10: >250	Very soluble in soil water at environmental pHs
n-Octanol/water partition coefficient (log K_{ow})	MCPP-P	0.48 (pH 7, 25°C)	Not expected to bioaccumulate in terrestrial biota
Dissociation constant (pK_a)	MCPP-P	3.68 (20°C)	Exists as an anion at environmental pH, therefore, expected to be mobile in soil
Abiotic transformation			
Hydrolysis	MCPP-P	Stable to hydrolysis at pH 5, pH 7 and pH 9	Hydrolysis is not an important route of transformation
Phototransformation on soil	MCPP-P	half-life = 32 days	Phototransformation is not an important route of transformation on soil under environmental conditions
Biotransformation			
Biotransformation in aerobic soil	MCPP-P	DT_{50} = 6.1-11.7 days DT_{90} = 20.3-38.8 days	Non-persistent in aerobic soil
Biotransformation in anaerobic soil	MCPP-P	No biotransformation	Persistent under anaerobic soil conditions as based on anaerobic biotransformation of the racemic mecoprop
Mobility			
Adsorption / desorption in soil	MCPP-P	K_{oc} = 135-167	Medium to high mobility in soil
Soil leaching	MCPP-P	R_f = 0.86	Mobile in soil
Field studies			
Field dissipation	MCPP-P	DT_{50} = 2.3-4.3 days	Non-persistent in soil under field conditions
Field leaching	MCPP-P	Residues leached to the 76.9 cm soil depth	Residues of MCPP-P are expected to leach through the soil profile

Table 3 summarizes the fate and behaviour of mecoprop-p (MCPP-P) in the aquatic environment.

Mecoprop-p has a water solubility >250 g/L at pH 7.0 and pH 10 indicating it is very soluble in water under environmental conditions. Mecoprop-p is not expected to bioaccumulate in aquatic biota as the log K_{ow} is 0.48. The measured vapour pressure of mecoprop-p at 20°C (3.0×10^{-5} mm Hg) indicates it has low volatility and the calculated Henry's law constant of $1/H = 2.4 \times 10^{6}$ indicates mecoprop-p is not expected to volatilize from bodies of water. Mecoprop-p does not absorb light at wavelengths greater than 300 nm and, thus, is not expected to undergo direct phototransformation in the aquatic environment.

Hydrolysis is not an important route of transformation as mecoprop-p is stable in water at pH 5, pH 7 and pH 9 after 31.3 days. In water, phototransformation is not an important route of transformation as the first-order half-lives of mecoprop-p are 9.8 days (pH 5), 14.4 days (pH 7) and 13.8 days (pH 9). Under aerobic aquatic conditions, mecoprop-p is slightly persistent to moderately persistent as the DT_{50}s are 14.8-60.4 days. Under anaerobic aquatic conditions, mecoprop-p does not undergo biotransformation and, thus, is not a route of transformation. On the basis of its K_{oc} values of 135-167, mecoprop-p is not expected to partition into the sediment of aquatic systems.

Table 3 Fate and behaviour of mecoprop-p (MCPP-P) in the aquatic environment.

Study type	Test material	Value	Comments
Physical and Chemical Properties			
Vapour pressure at 20°C	MCPP-P	3.0×10^{-5} mm Hg	Low volatility
Henry's law constant at 20°C	MCPP-P	$1/H = 2.4 \times 10^{6}$ $K = 1.0 \times 10^{-8}$ atm · m^3/ mole	Not expected to volatilize from bodies of water
Ultraviolet (UV) / visible spectrum	MCPP-P	No absorption at wavelengths >300 nm	Not expected to phototransform directly in the aquatic environment
Solubility in water at 20°C (g/L)	MCPP-P	pH 4: 6.65 pH 7: >250 pH 10: >250	Very soluble in water at environmental pHs
n-Octanol/water partition coefficient (log K_{ow})	MCPP-P	0.48 (pH 7, 25°C)	Not expected to bioaccumulate in aquatic biota
Abiotic transformation			
Hydrolysis	MCPP-P	Stable to hydrolysis at pH 5, pH 7 and pH 9	Hydrolysis is not an important route of transformation
Phototransformation in water	MCPP-P	9.8 days (pH5) 14.4 days (pH 7) 13.8 days (pH 9)	Phototransformation is not an important route of transformation in the aquatic environment
Biotransformation			
Biotransformation in aerobic water systems	MCPP-P	DT_{50} = 14.8-60.4 days	Slightly persistent to moderately persistent
Biotransformation in anaerobic water systems	MCPP-P	No biotransformation	Not a route of transformation

Monitoring Data

Mecoprop has been detected in Canadian surface waters and groundwater. For the ecoscenario exposure estimates, the acute concentration (2.9 µg/L) was estimated by determining the 95th percentile of the maximum concentration detected in each monitoring study/site whereas the chronic concentration (0.40 µg/L) was estimated by determining the 95th percentile of the arithmetic means of all samples at each site (detects and non-detects) from the monitoring studies (Appendix II).

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 (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. 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).

The risk assessment first utilizes a deterministic evaluation that integrates the environmental exposure represented by the EEC and the environmental toxicity as represented by the most sensitive test species to determine the likelihood of adverse ecological effects. One method of achieving this integration is through the estimation of a *Risk Quotient* (RQ). The RQ is usually calculated by comparing a threshold toxicity endpoint, usually a LC_{50}, LD_{50}, EC_{50}, EC_{25}, NOEC or NOEL for the most-sensitive test species, to an EEC based on the maximum cumulative application rate. The mathematical relationship among RQ, toxicity endpoint and the EEC is:

$$RQ = EEC \div \text{toxicity endpoint}$$

In addition, uncertainty factors are applied to the acute toxicity endpoints to account for interspecies variability. For fish and amphibians, the LC_{50} is divided by an uncertainty factor of ten. For terrestrial and aquatic invertebrates, algae and aquatic vascular plants, the LC_{50} or EC_{50} is divided by an uncertainty factor of two.

For describing the risk associated with the RQ, the Level of Concern (LOC) is considered. The LOC is equal to a RQ of 1.0 and functions as the cut-off criteria for estimating risk. Thus, if the LOC is exceeded (RQ>1) then, a concern is identified. For RQ < 1.0, there is a negligible risk as the LOC is not exceeded. In cases where the LOC is exceeded, a refined assessment is conducted in which the risk is based on exposure to mecoprop-p through spray drift and surface runoff.

Risks to Terrestrial Organisms

Table 4 summarizes the risks to terrestrial organisms resulting from the application of mecoprop-p. The effect endpoints considered in the risk assessment for terrestrial organisms are summarized in Table 5 of Appendix 1.

For earthworms and bees, mecoprop-p is not expected to pose an appreciable risk (RQ< 1) under field conditions.

For wild birds feeding on contaminated food on-field, mecoprop-p poses an acute oral risk (RQs = 1.1-3.1), an acute dietary risk (RQs = 1.2-9.7) and a risk to reproduction (RQ = 1.3) in some feeding guilds. For wild birds feeding on contaminated food off-field, mecoprop-p poses an acute dietary risk (RQ = 1.2) to one feeding guild. Although in these cases the LOC is exceeded (RQ >1) in birds feeding either on-field or off-field, the risk is based on the assumption that the bird's diet consists entirely of mecoprop-p-contaminated food, as expressed by the estimated daily exposure values. Under field conditions, however, it is not expected that birds would be feeding exclusively in fields treated with mecoprop-p or entirely in areas bordering these treated fields. In addition, the risk assessment does not consider feeding preference or avoidance behaviour toward contaminated food as these data are not available. On this basis, the risk to birds may be overestimated for field conditions.

For small mammals feeding on contaminated food on-field, mecoprop-p poses an acute oral risk (RQs = 1.3-4.5), a subchronic dietary risk (RQs = 1.1-24.7) and a risk to reproduction (RQs = 1.2-7.6) in some feeding guilds. For small mammals feeding on contaminated food off-field, mecoprop-p poses a subchronic dietary risk (RQs = 1.1-3.0) to some feeding guilds. Although in these cases the LOC is exceeded (RQ >1) in small mammals feeding either on-field or off-field, the risk is based on the assumption that the animal's diet consists entirely of mecoprop-p-contaminated food (as expressed by the EDE values). Under field conditions, however, it is not expected that small mammals would be feeding exclusively in fields treated with mecoprop-p or entirely in areas bordering these treated fields. In addition, the risk assessment does not consider feeding preference or avoidance behaviour toward contaminated food as these data are not available. On this basis, the risk to small mammals may be overestimated for field conditions.

The greatest risk was shown in non-target terrestrial plants (RQ = 9-35) in areas bordering treated fields where exposure to mecoprop-p results from off-target spray drift.

Table 4 Summary of the risk to terrestrial organisms.

Organism	Exposure	Endpoint value	RQ	LOC Exceeded
Invertebrates				
Earthworm	Acute	247 mg a.e./kg soil	0.001 0.002	No No
Bee	Oral	LD_{50} = 5.6 kg a.e./ha	0.19 0.24	No No
	Contact	LD_{50} = 56 kg a.e./ha	0.019 0.024	No No
Birds				
Bobwhite quail	Acute	46 mg a.e./kg bw/d	1.1-3.1	Yes
Mallard duck	Acute Dietary	14.6 mg a.e./kg bw/d	1.2-9.7	Yes

Organism	Exposure	Endpoint value	RQ	LOC Exceeded
Japanese quail	Reproduction	111.2mg a.e./kg bw/d	1.3	Yes
Mammals				
Rat	Acute	70 mg a.e./kg bw/d	1.3-4.5	Yes
Mouse	Subchronic Dietary	12.7 mg a.e./kg bw/d	1.1-24.7	Yes
Rat	Reproduction	41.4 mg a.e./kg bw/d	1.2-7.6	Yes
Vascular plants				
Vascular plants	Vegetative vigour	0.0069 kg a.e./ha (HD_5 of EC_{50}s)	9-35	Yes

Risks to Aquatic Organisms

Table 5 summarizes the risks to aquatic organisms resulting from the application of mecoprop-p. The endpoints considered in the risk assessment for aquatic organisms are summarized in Table 6 of Appendix 1.

In freshwater invertebrates, fish, amphibians and algae, there were no appreciable risks (RQs < 1) associated with the application of mecoprop-p.

In marine/estuarine plants, mecoprop-p poses a risk as the RQs were 1.4-3.5 and hence, exceeds the LOC.

Table 5 Summary of Risk to Aquatic Organisms.

Species	Exposure	Endpoint value (mg a.e./L)	RQ	LOC Exceeded
Freshwater Invertebrate *(Daphnia magna)*	Acute	41	<1	No
Freshwater Invertebrate *(Daphnia magna)*	Chronic	11.1	<1	No
Bluegill Sunfish *(Lepomis macrochirus)*	Acute	9.1	<1	No
Rainbow Trout *(Oncorhynchus mykiss)*	Chronic	49.6	<1	No
Amphibians	Acute	9.1	<1	No
Freshwater Algae *(Navicula pelliculosa)*	Acute	0.12	<1	No
Marine algae *(Skeletonema costatum)*	Acute	0.0085	1.4-3.5	Yes

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, mecoprop-p and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[1] *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of mecoprop-p were also considered, including transformation products formed in the environment, and contaminants and formulants in the technical product and the end-use product. Mecoprop-p and its transformation products were evaluated against the following Track 1 criteria: persistence in soil ≥182 days; persistence in water ≥182 days; persistence in sediment ≥365 days; persistence in air ≥2 days; bioaccumulation log K_{ow} ≥5 or BCF ≥5000 (or BAF ≥5000). In order for mecoprop-p or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The technical product and end-use product, including formulants, were assessed against the contaminants identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern, Part 3 Contaminants of Health or Environmental Concern.* The PMRA has reached the following conclusions (Table 4 of Appendix I summarizes the comparison to TSMP Track 1 criteria):

- Mecoprop-p does not meet Track 1 criteria.

- Mecoprop-p does not meet the Track 1 criterion for persistence because the half-life values in soil (6.1-11.7 days) and water (14.8-48.5 days), do not exceed the Track 1 criterion for soil and water.

- Mecoprop-p does not meet the Track 1 criterion for bioaccumulation, as its octanol-water partition coefficient (log K_{ow} = 0.48) is below the Track 1 criterion.

- Mecoprop-p (technical grade) does not contain any by-products or microcontaminants that meet the TSMP Track 1 criteria. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.

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*[2]**.** The list is used as described in the PMRA Notice of Intent NOI2005-01[3] and is based on existing policies

---

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

2 *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.*

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

and regulations including: DIR99-03; and DIR2006-02[4], 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:

> Technical grade mecoprop-p and the end-use product A.H. MARKS MCPP-p 600 Liquid Herbicide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

Value Assessment

A value assessment was not required for this application.

Conclusion

The PMRA has assessed all available information and is able to support the conversion of Marks Mecoprop-p Technical Acid (Registration Number 27441) to full registration.

[4] DIR2006-02, PMRA Formulants Policy.

List of Abbreviations

1/H	Henry's Law Constant
µg	micrograms
a.e.	acid equivalent
ADI	acceptable daily intake
AR	administered radioactivity
ARfD	acute reference dose
atm	atmosphere
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
bw	Body weight
CAF	composite assessment factor
cm	centimetres
CO_2	Carbon dioxide
d	day
DMA	dimethylamine
DMAS	dimethylamine salt
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the time required to observe a 90% decline in concentration)
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EEC	estimated environmental exposure concentration
EHE	2-ethylhexylester
EPA	United States Environmental Protection Agency
g	gram(s)
h	hour(s)
ha	hectare(s)
HD_5	hazard dose 5%
HDT	highest dose tested
Hg	mercury
HGPRT	hypoxanthine-guanine phosphoribosyl transferase
kg	kilogram(s)
K_{oc}	organic-carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
m^3	metre(s) cubed
MCPP	mecoprop
MCPP-P	mecoprop-P

MAS	maximum average score
mg	milligram(s)
MIS	maximum irritation score
mL	millilitre(s)
mm	millimetre(s)
MOE	margin of exposure
MRL	maximum residue limits
MTD	maximum tolerated dose
NA	not applicable
ND	not determined
nm	nanometres
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NZW	New Zealand white
PCPA	*Pest Control Product Act*
PHI	post harvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
q_1	linear low dose extrapolation
RAC	raw agricultural commodity
RED	Reregistration Eligibility Decision
R_f	retention factor
RQ	risk quotient
TSMP	Toxic Substances Management Policy
US	United States
UV	ultraviolet

Appendix I Tables and Figures

Table 1 Acute Toxicity of mecoprop-p

ACUTE STUDIES - TECHNICAL (mecoprop-p)				
Study type	**Species, strain (test compound)**	**Results**	**Comments**	**Reference**
Oral	rat, Wistar (mecoprop D-form)	LD_{50} ♂ = 1327; ♀ >681<1000 ♂♀ = 1050 mg/kg bw	Moderate toxicity **WARNING - POISON**	1097063
	Rat, Sprague-Dawley (mecoprop-p)	LD_{50} : ♂+♀ = 431 mg/kg bw	Highly toxic **DANGER - POISON**	
	Rat, Sprague-Dawley (mecoprop-p)	LD_{50} : ♂ = 803 (710-698) ♀ = 756 (651-861) ♂+♀ = 775 (666-885) mg/kg bw	Moderate toxicity **WARNING - POISON**	
	Rat, Sprague-Dawley (mecoprop-p DMA)	LD_{50} : ♂ = 834 (657-1064) ♀ = 696 (542-891) ♂+♀ = 763 (642-907) mg/kg bw	Moderate toxicity **WARNING - POISON**	
	Rat, Sprague-Dawley (mecoprop-p DMA)	LD_{50} : ♂ = ~ 903 ♀ = ~ 903 ♂+♀ = >681 <1000 mg/kg bw	Moderate toxicity **WARNING - POISON**	
	Rat, Sprague-Dawley (mecoprop-p EHE)	LD_{50} : ♂ = 1300 (1100-1600) ♀ = 1400 (1200-1900) ♂+♀ = 1400 (1200-1600) mg/kg bw	Slight toxicity	
Dermal	rat, Wistar (mecoprop D-form)	LD_{50} >4000 mg/kg bw	Low toxicity	1190440
	Rat, CD (mecoprop-p)	LD_{50} >2000 mg/kg bw	Low toxicity	
	Rat, Sprague-Dawley (mecoprop-p)	LD_{50} >2000 mg/kg bw	Low toxicity	
	Rat, Wistar (mecoprop-p DMA)	LD_{50} >4000 mg/kg bw	Low toxicity	
	Rabbit, NZW (mecoprop-p DMA)	LD_{50} >4000 mg/kg bw	Low toxicity	
	Rat, NZW (mecoprop-p EHE)	LD_{50} >2000 mg/kg bw	Low toxicity	
Intraperitoneal	Rat, Wistar (mecoprop D-form)	LD_{50}: ♂ >316 <464; ♀ = 383 ♂+♀ = 383 mg/kg bw	Not applicable	
Inhalation (4 h nose/head only)	Rat, Wistar (mecoprop D-form)	LC_{50} >5.6 mg/L (actual)	Low toxicity	
	rat, Sprague-Dawley (mecoprop-p)	LC_{50} >0.87 mg/L (actual)	Low toxicity	
	Rat, Wistar (mecoprop-p DMA)	LC_{50} ♂ = ~3.6; ♀ = 5.24~ ♂+♀ = 4.71 (3.89-6.45) mg/mL	Low toxicity	
Inhalation (4 h whole-body)	rat, Sprague-Dawley (mecoprop-p DMA)	LC_{50} >4.68 mg/L (actual)	Low toxicity	
	rat, Sprague-Dawley (mecoprop-p EHE)	LC_{50} >4.66 mg/L (actual)	Low toxicity	
Eye irritation	rabbit, New Zealand white (NZW) (mecoprop D-form)	MAS = 70/110 MIS at 1, 24, 48, 72 h = 38, 62, 66, 89, respectively	Severely irritating **DANGER CORROSIVE TO EYES**	
	rabbit, NZW (mecoprop-p)	MIS at 1, 24, 48, 72 h = 48, 48, 50, 61, respectively	Severely irritating **DANGER – EYE IRRITANT**	
	rabbit, white Vienna (mecoprop-p DMA)		Severely irritating **DANGER – EYE IRRITANT**	

ACUTE STUDIES - TECHNICAL (mecoprop-p)				
Study type	**Species, strain (test compound)**	**Results**	**Comments**	**Reference**
Skin irritation	rabbit, NZW (mecoprop D-form)	MIS: at 1, 24, 48 h, and days 7 and 14 after patch removal were 3.2, 2.3, 2.3, 1.0, 0, respectively	Moderately irritating (exposure period was prolonged for 24 h instead of the guideline requirement of 4 h)	
	rabbit, NZW (mecoprop-p)	MIS: 0	Non-irritating	
	rabbit, NZW (mecoprop-p)	MIS: at 1, 24, 48, 72 h, and days 7, 10, 13 = 0.8, 0.8, 0.7, 0.5, 0.3, 0.2, 0 (maximum = 8), respectively	Slightly irritating	
	rabbit, white Vienna (mecoprop-p DMA)	MIS: at 4, 24, 48, 72 h = 1.67, 0, 0, and 0 (maximum = 8), respectively	Mildly irritating **CAUTION - SKIN IRRITANT**	
	rabbit, NZW (mecoprop-p DMA)	MAS = 0.5/8 MIS: at days 1, 2, 3, 4 after dosing were 0.5, 0.5, 0.33, and 0 (maximum = 8), respectively	Slightly irritating	
Skin sensitization (Open epicutaneous test)	guinea pig, Pirbright White Dunkin Hartley (mecoprop racemate)	Negative	(Deficient - no positive control data)	
Skin sensitization (maximization)	guinea pig, Pirbright White Dunkin Hartley (mecoprop D-form)	Negative	Not a skin sensitizer	
	guinea pig, Pirbright White Dunkin Hartley (mecoprop-p)	Negative	Not a skin sensitizer	1185283
	guinea pig, Pirbright White Dunkin Hartley (mecoprop-p DMA)	Negative	Not a skin sensitizer	
Skin sensitization (Buehler)	guinea pig, albino (mecoprop-p)	Negative	Not a skin sensitizer	
	guinea pig, Dunkin Hartley (mecoprop-p DMA)	Positive	**Potential skin sensitizer**	
	guinea pig, Dunkin Hartley (mecoprop-p EHE)	Positive after 1st challenge Negative after 2nd challenge Results difficulty to interpret	Equivocal	
[a] MIS = maximum irritation score; [b] MAS = maximum average score for 24, 48 and 72 hours				

Table 2 Short- and Long-term Toxicity Profile of Technical Mecoprop-p and Mecoprop Racemate

SHORT-TERM TOXICITY [mecoprop-p (D-form of mecoprop), mecoprop racemate]			
Study type	**Species, strain / test compound / dose levels**	**Results and comments**	**Reference**
4-week dietary	mouse, B6C3F1 / mecoprop racemate 0, 100, 300, 900, 2700 ppm ♂: 0, 20, 63, 181, 614; ♀: 0, 31, 79, 267, 951 mg/kg bw/d	NOAEL ♂+♀ = 900 ppm; ♂ = 181; ♀ = 267 mg/kg bw/d LOAEL ♂+♀ = 2700 ppm; ♂ = 614; ♀ = 951 mg/kg bw/d (liver pathology)	
	mouse, B6C3F1 / mecoprop racemate 0, 2700, 4500, 7000 ppm ♂: 0, 764, 1800, 3913; ♀: 0, 1009, 2101, 4308 mg/kg bw/d	NOAEL not established LOAEL ♂+♀ = 2700 ppm ♂ = 764; ♀ = 1009 mg/kg bw/d (liver pathology)	
7-week dietary	Rat, Sprague-Dawley / mecoprop racemate and D-form racemate: 0, 50, 400 ppm ♂: 0, 4.41, 30.1; ♀: 0, 4.77, 37.5 mg/kg bw/d	NOAEL = 400 ppm (HDT) racemate: ♂ = 30.1, ♀ = 37.5 mg/kg bw/d D-form: ♂ = 35.2, ♀ = 38.0 mg/kg bw/d	

SHORT-TERM TOXICITY [mecoprop-p (D-form of mecoprop), mecoprop racemate]			
Study type	**Species, strain / test compound / dose levels**	**Results and comments**	**Reference**
	D-isomer: 0, 50, 400 ppm ♂: 0, 4.41, 35.2; ♀: 0, 4.76, 38.0 mg/kg bw/d		
90-day dietary	mouse; B6C3F1 / mecoprop-p 0, 100, 1000, 2500 ppm ♂: 0, 20, 224, 739; ♀: 0, 30, 330, 925 mg/kg bw/d	NOAEL ♂+♀ = 100 ppm; ♂ = 20, ♀ = 30 mg/kg bw/d LOAEL ♂ +♀= 1000 ppm; ♂ = 224, ♀ = 330 mg/kg bw/d (liver and kidney pathology)	1185284
	Rat, Wistar / mecoprop racemate 0, 50, 150, 450 ppm ♂: 0, 3.8, 11.3, 33.7; ♀: 0, 4.4, 13.3, 38.9 mg/kg bw/d	NOAEL > 450 ppm; ♂ = 33.7, ♀ = 38.9 mg/kg bw/d (HDT) MTD not reached	
	Rat, Wistar / mecoprop racemate and mecoprop D-form racemate: 0, 200, 800, 3200 ppm ♂: 0, 16.5, 68, 391; ♀: 0, 18.2, 76, 399 mg/kg bw/d D-isomer: 0, 200, 400, 800, 1600, 3200 ppm ♂: 0, 15.6, 32, 68, 146, 403 ♀: 0, 18.4, 38, 76, 170, 404 mg/kg bw/d	NOAELs - 800 ppm racemate: ♂ = 68; ♀= 76 mg/kg bw/d D-isomer: ♂ = 68; ♀ = 76 mg/kg bw/d LOAELs – racemate: 3200 ppm; ♂ = 391; ♀ = 398 mg/kg bw/d (bw) D-isomer: 1600 ppm; ♂ = 146; ♀ = 170 mg/kg bw/d (bw)	
90-day dietary / neurotoxicity	rat, Wistar / mecoprop-p 0, 75, 500, 2500 (♂), 3000 (♀) ppm ♂ = 0, 5.4, 35.2, 189; ♀ = 0, 6.0, 41.1, 240 mg/kg bw/d	NOAEL = 500 ppm; ♂ = 35; ♀ = 41 mg/kg bw/d LOAEL ♂ = 2500 ppm; 189 mg/kg bw/d ♀ = 3000 ppm; 240 mg/kg bw/d (pathology of liver and adrenal)	1185225
1-year dietary	dog, beagle / mecoprop-p 0, 60, 180, 600 ppm ♂ = 0, 1.8, 5.2, 18.3; ♀ = 0, 2, 5.7, 19 mg/kg bw/d	NOAEL = 180 ppm; ♂ = 5.2; ♀ = 5.7 mg/kg bw/d LOAEL = 600 ppm; ♂ = 18.3; ♀ = 19 mg/kg bw/d (bw)	1185285
21-day dermal	rabbit, NZW / mecoprop-p 0, 10, 100, 1000 mg/kg bw	NOAEL: 1000 mg/kg bw/d	
	rat, Wistar / mecoprop-p 0, 12, 120, 1000 mg/kg bw	NOAEL: 1000 mg/kg bw/d	
CHRONIC TOXICITY AND ONCOGENICITY			
18-month dietary oncogenicity	Mouse, B6C3F1/CrlBR / mecoprop-p 0, 25, 250, 2500 ppm ♂ = 0, 4, 40, 592; ♀ = 0, 4, 46, 732 mg/kg bw/d	NOAEL: ♂ = 40 mg/kg bw/d (HDT);♀ = 4 mg/kg bw/d LOAEL: ♂ = not established; ♀ = 46 mg/kg bw/d (kidney pathology) Oncogenic potential not adequately assessed	1185226
	Mouse, B6C3F1/CrlBR / mecoprop-p 0, 700 (♂), 800 (♀) ppm ♂ = 0, 122; ♀ = 0, 209 mg/kg bw/d	NOAEL: not established higher incidence of liver adenoma and carcinoma in ♀	
2-year dietary/ oncogenicity	rat, Wistar / mecoprop racemate 0, 20, 100, 400 ppm ♂ = 0, 1.1, 5.5, 22.2; ♀ = 0, 1.4, 6.9, 27.9 mg/kg bw/d	No systemic toxicity; inadequate dose levels tested (MTD not reached) Oncogenicity: no effects at dose levels tested	1185227 1185228 1185324 1185348
	rat, Wistar / mecoprop-p 0, 100, 600, 1200 ppm ♂ = 0, 5.3, 32.0, 64.6; ♀ = 0, 6.6, 39.9, 81.7 mg/kg bw/d	NOAEL: ♂ = 600 ppm, or 32 mg/kg bw/d ♀ = 100 ppm, or 6.6 mg/kg bw/d LOAEL: ♂ = 1200 ppm, or 64.6 mg/kg bw/d (bw) ♀ = 600 ppm, or 40 mg/kg bw/d (bw) no evidence of oncogenicity	
REPRODUCTION AND DEVELOPMENTAL TOXICITY			
2-generation reproductive toxicity	rat, Wistar / mecoprop racemate 0, 20, 100, 500 ppm	Parental systemic toxicity NOAEL > 500 ppm, or ♂ >47.3; ♀ >50.7 mg/kg bw/d Reproductive toxicity: NOAEL = 500 ppm, or 47.3 mg/kg bw/d Offspring toxicity: NOAEL = 100 ppm / 9.3 mg/kg bw/d LOAEL = 500 ppm, or 47.3 mg/kg bw/d (higher pup mortality during lactation days 0-4; but birth, viability, and lactation indices not affected)	1185229 1382211

SHORT-TERM TOXICITY [mecoprop-p (D-form of mecoprop), mecoprop racemate]			
Study type	**Species, strain / test compound / dose levels**	**Results and comments**	**Reference**
Developmental toxicity	rat, Sprague-Dawley / mecoprop racemate 0, 20, 50, 125 mg/kg bw/d	NOAEL, maternal toxicity = 20 mg/kg bw/d developmental toxicity = 50 mg/kg bw/d LOAEL, maternal toxicity = 50 (bw, food) developmental toxicity = 125 mg/kg bw/d No evidence of teratogenicity	
	Rat, Wistar / mecoprop-p 0, 20, 50, 100 mg/kg bw/d	NOAEL, maternal and developmental toxicity = 50 mg/kg bw/d LOAEL, maternal and developmental toxicity = 100 mg/kg bw/d No evidence of teratogenicity	1185230
	rabbit, Himalayan / mecoprop-p 0, 5, 20, 50 mg/kg bw/d	NOAEL, maternal and developmental toxicity = 50 mg/kg bw/d No evidence of teratogenicity	1185323 1185349 1185350
SPECIAL TOXICITY AND METABOLOSM/TOXICOKINETICS			
acute neurotoxicity	rat, Wistar / mecoprop-p 0, 175, 350, 700 mg/kg bw	Acute systemic toxicity: NOAEL = 175 mg/kg bw; LOAEL = 350 mg/kg bw (bw, clinical signs) No evidence of acute neurotoxicity	1185286
90-day neurotoxicity		See short-term study data	
Metabolism	Rat, Wistar / mecoprop-p	Absorption: rapid and extensive; plasma peak concentrations seen 2-4 h post-dosing. Distribution: tissue distribution was extensive, but the level declined rapidly and no evidence of bioaccumulation. Excretion: rapid; mainly in the urine; fecal elimination low; not eliminated in expired air. Metabolism: minimal; unchanged parent compound the main compound excreted.	1185287

GENOTOXICITY			
Study	**Species and strain or cell type / Test compound / Concentrations or doses**	**Results**	Reference
Gene mutations in bacteria *in vitro*	*Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, TA 1538 / mecoprop racemate	negative	
	Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537 / mecoprop-p	negative	1185335
	Salmonella typhimurium strains TA 98, TA 100, TA 1535 and TA 1537 / mecoprop-p	negative	
	Salmonella typhimurium strains TA 98, TA 100, TA 1535 and TA 1537 / mecoprop-p DMA	negative	
	Salmonella typhimurium strains TA 98, TA 100, TA 1535 and TA 1537 / mecoprop-p DMA	negative	
Gene mutations in mammalian cells *in vitro*	Chinese hamster ovary cells (HGPRT locus) / mecoprop-p	negative	1185344
	Chinese hamster ovary cells (HGPRT locus) / mecoprop-p DMA	negative	
	Chinese hamster ovary cells (HGPRT locus) / mecoprop-p EHE	negative	
Chromosome aberrations *in vitro*	human blood lymphocytes / mecoprop-p	positive at cytotoxic concentrations ≥300 µg/mL without S9 activation in assay 1 negative all concentration levels with (assay 1 and 2) or without S9 (assay 1) clastogenic at cytotoxic doses +S9	1185345 1185346
	human blood lymphocytes / mecoprop-p	positive at cytotoxic doses with S9 activation	
	human blood lymphocytes / mecoprop-p DMA	clastogenic at higher doses with S9 activation	

SHORT-TERM TOXICITY [mecoprop-p (D-form of mecoprop), mecoprop racemate]			
Study type	**Species, strain / test compound / dose levels**	**Results and comments**	**Reference**
	human blood lymphocytes / mecoprop-p EHE	clastogenic at high dose with S9 activation	
In vivo chromosome aberration in	Chinese hamster bone marrow cells / mecoprop D-form	negative	
	Chinese hamster bone marrow cells / mecoprop racemate	Positive at the high dose	
In vitro/in vivo unscheduled DNA synthesis	rat, Wistar / mecoprop-p 0, 50, 200, 500, 500 mg/kg bw	negative	1185347
In vivo sister chromatid exchange	Chinese hamster (bone marrow cells) / mecoprop racemate	negative	
In vivo mouse micronucleus assay	mouse, CD-1 / mecoprop-p 24 h: 0, 20, 100, 500 mg/kg bw; 48 & 72 h: 0, 2600 mg/kg bw	negative	
	mouse, CD-1 / mecoprop-p DMA 0, 144, 288, 576 mg/kg bw	negative	
	mouse, CD-1 / mecoprop-p EHE 0, 782, 1564, 3128 mg/kg bw	negative	

Table 3 Toxicology Endpoints for Use in Health Risk Assessment for Mecoprop-p

Exposure scenario	NOAEL, mg/kg bw/d	Study	Endpoint	CAF	ARfD / ADI / target MOE
Acute dietary (ARfD), general population	175	Acute rat neurotoxicity	Body weight, clinical signs, motor activity	100-fold	1.75
Acute dietary (ARfD), ♀ 13-49	50	Rat developmental	Body weight	100-fold	0.5
Chronic dietary (ADI), all population	10.3	Rat reproductive toxicity	Offspring toxicity	100-fold	0.01
Incidental ingestion, children	50	Rat developmental	Body weight		100
Acute 1-7 day dermal	1000	21-day rabbit dermal	No toxic effects		100
Acute 1-7 day inhalation	50	Rat developmental	Body weight		100
Acute aggregate oral/inhalation Acute aggregate dermal	50 1000	Rat developmental 21-day rabbit dermal	Body weight No toxic effects		100
Short-term dermal	1000	21-day rabbit dermal	No toxic effects		100
Short-term inhalation	50	Rat developmental	Body weight		100
Intermediate- and long-term dermal and inhalation	10.3	Rat reproductive toxicity	Offspring toxicity		1000*
CAF = standard 100-fold (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) X reduced PCPA factor of 1-fold * the 10-fold PCPA factor retained					

Table 4 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
Toxic or toxic equivalent as defined by the *Canadian Environmental Protection Act*[1]	Yes		Yes	CO_2 was the major transformation product in aerobic soil; 4-chloro-o-cresol (4-CC) was a minor transformation product that was short-lived in the upper soil strata.
Predominantly anthropogenic[2]	Yes		Yes	
Persistence[3]:	Soil	Half-life ≥ 182 days	Half-life = 6.1-11.7 days	
	Water	Half-life ≥ 182 days	Half-life =14.8-48.5 days	
	Sediment	Half-life ≥ 365 days	ND	
	Air	Half-life ≥ 2 days or evidence of long range transport	Half-life or volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (3.0 x 10^{-5} mm Hg) and Henry's Law Constant (K = 1.0 x 10^{-8} atm · m^3/ mole).	
Bioaccumulation[4]	Log $K_{OW} \geq 5$		0.48	
	BCF ≥ 5000		Value or not available	
	BAF ≥ 5000		Value or 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 toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (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}).

Table 5 Effects of Mecoprop-p (MCPP-P) on terrestrial organisms.

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity
Invertebrates				
Earthworm (*Eisenia foetida)*	Acute	MCPP-P DMAS	LC_{50} 494 mg a.e./kg soil	
Honey bee (*Apis mellifera*)	Oral	racemic MCPP[a] acid	LD_{50} > 10 µg a.e./bee (LD_{50} > 11.2 kg a.e./ha)	Relatively non-toxic[b]
	Contact	racemic MCPP[a] acid	LD_{50} > 100 µg a.e./bee (LD_{50} > 112 kg a.e./ha)	Relatively non-toxic[b]
Carabid beetle *(Pterostichus cupreus)*				
Birds				
Bobwhite quail (*Colinus virginianus)*	Acute oral	MCPP-P acid	LD_{50} = 462 mg a.e./kg bw	Moderately toxic[c]
	Acute dietary	MCPP-P DMAS	LC_{50} > 4630 mg a.e./kg diet	Slightly toxic[c]
	Reproduction		NA	
Mallard duck (*Anas platyrhynchos)*	Acute oral	MCPP-P acid	NA	
	Acute dietary	MCPP-P acid	LC_{50} > 2585 mg a.e./kg diet	Slightly toxic[c]
		MCPP-P DMAS	LC_{50} > 3908 mg a.e./kg diet	Slightly toxic[c]
	Reproduction		NA	
Japanese quail (*Coturnix japonica*)	Reproduction	MCPP-P DMAS	NOEC = 827 mg a.e./kg diet	
Mammals				
Rat	Acute oral	MCPP-P acid	LD_{50} = 700 mg a.e./kg bw	Slightly toxic[c]
	Dietary (90-day)	MCPP-P acid	NOEC = 800 mg a.e./kg diet	
	Reproduction (two generation)	MCPP-P acid	NOEC = 500 mg a.e./kg diet	
Mouse	Dietary (90-day)	MCPP-P acid	NOEC = 100 mg a.e./kg diet	
Vascular plants				
Vascular plant	Seedling emergence	MCPP-P acid	EC_{25} = 0.02 - >1.18 kg a.e./ha EC_{50} = 0.04 - >1.18 kg a.e./ha HD_5 of EC_{50}s = 0.0296 kg a.e./ha (seedling emergence) EC_{25} = 0.50 - >7.87 kg a.e./ha EC_{50} = 0.73 - >7.87 kg a.e./ha (percent survival) EC_{25} = 0.0090 – 0.86 kg a.e./ha EC_{50} = 0.024 - >1.18 kg a.e./ha HD_5 of EC_{50}s = 0.0227 kg a.e./ha (plant height) EC_{25} = 0.0046-0.61 kg a.e./ha EC_{50} = 0.0091-0.99 kg a.e./ha HD_5 of EC_{50}s = 0.0081 kg a.e./ha (plant dry weight)	

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity
	Vegetative vigour	MCPP-P DMAS	EC_{25} = 0.016 - >1.18 kg a.e./ha EC_{50} = 0.03- > 1.18 kg a.e./ha (plant height) EC_{25} = 0.0045 - >1.18 kg a.e./ha EC_{50} = 0.011- > 1.18 kg a.e./ha HD_5 of EC_{50}s = 0.0069 kg a.e./ha (plant dry weight)	

[a] Toxicity data on racemic mecoprop used as surrogate data for mecoprop-p (MCPP-P) isomer
[b] Atkins *et al*. (1981) classification
[c] US EPA classification
NA - data not available

Table 6 Effects of Mecoprop-p (MCPP-P) on aquatic organisms.

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[b]
Freshwater species				
Daphnia magna	Acute	MCPP-P acid	EC_{50} >90 mg a.e./L (mortality)	Slightly toxic
		MCPP-P acid	EC_{50} >82 mg a.e./L (immobility)	Slightly toxic
	Chronic (21-d)	Racemic MCPP-DMAS (EP)[a]	NOEC = 11.1 mg a.e./L	
Rainbow trout (*Oncorhynchus mykiss)*	Acute	MCPP-P DMAS	LC_{50} >123 mg a.e./L	Practically non-toxic
	Chronic	MCPP-P acid	LC_{50} = 95.7 mg a.e./L NOEC = 49.6 mg a.e./L	Practically non-toxic
Bluegill sunfish (*Lepomis macrochirus)*	Acute	MCPP-P acid	LC_{50} >91 mg a.e./L	Slightly toxic
Freshwater green algae (*Pseudokirchneriella subcapitata*)	Acute	MCPP-P DMAS (EP)	EC_{50} = 220 mg a.e./L	
		MCPP-P DMAS (EP)	EC_{50} = 108 mg a.e./L (biomass); EC_{50} >317 mg a.e./L (growth rate)	
		MCPP-P DMAS	EC_{50} = 159 mg a.e./L (biomass and growth rate)	
		MCPP-P acid	EC_{50} = 249 mg a.e./L (biomass); EC_{50} >672 mg a.e./L (growth rate)	
Freshwater blue-green algae (*Anabaena flos-aquae*)	Acute	MCPP-P DMAS	EC_{50} = 1.2 mg a.e./L (biomass)	
Freshwater diatom (*Navicula pelliculosa*)	Acute	MCPP-P DMAS	EC_{50} = 0.24 mg a.e./L (biomass)	
Duckweed (*Lemna* sp.)	Acute (7-d)	MCPP-P DMAS	EC_{50} = 18.7 mg a.e./L (biomass)	
	Acute (14-d)	MCPP-P DMAS	EC_{50} = 1.9 mg a.e./L (biomass)	

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[b]
Marine species				
Skeletonema costatum (marine alga)	Acute	MCPP-P DMAS	EC_{50} = 17 µg a.e./L (biomass)	

[a] Toxicity data on racemic mecoprop used as surrogate data for mecoprop-p (MCPP-P) isomer
[b] US EPA classification

Appendix II Monitoring Data

Water Monitoring Data

A search for mecoprop[1] water monitoring data in Canada resulted in a number of samples with detections being reported. The Federal Provincial and Territorial representatives from all of the provinces and territories in Canada were contacted, requesting water monitoring data for mecoprop. In addition, requests were submitted to Environment Canada, the Department of Fisheries and Oceans and the drinking water subcommittee through Health Canada. A response was received by all provinces and territories indicating that either monitoring data were not available or the available data were submitted.

US databases were searched for detections of mecoprop. Data on residues present in water samples taken in the US are important to consider in the Canadian drinking water assessment given the extensive monitoring programs that exist in the US. Runoff events, local use patterns, site specific hydrogeology as well as testing and reporting methods are probably more important influences on residue data rather than Northern versus Southern climate. As for the climate, if temperatures are cooler, residues may break down more slowly, on the other hand if temperatures are warmer, growing seasons may be longer and applications may be more numerous and frequent.

Mecoprop was not analyzed for in the US databases searched.

Approach for Evaluation

Data from Canadian monitoring studies in which mecoprop was quantified are summarized in Table 4 of Appendix I.

For both the ecoscenario assessment and the drinking water assessment, information was extracted from the available sources, tabulated and sorted into categories as follows:

- Residues in known drinking water sources (both surface and groundwater);
- Residues in ambient water that may serve as a drinking water source (both surface and groundwater);
- Residues in ambient water that are unlikely to serve as a drinking water source.

An important limitation of the monitoring data set is that, in many cases, the data were not accompanied with use data for mecoprop. For instance, the rate applied, when the application occurred and weather conditions prior to sampling were generally not known or reported. Without this information, it is difficult to 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

1 MCPP-P is the herbicidally active isomer of mecoprop. For analytical purposes the term “mecoprop” is used rather than specifying the isomer analyzed.

intervals immediately following application would increase the likelihood that the maximum concentration would be detected.

Thus, it is likely mecoprop was not used in some of the areas monitored, and that higher concentrations of mecoprop may occur in other areas not monitored. The mecoprop monitoring data likely underestimate the peak exposure because of the following limitations:

In general, the data are sparse in both time and location. In some of the studies available, mecoprop was analyzed in samples that were taken from non-mecoprop use areas. Mecoprop use information from the areas surrounding where the samples were collected is often not available.

Sampling in some of the studies was conducted during periods when mecoprop is not applied in Canada (i.e., October through March).

The concentrations of pesticides in surface water are directly related to the frequency and timing of monitoring in relation to pesticide application and runoff events. Therefore, timing and frequency of sampling is likely to be the most important factor influencing the concentration detected and the frequency of detections. Samples are often taken at arbitrary time intervals (i.e., once a month, once a week) and are unlikely to capture the absolute maximum concentration of mecoprop.

The following statistics are used to interpret the information available in each dataset and are summarized in Table 4 of Appendix I.

The detection frequency provides an indication of how often positive detections occur within the given data set. Detection frequency is primarily determined by the limits of detection and is influenced by pesticide use patterns and application rates. Consequently, a wide range of detection frequencies is likely to be expected.

The 95^{th} percentile concentration is calculated and reported. Maximum values should also be considered, especially when the 95^{th} percentile is not available, which occurs when there are insufficient detections to calculate a 95^{th} percentile.

The maximum concentration is reported and is used to determine the 95^{th} percentile concentration to estimate an acute exposure value.

The arithmetic mean with non-detects considered at ½ LOD is used to determine the 95^{th} percentile concentration to estimate a chronic exposure value.

Ecoscenario Exposure Estimates from Monitoring Data

The acute and chronic exposure estimates for mecoprop in Canadian surface water are presented in Table 1. The acute exposure value was estimated from monitoring data by determining the 95th percentile of the maximum concentration detected in each monitoring study/site. The chronic exposure value was estimated by determining the 95th percentile of the arithmetic means of all samples at each site (detects and non-detects) from the monitoring studies. The samples with values less than the LOD were given a value of ½ LOD. Groundwater data and data from water distribution systems were not included in the ecoscenario assessment.

Table 1 Concentrations of Mecoprop in Surface Water Estimated from Available Monitoring Data

Acute Concentration (µg/L)*	Chronic Concentration (µg/L)**
2.9	0.40

* 95th percentile of the maximum detected concentrations from surface water monitoring studies
**95th percentile of the mean concentration for each study site including ½ LOD for non-detects

Drinking Water Exposure Estimates from Monitoring Data

A search for mecoprop water monitoring data in Canada and the US resulted in a number of samples with detections being reported. A detailed summary of the Canadian and US water monitoring studies is provided in Table 4 Appendix I. Calculated EECs for acute and chronic exposure from groundwater and surface water are presented in Table 2.

Table 2 Concentrations of Mecoprop in Drinking Water Estimated from Available Monitoring Data

Ground Water		Surface Water	
Acute EEC (µg/L)*	Chronic EEC (µg/L)**	Acute EEC (µg/L)*	Chronic EEC (µg/L)**
0.069***	0.003***	2.09	0.36

* 95th percentile of the maximum detected concentrations from surface water monitoring studies
**95th percentile of the mean concentration for each study site including ½ LOD for non-detects
*** based on one monitoring study only

References

1.0 Chemistry

PMRA Document Number	Reference
1760404	Comparison of Old and New Processes, DACO: 2.11.3 CBI
1760405	Mecoprop-p Summary Dossier (A H Marks/ Nufarm Limited) Document J Confidential Information, DACO: 2.11.4 CBI
1760406	2007, The Analysis of 5 Batches of R(+) 2-(4-chloro-2-methylphenoxy)propionic acid, DACO: 2.13.3 CBI
1760407	2009, A discussion on the formation of MCPA as an impurity of concern in MARKS Mecoprop-p Technical Acid; Reg. No. 27441, DACO: 2.13.4 CBI
1760409	2009, Analysis for Tetra-to Octa-Chlorinated Dioxins and Fruans in Seven Batches of (+)--2-(4-chloro-2-methylphenoxy) propanoic acod (MCPP-P, Mecoprop-p), DACO: 2.13.4 CBI
1760410	2009, Analysis for Tetra-to Octa-Chlorinated Dioxins and Fruans in Seven Batches of (+)--2-(4-chloro-2-methylphenoxy) propanoic acod (MCPP-P, Mecoprop-p), DACO: 2.13.4 CBI
1760412	2009, Analysis for Tetra-to Octa-Chlorinated Dioxins and Fruans in Seven Batches of (+)--2-(4-chloro-2-methylphenoxy) propanoic acod (MCPP-P, Mecoprop-p), DACO: 2.13.4 CBI
1760414	2009, Analysis for Tetra-to Octa-Chlorinated Dioxins and Fruans in Seven Batches of (+)--2-(4-chloro-2-methylphenoxy) propanoic acod (MCPP-P, Mecoprop-p), DACO: 2.13.4 CBI

2.0 Human and Animal Health

PMRA Document Number	Reference
1418475	1983. Report of the study of the acute oral toxicity in rats of CMPP (mecoprop) (D-form) dated Dec. 29, 1983. Report RZ-No: 84/028. BASF. EPA DER 1256871; PMRA DER 93862.
1418476	1990. Mecoprop-p: Acute oral toxicity in the rat. LSR Report No 90/AMS015/0531. PMRA DER 93624.
1418477	1994. Mecoprop-p: Acute oral LD_{50} in the rat. Report SA 94095, Doc No 600362. Reg Doc #BASF 94/11744. PMRA DER 93861.
1418474	1985. Report of the study of the acute oral toxicity on the rat based on OECD of Duplosan KV/BAS 037 29 H. Report RZ-No: 85/060. BASF. PMRA DER 93863.
1418473	1992. Acute oral toxicity to rats of MCPP-P DMAS. Study Number: 920504D/JEL 46/AC. MRID 426147-01; EPA DER 1256886 & 1257085. PMRA DER 93870.
1418479	1983. Report of the study of the acute dermal toxicity in rats of CMPP (mecoprop) (D-form) dated May 25, 1984. Report RZ-No: 84/152. EPA DER 1256872; PMRA DER 93739.
1418481	1985. Report of the study of the acute dermal toxicity on the rat based on OECD of Duplosan KV/BAS 037 29 H. Report RZ-No: 85/061. PMRA DER 93745.
1418483	1990. Mecoprop-p: Acute percutaneous toxicity study in the rat. LSR Report No.

	90/AMS016/0498. PMRA DER 93795.
1418482	1994. Mecoprop-p: Acute dermal LD_{50} in the rat. Document No 600294. Doc # BASF 94/11743. PMRA DER 93827.
1418550	1992. Acute dermal toxicity to rabbit of MCPP-P DMAS. Study Number: 920477D/JEL 48/AC. MRID 426147-03; EPA DER 1256887 & 1257087. PMRA DER 93613.
1418484	1986. Acute inhalation toxicity LC_{50} - 4 hour (rat) - dust/aerosol study of MCPP: D-form (optisch aktive). Project No 1310424/651, Kli-fu/68, RZ-Report No: 86/379. EPA DER 1256873; PMRA DER 93614.
1418489	1985. Acute inhalation toxicity LC_{50} 4 hour (rat) - Liquid aerosol study of Duplosan KV (BAS 037 29 H). RZ-Report No: 85/199, Reg Doc #85/0199, BASF. PMRA DER 93803.
1418486	1990. Mecoprop-p: Acute inhalation toxicity study in the rat. LSR Report No. 90/AMS022/0278. First amendment, 1991. LSR Report No. 90/AMS022/0278. Final amendment, 1995. LSR Report No. 95/AMS022/0965. PMRA DER 93810.
1418551	1993. Acute inhalation toxicity to rats of MCPP-P DMAS. Study Number: JEL 67/930505, MRID 429163-01; EPA DER 1256888 & 1257088. PMRA DER 93802.
1418478	1983. Report on the study of the acute intraperitoneal toxicity in rats of CMPP (mecoprop) (D-form). Report RZ-No: 84/029, PMRA DER 93612.
1418490	1983. Report on the study of the irritation to the eye of the white rabbit based on Draize of CMPP (mecoprop) (D-form). RZ-No. 84/031, MRID 41013901; EPA DER 1256874; PMRA DER 94072.
1418491	1990. Mecoprop-p: Acute eye irritation/corrosion test in the rabbit. LSR Report 90/AMS018/0500. First amendment, 1990. PMRA DER 93615.
1418493	1984. Report on the study of the acute irritation to the eye of the white rabbit based on OECD of BAS 037 29 H/Duplosan KV. RZ-Report No: 84/263, PMRA DER 94073.
1418494	1983. Report of the study of the irritation to the intact and abraded dorsal skin of the white rabbit based on Draize of CMPP (mecoprop) D-form. BASF Report RZ-No: 84/030. MRID 41013904; EPA DER 1256875. PMRA DER 93887.
1418498	1990. Mecoprop-p: Acute dermal irritation / corrosion test in the rabbit. LSR Report 90/AMS017/0499, First amendment, LSR Report No. 90/AMS017/1134, December 17, 1990. PMRA DER 93616.
1418497	1994. Mecoprop-p - Acute dermal irritation test in the rabbit. Document No 600316. Reg Doc. #BASF 94/11742, BASF. PMRA DER 93886.
1418495	1992. Skin irritation to the rabbit of MCPP-P DMAS. Study Number: 920808D/JEL 72/SE. MRID 427298-02; EPA DER 1256890 & 1257089. PMRA DER 93888.
1418496	1984. Report of the study of the acute dermal irritation / corrosivity to the intact dorsal skin of the white rabbit based on OECD of BAS 037 29 H / Duplosan KV. Report RZ-No: 84/261. PMRA DER 93889.
1418572	1985. Report on the maximization test for the sensitizing potential of CMPP (mecoprop) - D-form in guinea pigs. Lab project 30H20/83-1, RZ-Report No: 85/392, MRID 41013907: EPA DER 1256876. PMRA DER 94028.
1185283	1995. Report on the maximization test for the sensitizing potential of mecoprop-P in guinea pigs. 30H002/912278. BCI# 95-0554. MRID 43749601. PMRA DER 93617. DACO 4.2.6

1213338	1995. Report on the maximization test for the sensitizing potential of mecoprop-P-DMA salt in guinea pigs. Lab project 30H0210/912275. PMRA DER 94029.
1213337	1993. Skin sensitization to the guinea pig of MCPP-P DMAS. Study Number: 920879D/JEL 77/SS. MRID 429555-02; EPA DER 1256891 & 1257090. PMRA DER 94030, 166844.
1418503	1984. Report on the study on the sensitizing effect of CMPP (mecoprop) in the guinea pig - Open Epicutaneous Test. Project No. 31H19/83, Registration Document No. BASF: 84/0240. PMRA DER 94031.
1418507	1990. Study on the oral toxicity of MCPP in mice - Administration in the diet for 4 weeks (supplementary range finding study). Report Project No. 50S0047/ 83077. PMRA DER 93620.
1418506	1990. Study on the oral toxicity of MCPP in mice - Administration in the diet for 4 weeks (range finding study). Report Project No. 50S0047/83075. PMRA DER 93675.
1651613	1986. Report on the comparative study of the racemate and D-form of mecoprop in rats after 7 week administration in the diet. Document BCI# 86/0087. PMRA DER 93689.
1185284	1993. Report on the Study of the Oral Toxicity of Mecoprop-p Acid in B6C3F1 Mice: Administration in the Diet for 3 Months. Report No. 35C0002/91002, BCI# 93-0906. MRID 430592-01; EPA DER 1256878 and 1257092. PMRA DER 93618. DACO 4.31
1418512	1977. Mecoprop - 3-Month oral toxicity study in the rat - Racemate (10 660 RP) - D-isomer (17 610 RP). IFREB-R 807266. Reg Doc # 77/10592. BASF. PMRA DER 94507.
1418510	April 1, 1985. Report on the study of the toxicity of MCPP in rats after 3 months administration in the diet. RZ-Report No. 85/092; BCI# 85-0092. PMRA DER 93704.
1185225	1995. Mecoprop-p: Subchronic Oral Dietary Toxicity and Neurotoxicity Study in Wistar Rats. Report No. 50C0002/91157; BCI# 95-1660, BASF Canada Inc. MRID 439082-01; EPA DER 1256877 and 1257094. PMRA DER 93609. DACO 4.3.1, 4.5.11
1185285	1997. Report on Mecoprop-p - Chronic Oral Toxicity Study in Beagle Dogs: Administration in the Diet for 12 Months. Report No. 33D0002/91166; BCI# 97-1083. PMRA DER 93619. DACO 4.3.2
1418556	1993. Twenty-one day dermal toxicity study in the rabbit with MCPP-p acid. JEL 50/921436. MRID 429164-01; EPA DER 1256879 and 1257107. PMRA DER 93621.
1185226	1996. Mecoprop-p: Carcinogenicity Study in B6C3FlICrlBR Mice, administration in the diet for 18 months. Report No. 7680002/91102; BCI# 96-1432. PMRA DER 93629. DACO 4.4.2
1418517	1999. Mecoprop-P - Carcinogenicity study in B6C3F1/Cr1BR mice - Administration in the diet for 18 months (Supplementary study). Project No 76S0002/91142. Reg Doc # BASF 99/10101, BASF. PMRA DER 94382.
1185348	1988. Report on the study on the chronic toxicity and oncogenic potential of MCPP in rats: Administration in the diet over 24 months. 71S0047/8352; BCI#88-0386. PMRA DER 93630. DACO 4.4.4

1185228	1988. Continuation of Report on the study on the chronic toxicity and oncogenic potential of MCPP in rats: Administration in the diet over 24 months. 71S0047/8352; BCI#88-0386. PMRA DER 93630. DACO 4.4.4
1602961	2008. Mecoprop-p - Dietary Two Year Carcinogenicity Study in the Rat. Study Number: PR1324; Report Number: PR1324-REG; Task Number: CO03366r2.
1185229	1996. Reproduction study with MCPP in rats - Continuous dietary administration over 2 generations (2 litters in the first and 1 litter in the second generation). 70R0047/83078; BCI# 92-1869. PMRA DER 93631. DACO 4.5.1
1382211	1992. Reproduction study with MCPP in rats - Continuous dietary administration over 2 generations (2 litters in the first and 1 litter in the second generation). 70R0047/83078; BCI# 92-1869. PMRA DER 93631. DACO 4.5.1
1418523	1980. Mecoprop oral teratogenicity study in the rat. Report No 1995-277/7b, PMRA DER 94446.
1185230	1993. Study of the prenatal toxicity of mecoprop-p in rats after oral administration (gavage). 30R0002/91013; BCI#92-1160. MRID 42815301; EPA DER 1256880 & 1257095. PMRA DER 93607. DACO 4.5.2
1185323	1993. Study of the prenatal toxicity of mecoprop-p in rabbits after oral administration (gavage). 40R0002/91014; BCI#92-1161. MRID 42815302; EPA DER 1256882 & 1257096. PMRA DER 93632. DACO 4.5.3
1185335	1993. Ames *Salmonella typhimurium* bacterial reverse mutation assay on MCPP-P acid. JEL53/921060, BCI#93-1660. MRID 428608-03; EPA DER 1256893 & 1257097. PMRA DER 93633. DACO 4.5.4
1418525	1993. Ames *Salmonella typhimurium* bacterial reverse mutation assay on MCPP-P DMAS. HRC Study JEL 51/921058. MRID 428608-01; EPA DER 1256892 & 1257100. PMRA DER 94176.
1185344	1993. Chinese hamster ovary/HGPRT locus assay MCPP-P acid. JEL87/931132, BCI#93-1410. MRID 431134-01; EPA DER 1256883 & 1257099. PMRA DER 93634. DACO 4.5.5
1418526	1993. Chinese hamster ovary / HGPRT locus assay - MCPP-P DMAS. HRC Study No JEL 60/921617. MRID 429368-02; EPA DER 1256896 & 1257101. PMRA DER 94239.
1185345	1994. Chromosome aberration assay in human lymphocytes *in vitro* with mecoprop-p acid. CCR Project 429401; BCI#94-1089. BCI#94-1368. MRID 431895-01; EPA DER 1256885 & 1257102. PMRA DER 93608. DACO 4.5.6
1185346	1994. 1st Amendment to report on Chromosome aberration assay in human lymphocytes *in vitro* with mecoprop-p acid. CCR Project 429401, BCI#94-1089. BCI#94-1368. MRID 431895-01; EPA DER 1256885 & 1257102. PMRA DER 93608. DACO 4.5.6
1382238	1990 (Draft June 19, 1990). *In vitro* assessment of the clastogenic activity of mecoprop-p in cultured human lymphocytes. LSR Report 90/0403. AMS/020; 90/AMS020/0403; PMRA DER 103617. DACO 4.5.6
1418527	1993. MCPP-P DMAS: metaphase chromosome analysis of human lymphocytes cultured in vitro. HRC Study No JEL 62/921576. MRID 429368-03; EPA DER 1256897 & 1257104. PMRA DER 94254.

1418586	1985. Report on the cytogenetic investigation in Chinese hamster after a single oral administration of MCPP D-form - Bone marrow chromosome analysis. Registration Document No. BASF 85/0225. PMRA DER 94255.
1185347	1994. *In vivo/in vitro* unscheduled DNA synthesis in rat hepatocytes with mecoprop-p acid. CCR Project 429402; BCI#94-1670. PMRA DER 93636. DACO 4.5.6, 4.5.7
1418585	1991. Mecoprop-p: Assessment of clastogenic action on bone marrow erythrocytes in the micronucleus test. LSR Report 90/AMS026/1269, PMRA DER 93635.
1418587	1993. MCPP-P DMAS micronucleus test. JEL 54/921201, MRID 428608-04; EPA DER 1256895 & 1257105. PMRA DER 94334.
1185286	1995. Report on mecoprop-p - Acute oral neurotoxicity study in Wistar rats. 20S0002/9115; BCI# 95-0415. MRID 43770801; EPA DER 1257106. PMRA DER 93638. DACO 4.5.10
1418531	1997. (^{14}C)-Mecoprop-p: Absorption, distribution, metabolism and excretion in the rat. Report 1149/3-1007. PMRA DER 93637.
1418533	1997. ^{14}C-Mecoprop-p-EHE and ^{14}C-mecoprop-p-DMA: Absorption, distribution, metabolism and excretion in the rat. Report 1149/14-1007. MRID 44362702. PMRA DER 94475.
1418558	1995. ^{14}C-Mecoprop-p-DMA salt [^{14}C-mecoprop-p-dimethyl-ammonium]: Metabolism/degradation in plasma, gastrointestinal tract, gastro-intestinal tract contents, and post mitochondrial liver fraction (S9). 1149/11-1011. MRID 43717201; EPA DER 1256898 & 1257093.
1185287	1994. (^{14}C)-2-Ethylhexyl Mecoprop-p: Metabolism/Degradation in Plasma, Gastro-Intestinal Tract, Gastro-Intestinal Tract Contents and Post-Mitochondrial Liver Fraction (S9). Report No. 1149/1-101. BCI#94-0551. PMRA DER 94496. DACO 4.5.9
1185325	1998. Statement on the use of data from studies with racemic mecoprop for the toxicological assessment of optically active mecoprop. DACO 4.8
1522671	2001, The Distribution and Metabolism of [14C]-Mecoprop-p in the Lactating Goat, DACO: 6.2,7.5
1522673	2007, Mecoprop-p Residues Study in Laying Hens: Request for a Waiver, DACO: 6.2
1522674	1998, 14C Mecoprop-p: Wheat Metabolism Study, DACO: 6.3
1522675	2000, 14C Mecoprop-p 2-ethylhexyl ester: Wheat Metabolism, DACO: 6.3
1522676	2000, Amendment to 14C Mecoprop-p 2-ethylhexyl ester: Wheat Metabolism, DACO: 6.3
1522677	2007, Summary of MCPP-p Cereal Grain Residue Program Conducted in Canada, DACO: 7.1
1522678	1996, Mecoprop-p and Dichlorprop-p Analytical Method for the Determination of Residues in Animal Products AR 125-96, DACO: 7.2.1,7.2.2,7.2.5
1522682	2002, Independent Laboratory Validation of the Method of Analysis AR 125-96 for the Determination of Mecoprop-p (MCPP-p) and Dichlorprop-p (2,4-DP-p) in Products of Animal Origin, DACO: 7.2.3
1522684	2007, Position Paper: Data Waiver Request for FDA Multiresidue Methods Testing for MCPA, 2,4-DB, MCPP-p, 2,4-DP-p and MCPB: OPPTS 860.1360 Multiresidue Method Test, DACO: 7.2.4
1522685	2002, Storage Stability of Mecoprop-p Residues in Cereals, DACO: 7.3

1522686	2006, Magnitude of Mecoprop-p Residues and Decline from Application of Mecoprop-p Dimethylamine Salt to Spring Wheat (in Canada), DACO: 7.4.1,7.4.2,7.4.5,7.4.6
1522689	2006, Magnitude of Mecoprop-p Residues and Decline from Application of Mecoprop-p Dimethylamine Salt to Barley (in Canada), DACO: 7.4.1,7.4.2,7.4.5,7.4.6
1522690	2006, Magnitude of Mecoprop-p Residues from Application of Mecoprop-p Dimethylamine Salt to Corn, DACO: 7.4.1,7.4.5,7.4.6
1522691	2007, Magnitude and Decline of Mecoprop-p Residues from Application of Mecoprop-p Dimethylamine Salt to Barley in Canada, DACO: 7.4.1,7.4.2,7.4.5,7.4.6
1522692	2007, Magnitude and Decline of Mecoprop-p Residues from Application of Mecoprop-p Dimethylamine Salt to Corn in Canada, DACO: 7.4.1,7.4.2,7.4.5,7.4.6
1522696	2007, Magnitude of MCPP and Metabolite Residues in Processed Fractions of Spring Wheat Following Treatment with Mecoprop-p Dimethylamine Salt in Canada, DACO: 7.4.1,7.4.2,7.4.5,7.4.6
1522700	2007, Magnitude and Decline of Mecoprop-p Residues from Application of Mecoprop-p Dimethylamine Salt to Spring Wheat in Canada, DACO: 7.4.1,7.4.2,7.4.6
1522703	2007, Waiver Request for Field Accumulation in Rotational Crops, DACO: 7.4.4
1522704	2007, Magnitude of Mecoprop-p Residues from Application of Mecoprop-p Dimethylamine Salt to Spring Wheat in Canada, DACO: 7.4.1,7.4.6
1522706	2007, Magnitude of Mecoprop-p Residues from Application of Mecoprop-p Dimethylamine Salt to Barley in Boissevain, Manitoba, Canada, DACO: 7.4.1,7.4.6
1522707	2007, Magnitude of Mecoprop-p Residues from Application of Mecoprop-p Dimethylamine Salt to Corn in Canada, DACO: 7.4.1,7.4.6
1522708	2007, Interim Draft Report A Confined Rotational Crop Study with 14C Mecoprop-p, DACO: 7.4.3

3.0 Impact on the Environment

PMRA Document Number	Reference
1256901	1993. Tier 2 Vegetative Vigor Nontarget Phytotoxicity Study Using MCPP-p acid. Pan-Ag Study No. BL91-484. MCPP-p Task Force II.
1256914	1993. The Effects of MCPP-P DMAS on Nontarget Plants: Seedling Germination/ Seedling Emergence. Study Number CAR 146-91E. MCPP-p Task Force II.

B. ADDITIONAL INFORMATION CONSIDERED

Published Information

1.0 Environment

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.

Fletcher, J.S., Nellessen, J.E., and Pfleeger, T.G. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. Environmental Toxicology and Chemistry 13:1383-1391.

Goring, C.A.I., D.A. Laskowski, J.H. Hamaker and R.W. Meikle. 1975. Principles of pesticide degradation in soil. Pages 135-172 in (R. Hague and V.H. Freed, eds.) *Environmental dynamics of pesticides*. Plenum Press, New York.

Harris, L.E. 1975. Guide for Estimating Toxic Residues in Animal Feeds or Diets. U.S.EPA, Washington. EPA/540/9-75-019 (NTIS reference #: PB 243 748).

Helling, C.S., and B.C. Turner. 1968. Pesticide mobility: Determination by soil thin-layer chromatography. Science 12: 562-563.

Hoerger F; Kenaga EE. 1972. Pesticide residues on plants: correlation of representative data as basis for estimation of their magnitude in the environment. In: Coulston F; Korte F. (eds). Global aspects of chemistry, toxicology and technology as applied to the environment, Vol. I. Thieme, Stuttgart, and Academic Press, New York. pp. 9-28.

Kenaga EE. 1973. Factors to be considered in the evaluation of the toxicity of pesticides to birds in their environment. In: Coulston F; Dote F. (eds). Global aspects of chemistry, toxicology and technology as applied to the environment, Vol. II. Thieme, Stuttgart, and Academic Press, New York. pp. 166-181.

Kennedy, J.M. and R.E. Talbert. 1977. Comparative persistence of dinitroaniline type herbicides on the soil surface. Weed Sci. 25(5): 373-381.

McCall, J.P., D.A. Laskowski, R.L. Swann and H.J. Dishburger. 1981. Measurement of sorption coefficients of organic chemicals and their use in environmental fate analysis. Pages 89-109 in Test protocols for environmental fate and movement of toxicants. Proceedings of a symposium. Association of Official Analytical Chemists. 94th Annual Meeting, October 21-22, 1980. Washington, D.C.

McEwen, F.L. and G.R. Stephenson. 1979. The Use and Significance of Pesticides in the Environment. John Wiley and Sons Inc. Toronto. 282 pp.

Nagy, K.A. 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecological Monographs 57:111-128.

Spector, W.S. 1956. Handbook of Biological Data. W.B. Saunders, Philadelphia, p. 78, 187.

U.S. EPA. 1975. Volatilization studies. Guidelines for registering pesticides in the United States. 40FR (123): 26889-26891.

U.S. EPA. 1985a. *Hazard Evaluation Division, Standard Evaluation Procedure, Avian Single-Dose Oral LD50 Test*. EPA 540/9-85-007. June, 1985. U.S. EPA, Washington, D.C.

U.S. EPA. 1985b. *Hazard Evaluation Division, Standard Evaluation Procedure, Avian Dietary LC50 Test*. EPA 540/9-85-008. June, 1985. U.S. EPA, Washington, D.C.

U.S. EPA. 1985c. *Hazard Evaluation Division, Standard Evaluation Procedure, Wild Mammal Toxicity Test.* EPA 540/9-85-004. June 1985. U.S. EPA, Washington, D.C.

Wolf, T.M. and B.C. Caldwell. 2001. Development of a Canadian spray drift model for the determination of buffer zone distances. Page 60. In: Expert Committee on Weeds - Comité d'experts en malherbologie (ECW-CEM). Proceedings of the 2001 National Meeting, Québec City. Saint-Anne-de-Bellevue, Quebec: ECW-CEM. Eds. D. Bernier, D.R.A. Campbell and D. Cloutier.

ISSN: 1911-8082

© Her Majesty the Queen in Right of Canada, represented by the Minister of Public Works and Government Services Canada 2011

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.