B21-1.0 MECOPROP

B21-1.1 Background Information

IUPAC: (RS)-2-(4-chloro-o-tolyloxy)propionic acid

CAS: 2-(4-chloro-2-methylphenoxy)propanoic acid

CASRN: 1929-86-8

MECOPROP USES:

Mecoprop was used to control weed resistant to 2,4-D such as chickweed, clovers, black medick and young knotweed (OMAFRA, 2002).

Mecoprop was an active ingredient of the herbicide product Trillion®. It was applied at the CFB Gagetown in 1986 (JW, 2006).

Table B21-1 Mecoprop Usage at CFB Gagetown[a]

Year	Total Area Treated (ha)	Total Mecoprop Applied (kg)
1986	91	50

[a] Adapted from JW, 2006.

B21-2.0 CHEMICAL AND PHYSICAL PROPERTIES

Formula: $C_{10}H_{11}ClO_3$

Activity: Mecoprop is a selective, hormone-type phenoxypropionic herbicide (EXTOXNET, 1996). Mecoprop will affect enzyme activity and growths in plants (RSCI, 1994). Mecoprop acts slowly and will require 3 to 4 weeks to demonstrate efficacy (Thomson, 1982).

Notes: Mecoprop can be used as an acid, ester or a salt. Various forms of mecoprop include: Mecoprop-dimethylammonium [CASRN: 32351-70-5], mecoprop-diolamine [CASRN: 1432-14-0], mecoprop-ethadyl, mecoprop-isoctyl [CASRN: 28473-03-2], mecoprop-methyl [CASRN: 2786-19-8], mecoprop-potassium [CASRN: 1929-86-8], mecoprop-sodium [CASRN: 19095-88-6], mecoprop-trolamine [CASRN: 53404-61-8]. Mecoprop exists in a mixture of two isomers, where the (R)-isomer of mecoprop is herbicidally active, and is referred to as mecoprop-P (OMAFRA, 2002).

Structure:

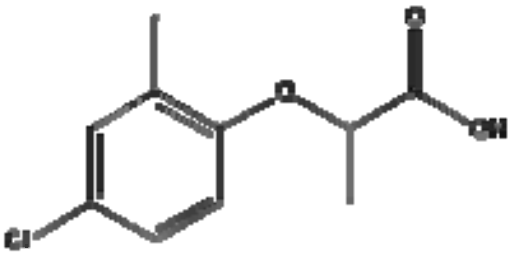

Figure 2-1 Mecoprop CASRN: 7085-19-0 Structure

Table B21-2 Chemical and Physical Properties of Mecoprop

Chemical/Physical Property	Result	Reference
Colour/Form	White to light brown crystalline solid	EXTOXNET, 1996
Dissociation Constant (pKa)	3.105-3.78	Mackay *et al*., 1997
Henry's Law constant	$7.43x10^{-5}$Pa m^3/mole	Mackay *et al*., 1997
	$1.36x10^{-16}$atm m^3/mole[a]	JW, 2006
Log K_{ow}	2.83-3.94	Mackay *et al*., 1997
Melting Point	92 - 95ºC	Mackay *et al*., 1997
Molecular Weight (g)	214.6	Mackay *et al*., 1997
	252.74[a]	JW, 2006
Odour	Odourless	EXTOXNET, 1996
Vapour Pressure	$<1.0x10^{-5}$– $3.10x10^{-5}$ Pa	Mackay *et al*., 1997
	5.21 x 10^{-11}mm Hg[a]	JW, 2006
Water Solubility	620-895 mg/L	Mackay *et al*., 1997
	$7.95x10^{5}$ mg/L[a]	JW, 2006

[a] Values pertain to the dimethyl amine salt of mecoprop.

B21-3.0 PMRA EVALUATION

PMRA has decided to discontinue sales of all racemic mecoprop formulations in their re-evaluation decision document, released on May 13, 2004.

B21-4.0 TOXICOLOGICAL SUMMARY

B21-4.1 Human Health Effects

Table B21-3 Human Health Effects Resulting from Acute and Chronic Exposure to Mecoprop[a,b]

Exposure	Effects	Response
Acute	Heent	Eye, nose, and mouth irritation are possible with direct contact.
	Cardiovascular	Tachycardia, bradycardia, ECG abnormalities, asystole, other dysrhythmias, and hypotension have been reported with overdose. Deaths have resulted from cardiorespiratory arrest.
	Respiratory	Ingestion of large amounts may cause bradypnea, respiratory failure, hyperventilation, or pulmonary edema.
	Neurologic	Low dose exposures: Vertigo, headache, malaise, and paresthesias may occur depending on the specific compound involved. Highdose exposures: Muscle twitching, spasms, profound weakness, polyneuritis, and unconsciousness may occur depending on the specific compound involved. Idiosyncratic reactions: Peripheral neuropathies.
	Gastrointestinal	Nausea, vomiting, and diarrhea have been reported. Necrosis of the gastrointestinal mucosa has been reported.
	Hepatic	Elevated LDH, AST (SGOT), and ALT (SGPT) have been reported.
	Genitourinary	Albuminuria and porphyria may occur; renal failure due to rhabdomyolysis is also possible.
	Fluid-electrolyte	Hypocalcemia, hyperkalemia, and hypophosphatemia.
	Hematologic	Thrombocytopenia is the primary hematologic effect. Leukopenia has also been reported.
	Dermatologic	Direct contact may cause skin irritation.
	Musculoskeletal	Muscle cramps, muscle rigidity, elevated creatinine kinase, and rhabdomyolysis were reported after ingestion of mecoprop.

[a] Rumack and Hall, 2006.
[b] MEDITEXT®, 2006.

B21-4.2.1 Oral Exposure

B21-4.2.1.1 Death

Table B21-4 Mammalian LD_{50} Values Resulting from Oral Exposure to Mecoprop

Test Organism (Species/Sex)	LD_{50} (mg/kg)	Reference
Acute		
Mice	369	IET, 1984
Mice	650	Meister, 1992; Thomson 1982; Budavari, 1989
Rats	650	IET, 1984
Rats	930-1,210	Meister, 1992; Thomson 1982; Budavari, 1989

B21-4.2.1.2 Systemic Effects

Table B21-5 Mammalian Systemic Effects Resulting from Oral Exposure to Mecoprop

Test Organism (Species)	Daily Dose (Duration)	Response	Reference
Sub-acute			
Weanling SPF-Wistar rats	0,50,400, or 3,200 mg/kg/day for 90 days	At highest dose levels, significantly decreased blood haemoglobin levels and erythrocyte counts was observed for both male and females. Furthermore, decreased in neutrophils were seen in females, and a significant increase alkaline phosphatase activity, and decreased relative kidney weights were seen in both sexes.	Verschuuren, 1996
Beagle dogs	0, 4, 16 or 64 mg/kg/day for 13 weeks	At the highest dose levels, the following effects were observed: Depressed body weight gain, increased relative weights of heart, liver, kidney, brain, and lungs, increased blood urea levels, decreased blood haemoglobin levels, decreased packed cell volume and red blood cells, and decreased lymphocyte and increased neutrophil counts.	DNHW, 1980
Chronic			
Rats	0, 100, 400, 1000 or 2500 mg/kg /day for 7 month[a]	Animals consuming 400 mg/kg and above showed reduced erythrocyte counts, haemoglobin, and packed cell volume. Relative liver weight was increased in females, and males. Relative kidney weights were increased in rats in all treatment groups.	Gurd *et al*., 1965
Wistar Rats (M)	20, 50, or 125 mg/kg/day for 52 weeks	Increased in relative kidney weights at the two highest doses.	BASF, 1988

[a] Diethanolamine salt of mecoprop used.

B21-4.2.1.3 Neurological Effects

No data found.

B21-4.2.1.4 Mammalian Reproductive/Developmental Effects

Table B21-6 Reproductive and Developmental Effects Resulting from Oral Exposure to Triclopyr

Test Organism (Triclopyr form)	Exposure	Dose (mg/kg/day) (Duration)	Response	Reference
Pregnant mice	Oral	0, 100, 200, 300, 400, 500 or 700 mg gestation days 6-15	At doses 300 mg/kg/day and above, embryotoxicity was observed. Skeletal malformations were prominent at dosages of 400 mg/kg/day and above.	Roll, V.R *et al*., 1983
Pregnant mice	Gavage	0-150 mg/kg/day on gestation days 4, 10, 13, and 18.	Increased number of fetuses with hydroureter. Mecoprop found to readily cross the placental barrier.	Buschmann *et al.*, 1986
Pregnant rats	Oral	20, 50, or 125 mg/kg/day, day 6-15 of gestation	Developmental toxicity: Increased incidence of delayed or absent ossification of the sternebrae. Maternal toxicity: none observed.	U.S. EPA, 1988
Pregnant rats	Gavage	0-330 mg/kg/day on gestation days 4, 10, 13, and 18	Increased number of fetuses with hydroureter. Mecoprop found to readily cross the placental barrier.	Buschmann *et al.*, 1986
Pregnant rabbits	Oral	12, 30, or 75 mg/kg/day gestation days 6-18	No teratogenic or fetotoxic effects in offsprings in the group of 15 pregnanat rabbits.	U.S. EPA, 1988

B21-4.2.1.5 No Observed Adverse Effect Levels in Mammals

Table B21-7 Mammalian NOAELs and LOAELs from Oral Exposure to Mecoprop

Test Organism (Species)	Effect	Value (mg/kg/day)	Endpoint	Reference
Sub-acute				
SPF-Wistar rats	NOAEL	3	Systemic effect on kidney and blood parameters.	Verschuuren, 1996
Beagle dogs	NOAEL	4	Systemic effect on blood parameters, and body weight gain.	DNHW, 1980
Chronic				
Wistar rats	NOAEL	1	Systemic effects on organ weights.	BASF, 1988
Rats	NOAEL	4	Systemic effects on blood parameters, and organ weights.	Gurd *et al*., 1965

Table B21-8 Mecoprop Mammalian Reproductive and Developmental NOAEL and LOAEL Values

Test Organism (Species)	Effect	Daily Value (mg/kg/day)	Endpoint	Reference
Rats	NOAEL	10	Reduced weight gain in pups at maternal toxic dose.	EC, 2003
	NOAEL	50	Decreased pup weight and skeletal variations at maternal toxic doses.	

B21-4.2.2 Dermal Exposure

B21-4.2.2.1 Death

No data found.

B21-4.2.2.2 Systemic Effects

No data found

B21-4.2.2.3 Neurological Effects

No data found.

B21-4.2.2.4 Reproductive/Developmental Effects

No data found.

B21-4.2.2.5 No Observed Adverse Effect Level

No data found.

B21-4.2.3 Inhalation Exposure

B21-4.2.3.1 Death

No data found.

B21-4.2.3.2 Systemic Effects

No data found.

B21-4.2.3.3 Neurological Effects

No data found.

B21-4.2.3.4 Reproductive/Developmental Effects

No data found.

B21-4.2.3.5 No Observed Adverse Effect Level

No data found.

B21-4.3 Carcinogenicity

From the 24 month rat study conducted by BASF in 1988, mecoprop was determined to have no influence on the incidence of tumourgenesis in rats. European Commission reported that

mecoprop had no overall carcinogenic potential relevant for humans. However, increased liver tumour incidence was observed in female mice at highest dose tested in a study on mecoprop-P (EC, 2003).

B21-4-4 Populations at Special Risk

No data found.

B21-4.5 Toxicokinetics

Mecoprop is rapidly absorbed in mammal *via* the oral route, and will be widely distributed systemically (EC, 2003). There is no potential for mecoprop tissue accumulation, however some residues can be found in adipose tissues after 8 days (EC, 2003). T here is limited mecoprop metabolism in mammals. Studies show that 45% of mecoprop will be excreted unchanged, where as the rest will go through hydroxylation. T he rate of mecoprop excretion is 90% over a period of 48 hours. Urinary excretion is the main route for mecoprop expulsion (81%, EC, 2003). Mecoprop is also excreted *via* the billary route (EC, 2003).

B21-4.6 Exposure Limits

Table B21-9 Existing RfD Values for Mecoprop Exposures

Reference Dose (mg/kg/day)	Route of Exposure	Reference	Endpoint	Study	Reference	NOAEL (mg/kg/day)	Uncertainty factor
Acute/Short-term (1-7 days)							
Not required (Acute RfD)	Oral	PSD, 2007	--	--	EU ANNEX I	--	--
Intermediate-term (7 days- Several months)							
0.04[a]	Oral	PSD, 2007	Systemic effects	--	EU ANNEX I	--	--
Long-term (6 months to lifetime)							
0.001	Oral	U.S. EPA, 1989	Increased absolute and relative kidney weights	90 day rat feeding study	BASF Aktiegesellschaft, 1985	3	3,000
0.003	Oral	WHO, 1996	Systemic effects on organ weights	1 and 2 year rat study	BASF, 1988	1	300
0.01	Oral	EC, 2003	Systemic effects on organ weights	2 year rat study	--	1.1	100

[a] Acceptable Operator Exposure limit (AOEL).

Intermediate- and long-term oral exposure limits of 0.04 mg/kg/day (PSD, 2007) and 0.01 mg/kg/day (EC, 2003), respectively, were selected for the risk assessment purposes of this report.

B21-5.0 ENVIRONMENTAL FATE AND EXPOSURE

Mecoprop has low vapour pressure (Table B21-10) so loss through volatilization would only occur to a minor extent. F urthermore, mecoprop also has a low Henry's Law Constant of $1.36x10^{-16}$atm m^3/mole (JW, 2006). This indicates that it would have little tendency to escape from an aqueous solution. Hence, mecoprop will not be expected to be found in air with the exception as a consequence of direct aerial application of compounds to agricultural and non agricultural areas. Since mecoprop is a chlorophenoxy herbicide, it is considered to have only marginal potential for leaching to groundwater (U.S. EPA, 1988). In waters with higher pH, phenoxy herbicide esters are usually hydrolysed to the anionic forms. Whereas in waters with lower pH, photodegradation dominate the degradation process (WHO, 1996). Mecoprop is moderately persistent, and can stay in soils up to two months (EXTOXNET, 1996). Mecoprop and its various salt formulations are mobile in a variety of soils (RSCI, 1994).Adsorption of mecoprop only increases after an increase in organic matter in the soil. Although, mecoprop has a potential to leach into groundwater, generally, it does not persist long enough to do so (U.S. EPA, 1988).

Table B21-10 Half-life of Mecoprop in the Environment

Conditions	Environmental Media	Half-life	Reference
Mean half-life	Air	1 day	Mackay *et al.*, 1997
Range half-life		10-30 hours	
Mean half-life	Water	1 week	
Range half-life		100-300 hours	
Mean half-life	Soil	1 week	
Range half-life		100-300 hours	

B21-6.0 SUMMARY

Mecoprop is a selective herbicide, and it will carry out the mechanism of action by affecting enzyme activity and growth in plants. As an herbicide, mecoprop can be used as an acid, ester or a salt. Although, mecoprop exists in a mixture of two isomers, only the (R)-isomer (Mecoprop-P) is active as an herbicide (OMAFRA, 2002). Being able to mimic plant hormones, mecoprop was used to control weeds resistant to 2,4-D such as chickweed, clovers, black medick and young knotweed (OMAFRA, 2002). In 1986, approximately 50 kg of mecoprop was applied over an area of 91 ha at CFB Gagetown (JW, 2006). Mecoprop is no longer registered for use as an herbicide in Canada and the United States.

Mecoprop has low acute toxicity through the oral route. Long-term oral exposures to mecoprop caused systemic effects in blood parameters, organ weights, and body weight gains in rodents. Adverse reproductive/developmental effects were also observed in rodents when mecoprop was administered orally.

B21-7.0 REFERENCES

BASF. 1988. Pathology report. Study on the chronic toxicity and oncogenic potential of MCPP in rats. Administration in the diet over 24 months. Ludwigshafen/Rhein, Department of Toxicology, BASFAktiengesselschaft, 1988 (project no. 71S0047/8352). Cited In: WHO, 1996.

BASF Aktiegesellschaft. 1985. MRID No. 00158359. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Budavari, Susan x 1989. (Ed) The Merck Index, Eleventh Edition. Merck and Company Inc. Rahway, NJ. Cited In: EXTOXNET, 1996.

Buschmann, J. *et al*. 1986. Comparative prenatal toxicity of phenoxyalkanoic herbicides: transplacental movement and effects on prenatal development. Teratology. 33:11A.

DNHW. Department of National Health and Welfare, Canada, unpublished data, 1980. Cited In: WHO, 1996.

EC. 2003. Commission Working Document-Review report for the active substance mecoprop. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 15 April 2003 in view of the inclusion of mecoprop in Annex I of Directive 91/414/EEC. Health & Consumer Protection Directorate-General, European Commission. April 14, 2003. Available at:http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1-50_en.pdf#search=%22mecoprop%22 [Sept 5, 2006]

EXTOXNET. 1996. Mecoprop. Extension Toxicology Network, Pesticide Information Profiles. Available at: http://pmep.cce.cornell.edu/profiles/extoxnet/haloxyfop-methylparathion/mecoprop-ext.html [Sept 1, 2006].

Gurd, M.R., Harmer, G.L.M. and Lessel, B. 1965. Summary of toxicological data—acute toxicity and 7-month feeding studies with mecoprop and MCPA. Food and cosmetics toxicology, 3:883. Cited In: WHO, 1996.

HSDB. 2005. Mecoprop. U.S. National Library of Medicine's Toxicology Data Network (TOXNET). Hazardous Substances Data Bank. Available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB. [Sept 1, 2006].

IET. 1984. 2,4-DP acid 24-month oral chronic dietary study in rats. Union Carbide.(unpublished report). Institute of Environmental Toxicology . Cited In: WHO, 1996.

JW. 2006. Final Report. Task 2A: The History and Science of Herbicide Use at CFB Gagetown From 1952 to Present. Report to: Department of National Defence. Jacques Whitford, May 19, 2006.

Mackay, D., Shiu, W.Y., and Ma, D.C. 1997. Illustrated handbook of physical-chemical properties and environmental fate for organic chemicals: Pesticide chemicals. Volume 5. Lewis Publishers, Boca Raton. New York.

MEDITEXT®. 2006. TOMES® Information System Micromedex, Inc., Englewood, Co; CCIS Volume 130, expires Nov, 2006. Cited in: HSDB, 2005.

Meister, R.T. 1992. Farm Chemicals Handbook '92. Meister Publishing Company. Willoughby, OH. Cited In: EXTOXNET, 1996.

OMAFRA. 2002. Compitox, Mecoprop: mecoprop. Excerpt from Chapter 4, Publication 75, Guide to Weed Control. Onatrio Ministry of Agriculture, food and Rural Affairs, Onario, Canada. Available at: http://www.omafra.gov.on.ca/english/crops/facts/notes/mecoprop.htm [Sept 5, 2006]

PSD. 2007. Toxicological Endpoints Database. U.K. Product Safety Directorate Databases. Available at: https://secure.pesticides.gov.uk/TEAWeb/tea_results.asp [Feb 16, 2007]

Roll, V.R. and Matthiaschk, G. 1983. [Comparative studies on the embryotoxicity of 2-methyl-4-chlorophenoxyacetic acid, mecoprop and dichlorprop in NMRI mice.] Arzneimittel-Forschung. 33:1479-1483 (in German).

RSCI. 1994. The Agrochemicals Handbook, Third Edition. Royal Society of Chemistry Information Systems, Unwin Brothers Ltd., Surrey, England. Cited In: EXTOXNET, 1996.

Rumack, B.H., and Hall, A.H. Eds. 2006. POISINDEX® Information system Micromedex, Inc., Englewood, CO. CCIS Volume 130, expires Nov 2006. Cited In: HSDB, 2005.

Thomson, W. T. 1982. Agricultural Chemicals Book II Herbicides Thomson Publications. Fresno, CA. Cited In: EXTOXNET, 1996.

U.S. EPA. 1988. Guidance for the reregistration of pesticide products containing mecoprop (MCPP) as the active ingredient. Environmental Protection Agency. Cited In: WHO, 1996.

U.S. EPA. 1989. 2-(2-Methyl-4-chlorophenoxy)propionic acid (MCPP). Integrated Risk Information System, U.S. Environmental Protection Agency. Available at: http://www.epa.gov/iris/subst/0067.htm [July 5, 2006]

Verschuuren, H.G., Kroes, R., Den Tonkelaar E.M. 1975. Short-term oral and dermal toxicity of MCPA and MCPP. Toxicology, 3(3):349-359. Cited In: WHO, 1996.

WHO. 1996. Chlorophenoxy herbicides (excluding 2,4-D and MCPA) in Drinking-water Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organization, Geneva, Switzerland. Available at: http://www.who.int/ water_sanitation_health/dwq/chemicals/chlorophenoxyherb.pdf [Sept 1, 2006].