Fact Sheet Date: June 2004

NEW YORK STATE
HUMAN HEALTH FACT SHEET

Ambient Water Quality Value for
Protection of Human Health and Sources of Potable Water

SUBSTANCE: Metolachlor OA (Metolachlor oxanilic acid)

CAS REGISTRY NUMBER: 152019-73-3

AMBIENT WATER QUALITY VALUE: 50 micrograms/liter (50 ug/L)

BASIS: General Organic Guidance Value (6 NYCRR 702.15(a)(2))

INTRODUCTION

Metolachlor (2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide) is a chloroacetanilide herbicide. There are four isomers of metolachlor: two S-enantiomers (named CGA-77102 by Ciba-Geigy Corporation, the US registrant of the pesticide products containing metolachlor) and two R-enantiomers (named CGA-77101 by the registrant) (Figure 1). A manufactured 50:50 mixture of the S- and R-enantiomers is called metolachlor (named CGA-24705 by the registrant). A manufactured 80:20 mixture of the S- and R-enantiomers is called alpha- or S-metolachlor (named CGA-77102 by the registrant). A separate fact sheet describes the derivation of an ambient water quality value for metolachlor, which applies to all four isomers of the metolachlor molecule (NYS, 2002a).

Recent studies have shown that environmental degradates of metolachlor are found in ambient water at levels higher than those of metolachlor itself (Kolpin et al., 2000). Metolachlor ethanesulfonic acid (also known as metolachlor ESA) is one commonly found degradate and a separate fact sheet describes the derivation of an ambient water quality value for metolachlor ESA (NYS, 2002b). A second commonly found degradate is metolachlor oxanilic acid (also known as metolachlor OA, CGA-51202, or 2-[(2-ethyl-6-methylphenyl)(2-methoxy-1-methylethyl)amino]-2-oxoacetic acid). This fact sheet describes the derivation of an ambient water quality value for metolachlor OA.

Metolachlor oxanilic acid is formed when the terminal chloroacetyl group (-CH_2Cl) of the parent molecule is transformed into a carboxyl group (-COOH) (Figure 1). Metolachlor OA was not one of the 39 compounds identified as metolachlor metabolites in studies with rats (Ciba-Geigy, 1994). Data on the health effects of oral exposure to metolachlor OA are limited to three studies in rats: an acute study, a 3-month subchronic study, and a developmental toxicity study (Novartis, 1997). These data were reviewed and evaluated. As described below, the general organic guidance value of 50 ug/L is selected as the ambient water quality value for metolachlor OA.

SPECIFIC MCL AND PRINCIPAL ORGANIC CONTAMINANT CLASS (702.3)

Metolachlor OA does not have a Specific MCL (maximum contaminant level) as defined in 700.1 and is not in a principal organic contaminant (POC) class as defined in 700.1. Consequently, an ambient water quality value cannot be derived under 702.3.

However, the New York State Department of Health (DOH) drinking-water regulations (10 NYCRR Part 5) does have a MCL of 50 ug/L for metolachlor OA, based on its categorization as an unspecified organic contaminant (UOC). This DOH general MCL applies as a drinking water standard to any organic compound that is not in a POC class and does not have a Specific MCL. However, this UOC MCL is not used as the basis for an ambient water quality value under 702.3.

ONCOGENIC EFFECTS (702.4)

Studies on the oncogenicity of metolachlor OA were not found. Metolachlor OA was inactive in short-term tests indicative of oncogenicity. These were point mutation tests in bacteria (Salmonella (four strains) and E. coli) with and without metabolic activation by rat liver S9 homogenate), gene mutation tests with chinese hamster cells V79 (with and without S9 activation), and a chromosome aberration test in mice (micronucleus test on bone marrow, in vivo) (Ciba-Geigy, 1988, 1992a,b; Novartis, 1999a). The data are insufficient to determine whether metolachlor OA is oncogenic. Thus, a value based on oncogenic effects cannot be derived.

NON-ONCOGENIC EFFECTS (702.5)

Acute single-dose toxicity studies in rats show that the oral and dermal LD_{50} doses of metolachlor OA are >2,000 mg/kg and >1,333 mg/kg, respectively (Ciba-Geigy, 1991a,b). Limited data from the only two non-acute studies on the oral toxicity of metolachlor OA (a subchronic and a developmental toxicity study in rats) show that reduced food consumption is an early indicator of its toxicity (Ciba-Geigy, 1992c,d).

In a subchronic study (Ciba-Geigy, 1992c), groups of male and female *Tif:RAIf* rats (10/sex/group) were fed diets containing 0, 300, 1,000 or 15,000 ppm metolachlor OA for 3 months. Estimated daily doses were 0, 18.7, 62.1 and 1,000 mg/kg/day for male rats and 0, 20.6, 67.3, and 1,020 mg/kg/day for female rats. A weight-of-evidence analysis (similar to that described in US EPA, 2000) was used to determine if any results, including those statistically significant ($p < 0.05$), were toxicologically significant.

There was no observed evidence of treatment-related clinical or eye toxicity, mortality, reductions in body weight or in food or water consumption, increases in serum enzymes levels indicative of liver toxicity (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and gamma-glutamyl transpeptidase), changes in urine content, relative organ weights (brain, liver, kidney, adrenal, testes, ovary) or histological lesions (27 tissues/organs).

Although there were minor changes in the levels of blood serum proteins (i.e., albumin and globulin levels at dietary levels of 1,000 ppm and 15,000 ppm) that were potentially dependent on exposure to metolachlor OA (Ciba-Geigy, 1992c), a weight-of-evidence analysis (Table 1) does not support a causal relationship between exposure to metolachlor OA and the observed effects. In the absence of other chronic or subchronic studies on *Tif:RAIf* rats, the analysis includes the results of subchronic dietary studies on different, but related strains of rats (i.e., SD rats and CD rats).

Although many factors can influence blood serum protein levels, the combination of low serum albumin level and high serum globulin level or either result alone is consistent with liver damage (ATSDR, 1993). These patterns were not consistently seen in rats exposed to metolachlor OA, metolachlor ESA, metolachlor, or S-metolachlor. In male rats exposed to

metolachlor OA, serum albumin level was reduced only at the mid-dose level (1,000 ppm) and serum globulin level was decreased (not increased) only at the high dose level (15,000 ppm). In female rats exposed to metolachlor OA, the only observed effect on serum proteins was a reduced albumin level at the highest dose (15,000 ppm). In rats exposed to metolachlor ESA, serum protein levels were not affected at dose levels as high as 20,000 ppm. In rats exposed to metolachlor or S-metolachlor (3,000 to 10,000 ppm), low serum albumin level or high serum globulin level were not observed consistently even though increased relative liver weights and liver histopathology (more reliable indicators of liver damage) were observed consistently. Overall, the inconsistency of the results among male rats and between male and female rats, the lack of any other observable liver effect of metolachlor OA, and the lack of supporting data from results of studies of rats fed metolachlor ESA, metolachlor, or S-metolachlor indicate that the observed changes in blood serum protein levels were not caused by exposure to metolachlor OA.

A second minor change potentially dependent on exposure to metolachlor OA was a reduced blood platelet count in male rats at the highest dose level of 15,000 ppm (Ciba-Geigy, 1992c). However, a comparison of the results from studies on metolachlor OA, metolachlor ESA, metolachlor, and S-metolachlor (Table 2) does not provide any data to support the results in males. Overall, the data do not support the conclusion that the observed decrease in the blood platelet count of male rats at the highest dose was caused by exposure to metolachlor OA.

Based on the analysis of the data on blood serum protein and blood platelet levels and the absence of any observable effects of metolachlor OA in rats, the no-observed-effect level (NOEL) and the lowest-observed-effect level (LOEL) of the study are $\geq$1,000 mg/kg/day and >1,000 mg/kg/day, respectively (i.e., there were no observed effects at the highest tested dose).

The subchronic dietary studies on different, but related strains of rats (*Tif:RAIf* and SD) also provide information on the relative toxicities of the metolachlor OA and S-metolachlor (Table 3). Numerous effects were observed in male and/or female SD rats fed diets containing $\geq$3,000 ppm of S-metolachlor (Ciba-Geigy, 1995b; US EPA, 1997). Important treatment-related effects were reduced body weight, increased serum levels of gamma-glutamyl transpeptidase, cholesterol, and proteins, increased liver and thyroid weights (relative), increased kidney weights (relative and absolute), and increased incidences of liver histopathology. In addition, male SD rats fed diets containing 30 ppm and 300 ppm of S-metolachlor also showed increased relative

liver weights, although the importance of this finding was minimized by Ciba-Geigy (1995b) and the US EPA (1997). Similar effects were not seen in male and female *Tif:RAIf* rats exposed to diets containing 15,000 ppm of metolachlor OA. Thus, the data show, under the conditions of the subchronic studies, differences in the toxicological effects of metolachlor OA and S-metolachlor in rats. The data show that S-metolachlor induced a broader range of effects at a lower dose than did metolachlor OA.

In a developmental toxicity study with metolachlor OA, pregnant *Tif:RAIf* rats were administered gavage doses of 0, 10, 100 or 1,000 mg/kg on day 6 through day 15 of gestation (Ciba-Geigy, 1992d). Dams were killed on day 21 of gestation and dams and fetuses were examined for reproductive and fetotoxic/teratogenic effects, respectively. A weight-of-evidence analysis (US EPA, 2000) was used to determine if any results, including those statistically significant ($p < 0.05$), were toxicologically significant.

There were no observed treatment-related clinical signs during the study. Mean maternal body weight and body-weight gain were similar among all groups, however, feed consumption by high-dosed dams was lower ($p < 0.05$) than that of controls during gestation days 6 to 11. There were no observed treatment-related effects on any reproductive parameters (pre- and post-implantation losses, resorptions/dam, litter size, sex ratios, or fetal body weights). There was no observed evidence of any treatment-related fetotoxic or teratogenic effects on external features, internal viscera, or the skeleton. The NOEL and LOEL for the maternal effects of metolachlor OA are 100 and 1,000 mg/kg/day (reduced food consumption during days 6 to 11 of gestation), respectively. The NOEL and LOEL for the fetal effects of metolachlor OA are $\geq$1,000 mg/kg/day and >1,000 mg/kg/day, respectively (i.e., there were no observed fetal effects at the highest tested dose).

A similar study was conducted in pregnant *Tif:RAIf* rats given gavage S-metolachlor doses of 0, 5, 50, 500, or 1,000 mg/kg/day on day 6 through day 15 of gestation (Ciba-Geigy, 1995a; US EPA, 1997). Maternal toxicity was observed at the two highest dose levels. Important treatment-related effects ($p < 0.05$) included increased incidences of abnormal behavioral (perhaps indicative of neurotoxicity), reduced food consumption, and reduced body weight and body weight gain. There was no observed evidence of any treatment-related fetotoxic or teratogenic effects on external features, internal viscera, or the skeleton. The NOEL and

LOEL for the maternal effects of S-metolachlor are 50 and 500 mg/kg/day, respectively. The NOEL and LOEL for the fetal effects of S-metolachlor are ≥1,000 mg/kg/day and >1,000 mg/kg/day, respectively (i.e., there were no observed fetal effects at the highest tested dose). Although neither compound induced fetal effects (under the conditions of developmental toxicity studies in *Tif:RAIf* rats), S-metolachlor induced a broader range of maternal effects at a lower dose than did metolachlor OA.

The two rat studies with metolachlor OA are comparable in quality. The developmental toxicity study is selected over the 3-month subchronic study as the basis of the acceptable daily intake for metolachlor OA because it provides a lower NOEL (100 mg/kg/day for maternal effects) than the subchronic study (≥1,000 mg/kg/day). This NOEL also is similar to a less-certain NOEL of 62 mg/kg/day that could be derived from the subchronic study under the health-protective assumption (not supported by the weight-of-evidence analysis) that the observed decrease in blood platelet count in male rats was caused by exposure to metolachlor OA. Thus, the developmental study is used to derive a potential water quality value for metolachlor OA based on non-oncogenic effects.

If an uncertainty factor of 3,000 is applied to the NOEL (100 mg/kg/day) from the subchronic study in rats, an acceptable daily intake of 0.033 mg/kg/day (33 ug/kg/day) can be derived for metolachlor OA using procedures consistent with those outlined in paragraphs (a) and (b) of 702.5. Under 702.5(b)(3), an uncertainty factor of 1,000 is selected because the acceptable daily intake is based on a NOEL from a short-term animal study and neither experimental results from prolonged exposures of humans nor valid results of long-term ingestion studies on experimental animals are available. However, 702.5(b) also states that the magnitude of the uncertainty factor used to obtain an acceptable daily intake shall reflect the quantity and quality of the toxicological data, the degree of confidence in the data and the nature of the effects of concern. Consequently, an additional uncertainty factor of 3 was used because there are gaps, and thus uncertainties, in the toxicological information of metolachlor OA, particularly with regard to non-oncogenic (including reproductive) and oncogenic effects of chronic exposure.

A water value of 230 ug/L can be derived assuming a 70-kg adult drinks 2 liters of water per day and allowing 20% of the acceptable daily intake (33 ug/kg/day) to come from drinking water (702.2(c) and 702.5(c)).

CHEMICAL CORRELATION (702.7)

Metolachlor OA is an environmental degradate of metolachlor, but it is not a known metabolite of metolachlor in rats. The ambient water quality value for metolachlor is 9 ug/L (based on oncogenic effects, i.e., liver cancer in rats) (NYS, 2002a).

Metolachlor is degraded to metolachlor OA when the chloroacetyl (-CH_2Cl) group, which is a reactive group in biological systems (Ashby and Tennant, 1991), is transformed into a less biologically reactive carboxyl group (-COOH) (see Figure 1). A reduction in the toxic potency of the molecule is associated with this change (Table 4). A similar removal of the chlorine during degradation of metolachlor to its ethanesulfonic acid metabolite (known as metolachlor ESA) is associated with a reduction in the toxic potency of the resulting molecule (NYS, 2002b). In another chloroacetanilide herbicide (alachlor), the removal and replacement of the chlorine atom by an sulfonic acid group to form alachlor ESA is also associated with a reduction in the toxic potency of the molecule (Heydens et al., 1996, 2000; US EPA, 1998). The reduced toxic potencies of metolachlor OA, metolachlor ESA, and alachlor ESA relative to the parent compound all suggest the removal of the chlorine atom changes the biological fate of the resulting molecule and reduces its toxic potency.

Experimental data on metolachlor OA and metolachlor show consistently that the former is less potent than the latter (Table 4). Metolachlor OA did not induce any observable signs of liver toxicity in *Tif:RAIf* rats at a dietary dose of 15,000 ppm for 3 months. This dose is three-times higher than the S-metolachlor dose (5,000 ppm, diet) that increased serum levels of biomarkers indicative of liver toxicity (e.g., liver enzymes), relative liver weight, and liver hypertrophy in SD rats. It is also five-times higher than the S-metolachlor dose (3,000 ppm, diet) that increased the relative liver weight of male and female SD rats in a second study, and 50-times higher than the S-metolachlor dose that increased the relative liver weight in male SD rats in the second study. These differences are particularly relevant because the liver is the target organ for metolachlor carcinogenesis. In addition, metolachlor OA was inactive (with and without metabolic activation) in short-term tests indicative of oncogenic potential.

Supplemental data also suggests differences in the target organs/organ systems of

metolachlor OA and metolachlor (Table 4). Metolachlor OA did not induce observable reductions in body weight and food consumption or observable increases in relative and absolute kidney weights in *Tif:RAIf* rats at a dietary dose of 15,000 ppm for 3 months. This dose is about five-times the dose (3,000 ppm, diet) that induced all those effects in SD rats exposed to S-metolachlor for 3 months. Metolachlor OA did not induce observable differences in abnormal behavior or reductions in body weight or body weight gain in pregnant *Tif:RAIf* rats exposed to 1,000 mg/kg/day on gestation days 6 through 15. This dose is twice the dose (500 mg/kg/day) that induced those effects in pregnant *Tif:RAIf* rats given S-metolachlor day on gestations days 6 through 15. However, both metolachlor OA (1,000 mg/kg/day) and S-metolachlor (500 and 1,000 mg/kg/day) reduced food consumption in pregnant female rats.

Collectively, the data suggest some differences in the toxic effects of metolachlor and metolachlor OA. The data also suggest that the toxic potency of metolachlor OA is less than that of metolachlor. These differences are consistent with the hypothesis that the chlorine atom of the metolachlor molecule plays an important role in the molecular events leading to the toxicity of metolachlor. Thus, there are insufficient data to derive a value for metolachlor OA based on chemical correlation to metolachlor. In addition, there are insufficient data for deriving a value based on chemical correlation to any other chemical.

SELECTION OF VALUE

According to 702.15(a), the selected ambient water quality value shall be the more stringent of the values derived using the procedures found in 702.3 through 702.7 or a general organic guidance value of 50 ug/L. Although a value of 230 ug/L can be derived by applying the procedures of 702.5 to the available non-oncogenic data on metolachlor OA, the value is based on a limited toxicological database. In particular, studies on the chronic (non-oncogenic) and reproductive effects of metolachlor OA were not found. In addition, studies on the oncogenic effects of metolachlor OA were not found. Accordingly, there are not adequate and sufficient data available to justify a value greater than 50 ug/L as described in 702.15(a)(2). Thus, the general organic guidance value of 50 ug/L is selected as the water quality value for metolachlor OA.

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SEARCH STRATEGY

Toxline (1966 to June 2003) was searched using the name or CAS Registry Number for metolachlor OA and the CAS Registry Number or name for metolachlor.

Bureau of Toxic Substance Assessment
New York State Department of Health/KGB02
June 2003

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Table 1. Results of Blood Serum Protein Levels Reported for Rats Fed Diets Containing Metolachlor OA, Metolachlor ESA, S-Metolachlor (Two Studies) for 90 Days or Metolachlor for 2 years.

Compound	Rat Strain	Dietary Level (ppm)	Total Protein	Albumin	Globulin (Total Protein - Albumin)	A/G Ratio	Liver Effects
Male Rats							
Environmental Degradates of Metolachlor							
OA[1]	*Tif:RAIf*	300	-*	-	-	-	-
		1,000	⬇**	⬇	-	-	-
		15,000	⬇	-	⬇	-	-
ESA[2]	SD	360	-	-	-	-	-
		1,200	-	-	-	-	-
		6,000	-	-	-	⬇	-
		20,000	-	-	-	-	-
Parent Compound							
metolachlor[3]	CD	3,000 (2 yrs)	-	not measured			⬆ liver cancer
S-metolachlor[2,4]	SD	3,000[4]	⬆	-	-	⬆	⬆ relative liver weight
		5,000[2]	⬆	-	⬆	-	⬆ relative liver weight;
		10,000[4]	⬆	-	-	⬆	⬆ relative liver weight; histological changes
Female Rats							
Environmental Degradates of Metolachlor							
OA[1]	*Tif:RAIf*	300	-*	-	-	-	-
		1,000	-	-	-	-	-
		15,000	-	⬇	-	-	-
ESA[2]	SD	360	-	-	-	-	-
		1,200	-	-	-	-	-
		6,000	-	-	-	-	-
		20,000	-	-	-	-	-
Parent Compound							
metolachlor[3]	CD	3,000 (2 yrs)	-	not measured			⬆ liver cancer
S-metolachlor[2,4]	SD	3,000[4]	-	-	-	⬆	⬆ relative liver weight
		5,000[2]	-	-	-	⬇	⬆ relative liver weight; hypertrophy
		10,000[4]	⬆	-	-	⬆	⬆ relative liver weight

* $p \geq 0.05$.
**$p < 0.05$ (⬆ or ⬇).
[1] Ciba-Geigy (1992c).
[2] Novartis (1999b).
[3] Ciba-Geigy (1983).
[4] Ciba-Geigy (1995b); US EPA (1997).

Table 2. Results of Blood Platelet Count Reported for Male Female Rats Fed Diets Containing Metolachlor OA, Metolachlor ESA, S-Metolachlor (Two Studies) for 90 Days or Metolachlor for 2 years.

Compound	Rat Strain	Dietary Level (ppm)	Sex	Platelet Count
Environmental Degradates of Metolachlor				
OA[1]	*Tif:RAIf*	300	M	-*
			F	-
		1,000	M	-
			F	-
		15,000	M	⬇**
			F	-
ESA[2]	SD	360	M	-
			F	-
		1,200	M	-
			F	-
		6,000	M	-
			F	
		20,000	M	-
			F	-
Parent Compound				
metolachlor[3]	CD	3,000 (2 yrs)	M & F	-
S-metolachlor[2,4]	SD	3,000[4]	M & F	-***
		5,000[2]	M & F	-
		10,000[4]	M & F	-***

* $p \geq 0.05$.
**$p < 0.05$ (⬆ or ⬇).
*** No treatment-dependent effect on platelet levels reported by either Ciba-Geigy (1995b) or US EPA (1997).

[1] Ciba-Geigy (1992c).
[2] Novartis (1999b).
[3] Ciba-Geigy (1983).).
[4] Ciba-Geigy (1995b); US EPA (1997).

Table 3. Results Reported for Rats Given Diets Containing S-Metolachlor (Two Studies) or Metolachlor OA Daily for 3 Months.

Effect*	Concentration in Diet (ppm)							
	SD Rats					*Tif:RAI f* Rats		
	S-Metolachlor[1]				S-Metolachlor[2]	Metolachlor OA[3]		
	30	300	3,000	10,000	5,000	300	1,000	15,000
Clinical Signs								
food consumption	-**	-	⬇***	⬇	-	-	-	-
body weight	-	-	⬇	⬇	⬇	-	-	-
Hematology								
blood platelet level	-	-	-	-	-	-	-	⬇ (M)+
Blood Chemistry								
serum gamma-glutamyl transpeptidase level	-	-	-	⬆	⬆	-	-	-
serum cholesterol level	-	-	-	-	⬆ (F)	-	-	-
protein level (albumin & globulin)	-	-	⬆ (M)	⬆	⬆ (M)	-	⬇ (M)+	⬇ (M)+
Relative Organ Weights								
liver	⬆ (M)	⬆ (M)	⬆	⬆	⬆	-	-	-
kidney	-	-	⬆++	⬆++	⬆	-	-	-
thyroid gland	not measured				⬆ (F)	-	-	-
Histopathology								
liver hypertrophy	-	-	-	-	⬆ (F)	-	-	-
eosinophilic intracytoplasmic inclusions in heptaocytes	-	-	-	⬆ (M)	-	-	-	-

* Observed in both male and female rats unless noted: (M) only in males or (F) only in females

** $p \geq 0.05$.

***$p < 0.05$ (⬇ or ⬆):

\+ Weight-of-evidence does not indicate a compound dependent effect.

++ Male rats also showed increased (⬆) absolute kidney weights.

[1] Ciba-Geigy (1995b); US EPA (1997).

[2] Novartis (1999b).

[3] Ciba-Geigy (1992c)

Table 4. Summary of Important Data on the Potential to Base the Ambient Water Quality Value for Metolachlor OA on the Water Quality Value for Metolachlor under 6 NYCRR 702.7 (Chemical Correlation).

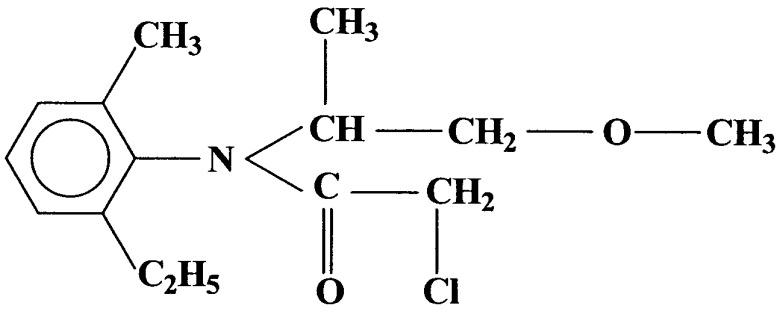
Parameter	Metolachlor	Metolachlor OA
1. Results of Chronic Dietary Studies in Rats (Basis for Metolachlor AWQ Value)		
liver cancer	yes (3,000 ppm)[1]	not tested
2. Structure		
functional groups	two identified: sole nitrogen (linking aromatic & aliphatic groups) & sole chlorine (attached to the terminal carbon atom in the chloroacetyl group (-CH_2Cl))	one: nitrogen still present, but formation of potential mutagenic metabolite is unlikely if minimal cleavage to the unsulfonated forms (i.e., metolachlor OA) occurs in the body (US EPA, 1998); chlorine atom is removed during conversion of chloroacetyl group to a carboxyl group
3. Pharmacokinetics		
percent oral dose absorbed by rats	85-99%	unknown
major rat metabolite of metolachlor	not applicable	no
4A. Primary Toxicology Data - Evidence For/Against Common Toxic Effect(s) on Liver (Important Data Because Liver is the Sole Site of Metolachlor Induced Carcinogenesis)		
Subchronic Dietary Studies in Rats		
strain (study)	SD (Novartis, 1999b)	*Tif:RAI f* (Ciba-Geigy, 1992c)
serum gamma-glutamyl transpeptidase levels	⬆[2] (5,000 ppm)	-[2](15,000 ppm)
serum cholesterol levels	⬆ (5,000 ppm)	- (15,000 ppm)
relative weight	⬆ (30, 300, & 3,000 ppm[3] & 5,000 ppm)	- (15,000 ppm)
hypertrophy	⬆ (5,000 ppm)	- (15,000 ppm)
4B. Supplemental Toxicology Data - Evidence For/Against Any Common Toxic Effects		
Subchronic Dietary Studies in Rats		
strain (study)	SD (Ciba-Geigy, 1995b)	*Tif:RAI f* (Ciba-Geigy, 1992c)
food consumption	⬇ (10,000 & 3,000 ppm)	- (15,000 ppm)
body weight	⬇ (10,000 & 3,000 ppm)	- (15,000 ppm)
relative & absolute kidney weights	⬆ (10,000 & 3,000 ppm)	- (15,000 ppm)
blood proteins (globulin & albumin levels)	⬆ (10,000 & 3,000 ppm)	- (15,000 ppm)
Developmental Gavage Studies in Tif:RAI f Rats - Maternal Effects *(Ciba-Geigy, 1992b; 1995a)*		
abnormal behavior (neurotoxicity)	⬆ (500 & 1,000 mg/kg/day)	- (1,000 mg/kg/day)
body weight & body weight gain	⬇ (500 & 1,000 mg/kg/day)	- (1,000 mg/kg/day)
food consumption	⬇ (500 & 1,000 mg/kg/day)	⬇ (1,000 mg/kg/day)

[1] NYS (2002a).

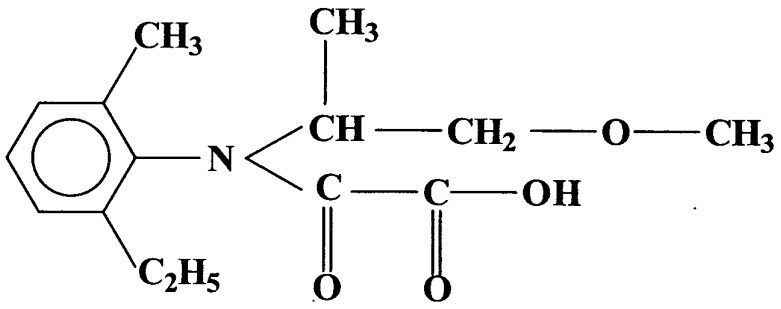
[2] Weight-of-evidence indicates a compound dependent effect (⬆ or ⬇) or no compound-dependent effect (-).

[3] Ciba-Geigy (1995b).

Figure 1. Metolachlor and an Environmental Degradate Metolachlor OA.



METOLACHLOR



METOLACHLOR OA
(Metolachlor oxanilic acid or CGA 51202)