Department of Pesticide Regulation

Julie Henderson
Director

Gavin Newsom
Governor

Yana Garcia
Secretary for Environmental Protection

M E M O R A N D U M

TO: Minh Pham, Chief
Environmental Monitoring Branch

VIA: Shelley DuTeaux, PhD MPH, Chief
Human Health Assessment Branch

FROM: Anna Kalashnikova, PhD, Staff Toxicologist
Risk Assessment Section
Pete Lohstroh, PhD, Senior Toxicologist
Toxicology and Dose Response Assessment Section

Svetlana Koshlukova, PhD, Senior Toxicologist
Risk Assessment Section

DATE: May 30, 2024

SUBJECT: HUMAN HEALTH REFERENCE LEVELS FOR METOLACHLOR/S-METOLACHLOR AND DEGRADATES IN GROUNDWATER

On February 7, 2024, the Department of Pesticide Regulation's (DPR) Human Health Assessment Branch (HHA) was requested by the Environmental Monitoring Branch (EMB) to provide DPR Groundwater Human Health Reference Levels (HHRLs) for metolachlor/S-metolachlor and their degradates, metolachlor ethanesulfonic acid (ESA), metolachlor oxanilic acid (OXA), hydroxymetolachlor (metolachlor-2-hydroxy), and dechlorometolachlor, for screening detections of these residue levels in groundwater (see request, Appendix 1). This memorandum is in response to the request.

Conclusions and Recommendations:

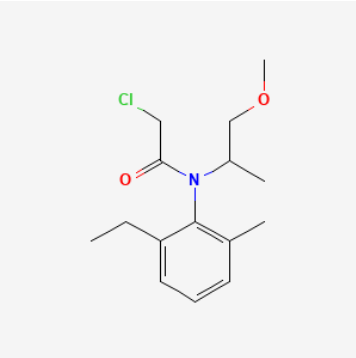
1. HHA calculated DPR Groundwater Human Health Reference Levels (HHRLs) to be used for detections of metolachlor/S-metolachlor residue in groundwater using (1) acute and chronic consumption rates for drinking water from the National Health and Nutrition Examination Survey (NHANES) 2005–2010 database; and (2) toxicological endpoints established by the United States Environmental Protection Agency (US EPA).
2. Based on the structural similarity to parent compounds metolachlor and its isomer S-metolachlor, the degradates ESA, OXA, hydroxymetolachlor and deschlorometolachlor

are considered to have equivalent toxicity and should be summed when they are detected in the same samples.

3. Maximum residue concentrations of metolachlor/S-metolachlor equal to or less than the DPR Groundwater HHRL of 1368 parts-per-billion (ppb) in drinking water are not expected to pose a risk to human health, including for sensitive subpopulations.

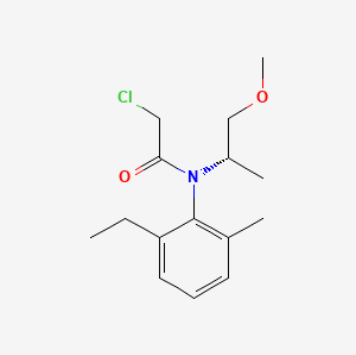
Background

Technical Name: Metolachlor
Chemical Name: 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(1-methoxypropan-2-yl)acetamide
Chemical Abstracts Service Registry Number (CAS #): 51218-45-2
Molecular Weight: 283.79 g/mol
Chemical Structure:



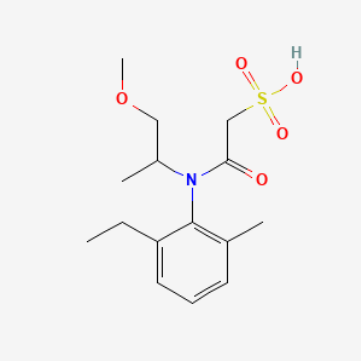
(NIH, 2024b)

Technical Name: S-metolachlor
Chemical Name: 2-chloro-N-(2-ethyl-6-methylphenyl)-N-[(2S)-1-methoxypropan-2-yl]acetamide
Chemical Abstracts Service Registry Number (CAS #): 87392-12-9
Molecular Weight: 283.79 g/mol
Chemical Structure:



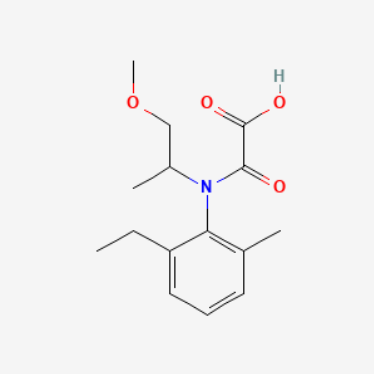
(NIH, 2024d)
Technical Name: Metolachlor ethanesulfonic acid (ESA)

Chemical Name: 2-[(2-ethyl-6-methylphenyl)(1-methoxypropan-2-yl)amino]-2-oxoethanesulfonic acid
Chemical Abstracts Service Registry Number (CAS #): 171118-09-5
Molecular Weight: 329.4 g/mol
Chemical Structure:



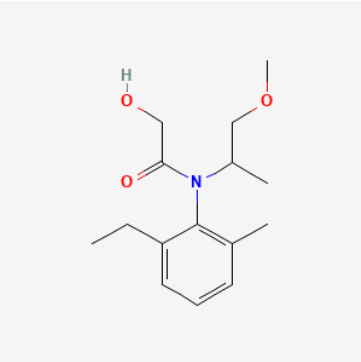
(NIH, 2024c)

Technical Name: Metolachlor oxanilic acid (OXA)
Chemical Name: [(2-ethyl-6-methylphenyl)(1-methoxypropan-2-yl)amino](oxo)acetic acid
Chemical Abstracts Service Registry Number (CAS #): 152019-73-3
Molecular Weight: 279.33 g/mol
Chemical Structure:



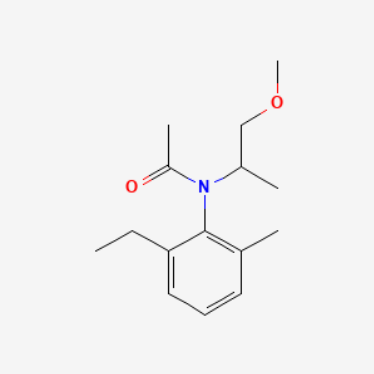
(NIH, 2024f)

Technical Name: Hydroxymetolachlor (Metolachlor-2-hydroxy)
Chemical Name: N-(2-ethyl-6-methylphenyl)-2-hydroxy-N-(1-methoxypropan-2-yl)acetamide
Chemical Abstracts Service Registry Number (CAS #): 131068-72-9
Molecular Weight: 265.35 g/mol
Chemical Structure:



(NIH, 2024a)

Technical Name: Dechlorometolachlor
Chemical Name: N-(2-ethyl-6-methylphenyl)-N-(1-methoxypropan-2-yl)acetamide
Chemical Abstracts Service Registry Number (CAS #): 126605-22-9
Molecular Weight: 249.35 g/mol (NIH, 2023)
Chemical Structure:



(NIH, 2024e)

Metolachlor is a chloroacetanilide herbicide that consists of 50% each of the R-enantiomer and the herbicidally-active S-enantiomer (US EPA, 2019b). S-metolachlor is S-enantiomer enriched form of metolachlor, comprised of 88% S-isomer and 12% R-isomer (US EPA, 2019b). Metolachlor/S-metolachlor are primarily used for control of grass weeds in agricultural field crops, including corn, cotton, grasses grown for seed, legume vegetables, peanuts, potatoes, safflower, sorghum, sunflower, and tomatoes. They are also registered for use to control weeds on residential lawns, commercial turf (including golf courses, sports fields, recreation areas, and sod farms), ornamentals and horticultural nurseries (US EPA, 2018c). Metolachlor/S-metolachlor are not restricted materials (DPR, 2024a). Tolerances has been established on multiple crops, including root, legume, cucurbit and fruiting vegetables (eCFR, 2020). Pesticide products using metolachlor/S-metolachlor as active ingredients were first registered by US EPA in 1976 (US EPA, 1995). In California, metolachlor and S-metolachlor were registered in 1982 and 2003, respectively (DPR, 2024e). As of March 2024, there were eight active registrations under

metolachlor, and eleven under S-metolachlor, in California (DPR, 2024e). According to the most currently available data from the DPR's Pesticide Use Reporting (PUR) database, 320,470 pounds of metolachlor/S-metolachlor active ingredient were used in 4976 California agricultural and landscape applications in 2021 (DPR, 2021).

Degradates

The US EPA Residue of Concern Knowledgebase Subcommittee (ROCKS) identified the degradates OXA (CGA-51202), hydroxymetolachlor (CGA-40172), and 2-((2-Ethyl-6-methylphenyl)amino)-2-oxoacetic acid (CGA-50720) as residues of concern for drinking water based on their structural similarities to parent compounds (US EPA, 2014b; US EPA, 2019c). ESA (CGA-354743) was not included because it was considered to be significantly less toxic than the parent compounds based on the structural considerations (US EPA, 2014b; US EPA, 2019c). Dechlorometolachlor (CGA-41507) was also not included (US EPA, 2014b).

DPR identified the parent chemicals metolachlor and S-metolachlor, as well as the degradates OXA, ESA, hydroxymetolachlor, and dechlorometolachlor as residues of concern in drinking water. For this evaluation, these degradates are considered to be metolachlor equivalents on the basis of structural similarity to the parent compounds and their toxicity data (see below) and their residues should be summed if they are detected in the same samples (US EPA, 2019b; US EPA, 2019c; eCFR, 2020).

DPR Pesticide Contamination Prevention Act (PCPA) Review of Metolachlor/S-Metolachlor

In 2017, DPR initiated the Pesticide Contamination Prevention Act (PCPA) review process for metolachlor/S-metolachlor based on detections of the degradates ESA and OXA in 62 well water samples collected in California between 2001 and 2015, at concentrations ranging from 0.05 to 20.2 ppb (DPR, 2016; DPR, 2017b). These detections were determined to be from legal agricultural uses of metolachlor and S-metolachlor (DPR, 2012; DPR, 2017b). After a hearing before the PCPA Pesticide Registration and Evaluation Committee (PREC) subcommittee, DPR's Director issued a response concurring with subcommittee findings and recommendations that ESA or OXA currently have not polluted and do not threaten to pollute groundwater (DPR, 2017a).

Review of Regulatory Documents and Databases

A review of pertinent regulatory documents was performed to ensure that the most scientifically supportable toxicological data were used for this evaluation (summarized in Table 1, below). A comprehensive systematic review was beyond the scope of the request.

Table 1. Review of Regulatory Documents and Databases

Regulatory Agency	Year	Title	Reference(s)
US EPA	1995	Reregistration Eligibility Decision (RED) Metolachlor	US EPA (1995)
US EPA	2007	Drinking Water: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List	US EPA (2007)
DPR	2009	Guidance for Dietary Exposure Assessment	DPR (2009)
DPR	2012	Study GW 09: Ground Water Protection List Monitoring for Metolachlor and Alachlor	DPR (2012)
US EPA	2014	Dietary Exposure Evaluation Model User's Guide. Office Of Pesticide Program, United States Environmental Protection Agency.	US EPA (2014a)
US EPA	2014	Metolachlor and S-Metolachlor. Recommended Environmental Degradates to Include in Drinking Water Assessment.	US EPA (2014b)
DPR	2016	Legal Agricultural Use Determination for Metolachlor/S-Metolachlor Degradate Detections in California	DPR (2016)
DPR	2017	Director's Response Concerning Detections of Metolachlor/S-Metolachlor Degradates in Groundwater of the State	DPR (2017a)
DPR	2017	Metolachlor/S-Metolachlor Findings by the Subcommittee of the Pesticide Registration and Evaluation Committee	DPR (2017b)
DPR	2017	Summary of Toxicology Data Metolachlor, S-Metolachlor, Metolachlor Oxanilic Acid, Metolachlor Ethanesulfonic Acid	DPR (2017c)
OEHHA	2017	Metolachlor and Metolachlor Degradates Ethanesulfonic Acid and Oxanilic Acid in Groundwater	OEHHA (2017)
US EPA	2018	2018 Edition of the Drinking Water Standards and Health Advisories Tables	US EPA (2018a)
US EPA	2018	Label Review Manual, Chapter 7: Precautionary Statements	US EPA (2018b)
US EPA	2018	S-metolachlor - Human Health Risk Assessment for the Establishment of Permanent Tolerances for Use of the Herbicide on Sugarcane (PP#6F8519).	US EPA (2018c)
USGS	2018	Health-Based Screening Levels for Evaluating Water-Quality Data	USGS (2018)
US EPA	2019	Environmental Protection Agency 40 CFR Part 180 [EPA–HQ–OPP–2017–0476; FRL–9991–75] Metolachlor; Pesticide Tolerances	US EPA (2019a)
US EPA	2019	Metolachlor and S-Metolachlor: Draft Human Health Risk Assessment for Registration Review	US EPA (2019b)
US EPA	2019	Metolachlor/S-Metolachlor: Draft Ecological Risk Assessment for Registration Review	US EPA (2019c)
US EPA	2020	S-Metolachlor: Human Health Risk Assessment for Petition for the Establishment of Tolerances and Registration for Use in/on Rosema1y and Dill (PP#9E8800) and Amended Use in/on Soybean (PP# 9F8764)	US EPA (2020)

Table 1. Review of Regulatory Documents and Databases

Regulatory Agency	Year	Title	Reference(s)
eCFR	2020	Code of Federal Regulation. § 180.355 Metolachlor; tolerances for residues	eCFR (2020)
DPR	2021	2021 Annual Statewide Pesticide Use Report Chemical Totals	DPR (2021)
US EPA	2021	2021 Human Health Benchmarks for Pesticides	US EPA (2021a)
US EPA	2021	Human Health Benchmarks for Pesticides: Updated 2021 Technical Document	US EPA (2021b)
DPR	2023	Groundwater Protection Program Fact Sheet	DPR (2023)
US EPA	2023	Integrated Risk Information System (IRIS) Glossary.	US EPA (2023)
DPR	2024	California Code of Regulations (Title 3. Food and Agriculture) Division 6.	DPR (2024a)
DPR	2024	California Pesticide Illness Query CalPIQ	DPR (2024b)
DPR	2024	Environmental Monitoring Programs and Projects	DPR (2024c)
DPR	2024	Pesticide Use Reporting (PUR)	DPR (2024d)
DPR	2024	Search for Chemical Ingredient by Partial Name, Chemical Code or CAS Number.	DPR (2024e)
OEHHA	2024	The Proposition 65 List.	OEHHA (2024)
US EPA	2024	Human Health Water Quality Criteria and Methods for Toxics	US EPA (2024a)
US EPA	2024	Incident Data System (IDS) - Incidents Submitted in Aggregate	US EPA (2024b)
DPR: Department of Pesticide Regulation; eCFR: online version of Code of Federal Regulation; US EPA: United States Environmental Protection Agency; USGS: United States Geological Survey; OEHHA: Office of Environmental Health Hazard Assessment			

Summary of Toxicology

Metolachlor has an acute Toxicity Category[1] value of III for oral hazards and Toxicity Category IV for dermal and inhalation hazards based on median lethal doses. It is a dermal sensitizer, a slight eye irritant (Toxicity Category III), and a minimal irritant to skin (Toxicity Category IV) (US EPA, 2019b). S-Metolachlor has the same toxicity categories, except that it is a Category III acute dermal toxicant. OXA has is in acute Toxicity Category III for oral hazards, Toxicity Category II for dermal hazards and is a Toxicity Category I eye irritant (DPR, 2017c). ESA is in acute Toxicity Category IV for oral hazards, is in Toxicity Category II for eye irritation, and is otherwise similar in acute hazards to S-metolachlor (DPR, 2017c). US EPA classified metolachlor/S-metolachlor as "not likely to be carcinogenic to humans" at doses that do not induce cellular proliferation in the liver (US EPA, 2019b).

[1] Acute Toxicity Categories. US EPA Label Review Manual Chapter 7: Precautionary Statements. US Environmental Protection Agency, Office of Pesticide Programs, Registration Division. Revised March 2018. Available at https://www.epa.gov/sites/default/files/2018-04/documents/chap-07-mar-2018.pdf (US EPA, 2018b).

Metolachlor/S-metolachlor is not included on Proposition 65 (the California Safe Drinking Water and Toxic Enforcement Act of 1986) list for chemicals known to cause cancer, reproductive toxicity, or developmental toxicity (OEHHA, 2024).

Effects seen in chronic toxicity studies with metolachlor included decreased body weights and food consumption in mice, rats and dogs, and increased absolute and relative (to body and brain) liver weights and microscopic liver lesions in rats (US EPA, 2018c). The most common effect in all experimental animals following long term exposures was reduced body weight. Subchronic studies were conducted with both metolachlor and S-metolachlor, whereas all chronic studies were performed with metolachlor only. Besides decreased body weights/body weight gains, subchronic exposure to S-metolachlor resulted in reduced food consumption and food efficiency (a measure of the ingested food conversion into an experimental animal's body weight), and increased kidney weights. In a rat developmental study, exposure to high dose of metolachlor resulted in slightly decreased numbers of implantations per dam, decreased numbers of live fetuses/dam, increased numbers of resorptions/dam and significant decreases in mean fetal body weight (US EPA, 2018c).

DPR's Pesticide Illness Surveillance Program (PISP) maintains a database of pesticide-related illnesses and injuries reported in California. Between 1992 and 2019 (the most recent data available) there were 24 cases reported to the PISP involving exposure to metolachlor alone or in combination with other active ingredients. In cases related to exposure to metolachlor alone symptoms included burning, painful, and red eyes, and itchy skin rash (DPR, 2024b).

HHA has evaluated all required toxicity data submitted for metolachlor as part of registration in California but has not conducted a human health risk assessment (DPR, 2017c).

Metolachlor/S-metolachlor

For the purpose of this evaluation, HHA adopted the toxicological endpoints and points of departure (PODs) established by US EPA for metolachlor/S-metolachlor (US EPA, 2019b; US EPA, 2020). US EPA did not derive an acute POD but established a short-term (1-30 days) incidental oral POD. This POD was a no observed adverse effect level (NOAEL) of 26 mg/kg/day based on decreased pup body weights in F1 and F2 litters at the LOAEL of 86 mg/kg/day in a two-generation reproduction study in rats with metolachlor (US EPA, 2019b; US EPA, 2020). US EPA calculated an incidental oral short-term reference dose (RfD[2]) of 0.26 mg/kg/day by dividing the POD by a total uncertainty factor (UF_{TOTAL}) of 100 comprised of 10x

[2] An RfD is an estimate of a daily oral exposure for specific duration (acute or chronic) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Available at https://www.epa.gov/iris/iris-glossary (US EPA, 2023)

for interspecies extrapolation (UF_A) and 10x for intraspecies variation (UF_H) (US EPA, 2019b; US EPA, 2020).

US EPA chronic POD was the same as the incidental oral NOAEL (26 mg/kg/day) from two-generation reproduction study in rats. The chronic RfD (cRfD) was the same as the acute RfD (0.26 mg/kg/day) (US EPA, 2019b; US EPA, 2020).

Limited toxicity data were submitted to DPR for the degradates ESA and OXA but no data were submitted for hydroxymetolachlor, or dechlorometolachlor (DPR, 2017c). Three-month oral subchronic studies using rats and dogs showed some evidence of liver toxicity for ESA and OXA, in common with the parent; there was no evidence of developmental toxicity for either (DPR, 2017c). In these studies, ESA and OXA demonstrated lower toxicity than metolachlor/S-metolachlor (DPR, 2017c). US EPA did not established RfDs for the degradates ESA/OXA, hydroxymetolachlor, or dechlorometolachlor (DPR, 2017c; US EPA, 2019b; US EPA, 2020).

Calculation of Human Health Reference Levels

An HHRL is the threshold pesticide residue for a maximum water intake that results in the maximum safe oral exposure. HHRLs were calculated using the acute and chronic RfDs for metolachlor as the maximum safe exposure, and the 95th percentile of acute and chronic (mean) drinking water intake rates for non-nursing infants as the maximum water intake. Non-nursing infants are the population identified as having the highest consumption of drinking water per kilogram of bodyweight among the standard populations that HHA evaluates, including the general US population and other sensitive subpopulations such as children 1–2 years of age and women of childbearing age (13–49 years). The water consumption rates were extracted from the Dietary Exposure Evaluation Model - Food Commodity Intake Database (DEEM-FCID, version 4.02, 05-10-c) and the What We Eat in America (WWEIA) database. WWEIA is the dietary intake interview component of the National Health and Nutrition Examination Survey (NHANES). It is a collection of two-day dietary survey data (including drinking water consumption) from 2005 to 2010 for the US population and select subgroups (US EPA, 2014a). HHA uses the 95th percentile of the exposure levels for each population subgroup as the default upper bound for acute exposures, while two-day nonconsecutive food intake is used as a surrogate for chronic consumption patterns (DPR, 2009).

HHA calculated acute and chronic HHRLs for metolachlor/S-metolachlor and their degradates of concern in groundwater. The results were summarized in Table 2. The lower reference value, the acute HHRL level of **1368** ppb, was selected as the DPR Groundwater HHRL for residues of metolachlor/S-metolachlor and their degradates in groundwater. Maximum residue concentrations of metolachlor/S-metolachlor and their degradates in groundwater equal to or less than the DPR Groundwater HHRL of 1368 ppb are not expected to pose a risk to human health, including for sensitive subpopulations.

Other Reference or Regulatory Levels for Metolachlor in Drinking Water

DPR considers other reference and regulatory levels for drinking water in the development of HHRLs, especially with regards to maintaining current best practices for dietary and drinking water exposure assessments. Common federal reference levels for drinking water include US EPA enforceable Maximum Contaminant Levels (MCLs[3]), non-legally enforceable Health Advisories (HAs[4]), and Human Health Benchmark for Pesticides (HHBP[5]), and United States Geological Survey (USGS) Health-Based Screening Levels (HBSLs[6]). US EPA has not issued either an MCL or an HHBP for metolachlor but has provided HAs. One- and ten-day HAs of 2000 ppb are expected to be protective for a 10-kg child consuming 1 liter of water per day. Other HAs include a Drinking Water Equivalent Level (DWEL) of 3500 ppb and a non-carcinogenic lifetime HA (NCHA) exposure level of 700 ppb for lifetime exposure (US EPA, 2018a). DWELs apply to situations where 100% of the residue intake are assumed to be from water sources while NCHA exposure levels incorporate a relative source contribution (RSC) factor of 0.2, assuming that the exposure from water sources will be 20% of the total exposure while other intakes will make up the remainder (80%). This RSC factor is routinely used by regulatory agencies for deriving chronic screening levels for drinking water (US EPA, 2000; US EPA, 2015; US EPA, 2024a). USGS's non-cancer HBSL for metolachlor was 600 ppb (USGS, 2018). OEHHA issued PHCs[7] for metolachlor, ESA, and OXA of 7 ppb, 1300 ppb, and 3200 ppb, respectively (OEHHA, 2017). DPR's Groundwater HHRL for metolachlor/S-metolachlor differed from US EPA's HAs, USGS's HBSL, and OEHHAs PHC because they were calculated using different parameters/assumptions such as water consumption rates, RfDs, and used RSC factors. The DPR Groundwater HHRL of 1368 ppb is the only reference level that is specifically

[3] Maximum Contaminant Levels (MCLs) are used for the protection of public drinking water systems and do not apply to privately owned wells or any other individual water system. Available at https://www.epa.gov/system/files/documents/2022-01/dwtable2018.pdf (US EPA, 2018a).

[4] Health Advisories (HAs) are estimated acceptable drinking water levels for chemicals based on information of adverse health effects and are not legally enforceable Federal standards, but rather serve as technical references to be used by federal, state, and local officials. Available at https://www.epa.gov/system/files/documents/2022-01/dwtable2018.pdf (US EPA, 2018a).

[5] The 2021 US EPA Human Health Benchmark for Pesticides (HHBPs) contain 430 pesticides that currently have no federal drinking water standards. HHBPs are not legally enforceable, but rather are provided by US EPA for pesticides that have no drinking water standards or health advisory (HA). Available at https://www.epa.gov/system/files/documents/2021-07/hh-benchmarks-technical-document-2021.pdf (US EPA, 2021b).

[6] USGS Health-Based Screening Levels (HBSLs) are "non-enforceable water-quality benchmarks" that were developed using (1) the latest US EPA Office of Water methods for establishing drinking-water guidelines and (2) the most recent US EPA peer-reviewed publicly available toxicity information. Available at https://water.usgs.gov/water-resources/hbsl/ (USGS, 2018).

[7] PHCs are developed by OEHHA using the general approach of the Public Health Goal (PHG) program for exposure to chemicals in drinking water for a lifetime OEHHA. 2017. Metolachlor and Metolachlor Degradates Ethanesulfonic Acid and Oxanilic Acid in Groundwater. *California Environmental Protection Agency*..

intended to be used for screening maximum detected residue concentrations of metolachlor/S-metolachlor in groundwater.

Table 2. DPR HHRLs[a] for Metolachlor/S-Metolachlor[b]

Residue	Acute or Chronic	Consumption Rates for Non-Nursing Infants[c] (L water/kg-BW)	RfD[d] (mg/kg/day)	HHRL (ppb)	US EPA Health Advisories[e]		
					1-Day/10-Day[e] (10-kg Child) (ppb)	DWEL[e] (ppb)	NCHA[e] (ppb)
Metolachlor/ S-metolachlor	Acute	0.19	0.26	**1368**	2000	3500	700
	Chronic	0.10	0.26	2600			
BW: bodyweight; DWEL: Drinking Water Equivalent Level; HHRL: Human Health Reference Level; L: liter; NCHA: non-carcinogenic lifetime health advisory; RfD: reference dose; ppb: parts-per-billion.							

[a] The DPR HHRLs (ppb) for screening maximum pesticide residue levels were calculated as [RfD (mg/kg/day) x 1000] / [Daily water intake (L/kg/day)]. Daily water intake is 95th percentile for acute or chronic (mean) water consumption rates for non-nursing infants (see Note c).

[b] Metolachlor's degradates of concern, OXA, ESA, hydroxymetolachlor, and dechlorometolachlor, are considered equivalent to metolachlor.

[c] 95th percentile water consumption rates for non-nursing infants from NHANES database (2005–2010). Acute and chronic water consumption data were extracted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database (DEEM-FCID, version 4.02, 05-10-c). A residue level of 1 ppm consumption defaults to the consumption rates by dimensional analysis (acute = 0.194566 L water/kg BW and chronic = 0.099559 L water/kg BW). The values were rounded to two decimal points for the calculation of HHRLs.

[d] Acute and chronic RfDs (mg/kg/day) were established by US EPA (US EPA, 2019b; US EPA, 2020) as described in the text.

[e] US EPA Health Advisories (HAs) are not legally enforceable Federal standards. HAs serve as a technical guidance to assist Federal, State, and local officials (US EPA, 2018a). 1-Day and 10-day parameters are concentrations intended to protect a 10-kg child consuming 1 liter of water per day for up to one day (1-day) and 10 days (10-day) exposure, respectively. A DWEL is a drinking water lifetime maximum noncarcinogenic safe exposure level assuming 100% exposure from that medium. A noncancer lifetime health advisory (NCHA) incorporates a relative source contribution (RSC) factor above DWEL, assuming that the exposure from water sources will be 20% of the total exposure while other intakes will make up the remainder (80%).

The recommended DPR Groundwater HHRL for screening residue concentrations of metolachlor/S-metolachlor and their degradates of concern in drinking water is **bolded**.

Conclusions

HHA calculated a DPR Groundwater Human Health Reference Level (HHRL) to be used when metolachlor/S-metolachlor and their degradates of concern (metolachlor ethanesulfonic acid (ESA), metolachlor oxanilic acid (OXA), hydroxymetolachlor and deschlorometolachlor)) are detected in groundwater. Maximum concentrations of these residues, individually or in summation if detected in the same samples, equal to or less than the DPR Groundwater HHRL of **1368** ppb are not expected to pose a risk to human health, including for sensitive subpopulations.

Anna Kalashnikova

Anna Kalashnikova, PhD
Staff Toxicologist, Risk Assessment Section

Svetlana Koshlukova

Svetlana Koshlukova, PhD
Senior Toxicologist, Risk Assessment Section

Peter N. Lohstroh

Peter N. Lohstroh, PhD
Senior Toxicologist, Toxicology and Dose Response Assessment Section

References

DPR. 2009. Guidance for Dietary Exposure Assessment. Human Health Assessment Branch. Environmental Protection Agency, Sacramento, CA.

DPR. 2012. Study GW 09: Ground Water Protection List Monitoring for Metolachlor and Alachlor. Environmental Monitoring Branch. Environmental Protection Agency, Sacramento, CA. https://www.cdpr.ca.gov/docs/emon/pubs/ehapreps/study_gw09_2012.pdf.

DPR. 2016. Legal Agricultural Use Determination for Metolachlor/S-Metolachlor Degradate Detections in California. Environmental Monitoring Branch. Environmental Protection Agency, Sacramento, CA. https://www.cdpr.ca.gov/docs/emon/grndwtr/metolachlor_lau.pdf.

DPR. 2017a. Director's Response Concerning Detections of Metolachlor/S-Metolachlor Degradates in Groundwater of the State. https://www.cdpr.ca.gov/docs/emon/grndwtr/metolSmetol_directors_response.pdf.

DPR. 2017b. Metolachlor/ S-Metolachlor: Findings and Recommendations. Subcommittee of the Pesticide Registration and Evaluation Committee. Environmental Protection Agency, Sacramento, CA. https://www.cdpr.ca.gov/docs/emon/grndwtr/metolachlor_findings_and_recs.pdf.

DPR. 2017c. Summary of Toxicology Data. Metolachlor, S-Metolachlor, Metolachlor Oxanilic Acid, Metolachlor Ethanesulfonic Acid. Human Health Assessment Branch. Environmental Protection Agency, Sacramento, CA.

DPR 2021. 2021 Annual Statewide Pesticide Use Report Chemical Totals. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. https://www.cdpr.ca.gov/docs/pur/pur21rep/pur_data/pur2021_subtotals_indexed_by_chemical.pdf.

DPR. 2023. Groundwater Protection Program Fact Sheet. Environmental Monitoring Branch. Environmental Protection Agency, Sacramento, CA. https://www.cdpr.ca.gov/docs/dept/factshts/pesticide_drinking_water_gw.pdf.

DPR. 2024a. California Code of Regulations (Title 3. Food and Agriculture) Division 6. Pesticides and Pest Control Operations. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. Retrieved August 6, 2023 from https://www.cdpr.ca.gov/docs/legbills/calcode/040101.htm.

DPR 2024b. California Pesticide Illness Query (CalPIQ). Human Health Assessment Branch. Department of Pesticide Regulation, California Environmental Protection Agency,

Sacramento, CA. Retrieved March 1, 2024 from https://apps.cdpr.ca.gov/calpiq/calpiq_input.cfm.

DPR. 2024c. Environmental Monitoring Programs and Projects. Environmental Monitoring Branch. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. . https://www.cdpr.ca.gov/docs/emon/ehap.htm.

DPR. 2024d. Pesticide Use Reporting (PUR)https://www.cdpr.ca.gov/docs/pur/purmain.htm.

DPR 2024e. Search for Chemical Ingredient by Partial Name, Chemical Code or CAS Number. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. .

eCFR. 2020. Code of Federal Regulation. § 180.368 Metolachlor; tolerances for residues. United States Environmental Protection Agency. Retrieved March 1, 2024 from https://www.ecfr.gov/current/title-40/chapter-I/subchapter-E/part-180/subpart-C/section-180.368.

NIH 2023. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 94411, 2-Amino-n-isopropylbenzamide. Retrieved August 4, 2023 from https://pubchem.ncbi.nlm.nih.gov/compound/2-Amino-n-isopropylbenzamide.

NIH. 2024a. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 183006, Metolachlor-2-hydroxy. Retrieved February 15, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/183006.

NIH. 2024b. National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 4169, metoachlor. Retrieved February 15, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/4169

NIH. 2024c. National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 6426849, Metolachlor ethanesulfonic acid. Retrieved February 15, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/Metolachlor-ethanesulfonic-acid.

NIH. 2024d. National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 11140605, S-metoachlor. Retrieved February 15, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/S-Metolachlor.

NIH. 2024e. National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 11831821, Metolachlor deschloro. Retrieved February 15, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/Metolachlor-deschloro.

NIH. 2024f. National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 15842092, Metolachlor OA. Retrieved February 15, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/Metolachlor-OA.

OEHHA. 2017. Metolachlor and Metolachlor Degradates Ethanesulfonic Acid and Oxanilic Acid in Groundwater. *California Environmental Protection Agency*.

OEHHA 2024. The Proposition 65 List. The Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA, USA. Retrieved March 1, 2024 from https://oehha.ca.gov/proposition-65/proposition-65-list.

US EPA. 1995. Reregistration Eligibility Decision (RED) Metolachlor.

US EPA. 2000. Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000). *United States Environmental Protection Agency.* .

US EPA. 2007. Drinking Water: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List. *United States Environmental Protection Agency*.

US EPA 2014a. Dietary Exposure Evaluation Model User's Guide. Office Of Pesticide Program, United States Environmental Protection Agency. https://www.epa.gov/sites/production/files/2015-09/documents/deem-user-guide-sep30-14.pdf.

US EPA. 2014b. Metolachlor and S-Metolachlor. Recommended Environmental Degradates to Include in Drinking Water Assessment.

US EPA 2015. Human Health Ambient Water Quality Criteria: 2015 Update. Office of Water, United States Environmental Protection Agency. https://www.epa.gov/sites/default/files/2015-10/documents/human-health-2015-update-factsheet.pdf.

US EPA 2018a. 2018 Edition of the Drinking Water Standards and Health Advisories Tables. Office of Water, United States Environmental Protection Agency. https://www.epa.gov/system/files/documents/2022-01/dwtable2018.pdf.

US EPA 2018b. Label Review Manual, Chapter 7: Precautionary Statements. Office of Pesticide Program, United States Environmental Protection Agency. https://www.epa.gov/sites/production/files/2018-04/documents/chap-07-mar-2018.pdf.

US EPA. 2018c. S-metolachlor - Human Health Risk Assessment for the Establishment of Permanent Tolerances for Use of the Herbicide on Sugarcane (PP#6F8519).

US EPA 2019a. Environmental Protection Agency 40 CFR Part 180 [EPA–HQ–OPP–2017–0476; FRL–9991–75] Bentazon; Pesticide Tolerances. Federal Register / Vol. 84, No. 84. https://www.regulations.gov/document/EPA-HQ-OPP-2017-0476-0003.

US EPA. 2019b. Metolachlor and S-Metolachlor: Draft Human Health Risk Assessment for Registration Review.

US EPA. 2019c. Metolachlor/S-Metolachlor: Draft Ecological Risk Assessment for Registration Review.

US EPA. 2020. S-Metolachlor: Human Health Risk Assessment for Petition for the Establishment of Tolerances and Registration for Use in/on Rosema1y and Dill (PP#9E8800) and Amended Use in/on Soybean (PP# 9F8764).

US EPA 2021a. 2021 Human Health Benchmarks for Pesticides. Office of Ground Water and Drinking Water, United States Environmental Protection Agency. Retrived August 2, 2023 from https://www.epa.gov/sdwa/2021-human-health-benchmarks-pesticides.

US EPA 2021b. Human Health Benchmarks for Pesticides: Updated 2021 Technical Document. Office of Ground Water and Drinking Water, United States Environmental Protection Agency. https://www.epa.gov/system/files/documents/2021-07/hh-benchmarks-technical-document-2021.pdf.

US EPA 2023. Integrated Risk Information System (IRIS) Glossary. Integrated Risk Information System, United States Environmental Protection Agency. https://www.epa.gov/iris/iris-glossary.

US EPA 2024a. Human Health Water Quality Criteria and Methods for Toxics. United States Environmental Protection Agency. Retrieved March 1, 2024 from https://www.epa.gov/wqc/human-health-water-quality-criteria-and-methods-toxics.

US EPA. 2024b. Incident Data System (IDS) - Incidents Submitted in Aggregate. United States Environmental Protection Agency. Retrieved August 4, 2023 from https://ordspub.epa.gov/ords/pesticides/f?p=359:5.

USGS 2018. Health-Based Screening Levels for Evaluating Water-Quality Data. United State Geological Survey. https://water.usgs.gov/water-resources/hbsl/.

Appendix 1: DPR Memo: Human Health Reference Level Request for Metolachlor/S-metolachlor and Degradates in Groundwater 7 February 2024 (1 Page)

Department of Pesticide Regulation

Julie Henderson
Director

Gavin Newsom
Governor

Yana Garcia
Secretary for Environmental Protection

MEMORANDUM

TO: Shelley DuTeaux
Environmental Program Manager II
Human Health Assessment Branch

VIA: Minh Pham *Original Signed by 2/7/24*
Environmental Program Manager II
Environmental Monitoring Branch

FROM: Joy Dias *Original Signed by 2/7/24*
Environmental Program Manager I
Environmental Monitoring Branch

DATE: February 7, 2024

SUBJECT: HUMAN HEALTH REFERENCE LEVEL REQUEST FOR METOLACHLOR/S-METOLACHLOR AND DEGRADATES IN GROUNDWATER

The Environmental Monitoring Branch (EMB) monitors the environment to determine the fate of pesticides and protects the public and the environment from pesticide contamination by analyzing hazards and developing pollution prevention strategies. Consistent with EMB's mission, the Groundwater Protection Program (GWPP) routinely monitors for metolachlor/s-metolachlor and their degradates, metolachlor ethanesulfonic acid (ESA) and metolachlor oxanilic acid (OXA), due to their status as 3CCR 6800(b) pesticides and occurrence in groundwater. The GWPP also gathers data from all public agencies that report groundwater monitoring data of pesticides and their degradates and enters the data into the Well Inventory Database (WIDB). The United States Geological Survey has also reported detections of the degradates hydroxymetolachlor and dechlorometolachlor.

To determine whether detections of metolachlor/s-metolachlor or any of their degradation products pose a significant risk to human health, EMB requests that the Human Health Assessment Branch provide a human health reference level to use for screening detections in groundwater.

Chemical	DPR Chemical Code	CAS Number
Metolachlor	1996	51218-45-2
S-metolachlor	5133	87392-12-9
Metolachlor ethanesulfonic acid (ESA)	5806	171118-09-5
Metolachlor oxanilic acid (OXA)	5807	152019-73-3
Hydroxymetolachlor	6405	131068-72-9
Dechlorometolachlor	6475	126605-22-9

cc: Carissa Ganapathy, Senior Environmental Scientist (Supervisory)