



Julie Henderson  
Director

Yana Garcia  
Secretary for  
Environmental Protection

MEMORANDUM

TO: Minh Pham  
Environmental Program Manager II  
Environmental Monitoring Branch

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

FROM: Chunbo Zhang, PhD, Staff Toxicologist  
Pete Lohstroh, PhD, Senior Toxicologist  
Toxicology and Dose Response Assessment Section

Svetlana Koshlukova, PhD, Senior Toxicologist  
Risk Assessment Section

DATE: July 17, 2024

SUBJECT: HUMAN HEALTH REFERENCE LEVELS FOR METHOXYFENOZIDE  
RESIDUES IN SURFACE WATER AND GROUNDWATER

---

The Human Health Assessment (HHA) Branch at the Department of Pesticide Regulation's (DPR) was requested by the Environmental Monitoring Branch (EMB) to provide Human Health Reference Levels (HHRLs) for methoxyfenozide for evaluations of detected or model-estimated concentrations of its residues in drinking water from surface water or groundwater sources. This memorandum updates HHRLs of methoxyfenozide, which reflects HHA's revised approach by establishing separate HHRLs for surface water and groundwater. These updated HHRLs supersede the corresponding DPR HHRLs for methoxyfenozide established in 2022 and 2023 (DPR, 2022b; DPR, 2023).

**Human Health Reference Levels (HHRLs):**

1. HHA calculated Human Health Reference Levels (HHRLs) to be used for detected or model-estimated concentrations of methoxyfenozide in surface water and 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. A DPR Acute Surface Water HHRL for methoxyfenozide at 895 parts-per-billion (ppb) applies to the evaluation of **maximum** residue levels of methoxyfenozide in drinking

water from surface water sources. Maximum methoxyfenozide residue concentrations in surface water equal to or less than the DPR Acute Surface Water HHRL of 895 ppb are not expected to pose a risk to human health, including for sensitive subpopulations. The DPR Acute Surface Water HHRL supersedes the corresponding HHRL (504 ppb) previously issued in 2023 (DPR, 2023).

3. A DPR Chronic Surface Water HHRL for methoxyfenozide at 200 ppb applies to the evaluation of **average** residue levels in surface water. Average methoxyfenozide residue concentrations in surface water equal to or less than the DPR Chronic Surface Water HHRL of 200 ppb are not expected to pose a chronic risk to human health, including for sensitive subpopulations. This DPR Chronic Surface Water HHRL supersedes a corresponding HHRL (205 ppb) previously issued in 2023 (DPR, 2023).
4. The DPR Groundwater HHRL for methoxyfenozide at 895 ppb are for evaluations of **maximum** residue levels of methoxyfenozide in drinking water from groundwater water sources. Maximum methoxyfenozide residue concentrations in groundwater equal to or less than the DPR HHRL of 895 ppb are not expected to pose a risk to human health, including for sensitive subpopulations. This DPR Groundwater HHRL supersedes the corresponding HHRL (504 ppb) previously issued in 2022 (DPR, 2022b; DPR, 2023).

## **Background**

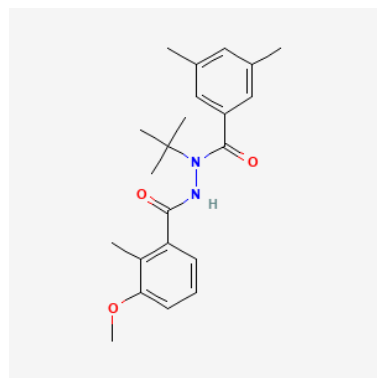
**Technical Name:** Methoxyfenozide

**Chemical Name:** N'-tert-butyl-N'-(3,5-dimethylbenzoyl)-3-methoxy-2-methylbenzohydrazide  
3-methoxy-2-methylbenzoic acid 2-[3,5-dimethylbenzoyl]-2-[1,1-dimethylethyl] hydrazide

**Chemical Abstracts Service Registry Number (CAS #):** 161050-58-4

**Molecular Weight:** 368.5 g/mol (NIH, 2024)

**Chemical Structure:**



(NIH, 2024)

Methoxyfenozide is a bis-diacylhydrazine insecticide that acts as an insect growth regulator. It mimics the action of the insect molting hormone 20-hydroxyecdysone by inducing precocious incomplete molts in invertebrates, which ultimately results in their death (US EPA, 2007; US EPA, 2018c). Methoxyfenozide is used for control of lepidopterous insects on a variety of food and feed crops (US EPA, 2015b; US EPA, 2023a). Methoxyfenozide was first registered in California in 2003 (DPR, 2024d). As of July 2024, there are 13 active registrations in California (DPR, 2024d). According to the most recent available data from the DPR's Pesticide Use Reporting (PUR) database, 541,000 pounds of methoxyfenozide active ingredient were used in 34,614 California agricultural applications in 2022 (DPR, 2022a).

In 2016, US EPA determined that methoxyfenozide and two other diacylhydrazines, halofenozide and tebufenozide, form a candidate common mechanism group (CMG), and in 2023 conducted a screening level dietary (food and drinking water) cumulative risk assessment for methoxyfenozide and tebufenozide based on a common mechanism of action (US EPA, 2016; US EPA, 2023a). The assessment concluded that cumulative exposures were not of concern (US EPA, 2023a).

### **Regulatory Document Review**

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**

<b>Regulatory Agency</b>	<b>Year</b>	<b>Title</b>	<b>Reference(s)</b>
DPR	2000	Summary of Toxicology Data Methoxyfenozide	DPR, 2000
US EPA	2000	Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)	US EPA, 2000
US EPA	2007	Ecological Risk Assessment for the Methoxyfenozide Section 3 New Uses (Variety of Uses)	US EPA, 2007
DPR	2009	Guidance for Dietary Exposure Assessment	DPR, 2009
US EPA	2014	Dietary Exposure Evaluation Model User's Guide	US EPA, 2014a
US EPA	2014	Methoxyfenozide. Revised Human Health Risk Assessment to Support Proposed New Section 3 Use on Pineapple	US EPA, 2014b
US EPA	2015	Human Health Ambient Water Quality Criteria: 2015 Update	US EPA, 2015a

**Table 1. Review of Regulatory Documents and Databases**

Regulatory Agency	Year	Title	Reference(s)
US EPA	2015	Methoxyfenozide. Human Health Draft Risk Assessment for Registration Review and New Use Risk Assessment to Support the Registration of Proposed Use on Chives, and Crop Group Expansions for Stone Fruit and Tree Nuts	US EPA, 2015b
US EPA	2016	Diacylhydrazines Cumulative Screening Risk Assessment: Methoxyfenozide and Tebufenozide	US EPA, 2016
EFSA	2017	Peer Review of the Pesticide Risk Assessment of the Active Substance Methoxyfenozide	EFSA, 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	Methoxyfenozide. Human Health Risk Assessment to Support the Proposed Establishment of a Tolerance (without Section 3 Registration) on Imported Tea	US EPA, 2018c
USGS	2018	Health-Based Screening Levels for Evaluating Water-Quality Data.	USGS, 2018
EFSA	2020	Focused Assessment of Certain Existing MRLs of Concern for Methoxyfenozide	EFSA, 2020
DPR	2021	Evaluating Risk from Exposure to Illegal Pesticides on Fresh Agricultural Commodities	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	2022	2022 Annual Statewide Pesticide Use Report Chemical Totals	DPR, 2022a
DPR	2022	Risks from Human Exposure to Methoxyfenozide Residues in Groundwater	DPR, 2022b
US EPA	2022	Methoxyfenozide. Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessment for the Section 3 Regional Registration on Rice	US EPA, 2022a
US EPA	2022	Methoxyfenozide. Human Health Risk Assessment for the Petition to Establish Permanent Tolerances, and Associated Section 3 Registration, for Residues Resulting from Use of the Insecticide on Rice, and Crop Group Conversions and Expansions	US EPA, 2022b
DPR	2023	Risks from Human Exposure to Methoxyfenozide in Surface Water	DPR, 2023
OEHHA	2023	The Proposition 65 List	OEHHA, 2023
US EPA	2023	Methoxyfenozide. Human Health Risk Assessment for the Petition to Establish Permanent Tolerances without a U.S. Registration on Coffee Beans and Sugar Cane	US EPA, 2023a

**Table 1. Review of Regulatory Documents and Databases**

Regulatory Agency	Year	Title	Reference(s)
US EPA	2023	Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions	US EPA, 2023b
DPR	2024	California Code of Regulations (Title 3. Food and Agriculture) Division 6. Pesticides and Pest Control Operations	DPR, 2024a
DPR	2024	California Pesticide Illness Query (CalPIQ)	DPR, 2024b
DPR	2024	Environmental Monitoring Programs and Projects	DPR, 2024c
DPR	2024	Search for Chemical Ingredient by Partial Name, Chemical Code or CAS Number	DPR, 2024d
DPR	2024	Surface Water Database (SURF)	DPR, 2024e
eCFR	2024	Code of Federal Regulation. § 180.544 Methoxyfenozide; Tolerances for Residues	eCFR, 2024
OEHHA	2024	Public Health Goals (PHGs)	OEHHA, 2024
US EPA	2024	CompTox Chemicals Dashboard: Methoxyfenozide	US EPA, 2024a
US EPA	2024	Endocrine Disruptor Screening Program (EDSP) Estrogen Receptor Bioactivity	US EPA, 2024b
US EPA	2024	Human Health Water Quality Criteria and Methods for Toxicants	US EPA, 2024c
US EPA	2024	Incident Data System (IDS) - All Aggregate Summary Incidents: Methoxyfenozide	US EPA, 2024d
US EPA	2024	Integrated Risk Information System (IRIS) Glossary	US EPA, 2024e
US EPA	2024	Methoxyfenozide; Pesticide Tolerances; Correction	US EPA, 2024f
DPR: Department of Pesticide Regulation; eCFR: online version of Code of Federal Regulation; EFSA: European Food Safety Authority; US EPA: United States Environmental Protection Agency; USGS: United States Geological Survey; OEHHA: Office of Environmental Health Hazard Assessment.			

**Summary of Toxicology**

Methoxyfenozide was placed in Toxicity Category<sup>1</sup> IV for acute oral and inhalation hazards and Toxicity Category III for dermal hazards based on median lethal doses. It is not a skin sensitizer or a skin irritant (Toxicity Category IV) but is a very mild eye irritant (Toxicity Category IV) (US EPA, 2023a). US EPA classified methoxyfenozide as "not likely to be carcinogenic to humans" based on carcinogenicity studies in rats and mice (US EPA, 2015b; US EPA, 2023a).

<sup>1</sup> 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)

US EPA concluded that “quantifications of acute dietary and human cancer risks are not required” (US EPA, 2018c). In the available database, methoxyfenozide did not show reproductive, developmental, or neurotoxic effects in laboratory animals (US EPA, 2015b).

Methoxyfenozide is not included on the 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, 2023).

In 2-week repeated oral studies, thyroid gland hypertrophy/hyperplasia and increased adrenal hypertrophy were observed in rats, and hematological changes and increased spleen weights were observed in dogs (US EPA, 2015b; US EPA, 2023a). Hepatocellular hypertrophy and increased liver weights were noted in a 90-day oral toxicity study in rats (US EPA, 2015b; US EPA, 2023a). Chronic toxicity studies showed changes in the liver, thyroid glands, adrenal glands, and the hematopoietic system in rats and hematological and clinical chemical changes in dogs (DPR, 2000; US EPA, 2015b; EFSA, 2017; US EPA, 2023a).

DPR’s Pesticide Illness Surveillance Program (PISP) maintains a database of pesticide-related illnesses and injuries reported in California from 1992 to 2019 (the most recent data available). There were 118 cases involving exposure to methoxyfenozide alone or in combination with other active ingredients. In two cases, exposure was to methoxyfenozide alone. One case exhibited serious symptoms including coughing, tightness of nose and throat, difficulty breathing, and nausea. Two weeks following the exposure, wheezing throughout lungs was recorded. Twelve days later, red nose & throat with white discharge were noted (DPR, 2024b).

Although HHA has evaluated all required toxicity data submitted as part of registration in California, HHA has not conducted a human health risk assessment for methoxyfenozide (DPR, 2000). For purposes of this evaluation, HHA reviewed relevant regulatory documents (Table 1) and adopted points of departure (PODs<sup>2</sup>) established by US EPA for calculations of acute and chronic reference doses (RfDs<sup>3</sup>) (US EPA, 2022a; US EPA, 2023a)

US EPA has not established an acute POD (aPOD) for methoxyfenozide. Previously, DPR adopted the aPOD established by European Food Safety Authority (EFSA), which is a no

---

<sup>2</sup> Point of departure (POD) is the dose-response point that marks the beginning of a low-dose extrapolation. A POD can be the lower bound dose for an estimated incidence or from a dose-response model (BMD), or a NOAL/NOAEL. Available at <https://www.epa.gov/iris/iris-glossary> (US EPA, 2024e).

<sup>3</sup> 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, 2024e).

observed adverse effect level (NOAEL) of 9.8 mg/kg/day based on hemolytic anemia observed at the lowest observed adverse effect level (LOAEL) of 106 mg/kg/day in a 1-year dietary toxicity study in dogs (EFSA, 2017; DPR, 2022b; DPR, 2023). After reevaluating available documents, DPR determined that the incidental oral short-term POD (1-30 days) established by US EPA is more appropriate for use as an aPOD for the reasons described below. The incidental POD established by US EPA was a NOAEL of 16.8 mg/kg/day based on hematological changes and increased spleen weights at the lowest observed adverse effect level (LOAEL) of 90.8 mg/kg/day in a 2-week oral study in dogs (US EPA, 2015b; US EPA, 2023a). The NOAEL of 16.8 mg/kg/day was the most sensitive dose in the available acute and short-term toxicity studies, and was a more appropriate duration for use as an aPOD than the previous one that was based on effects seen after chronic exposure (US EPA, 2015b; EFSA, 2017). Supportive evidence comes from a 2-week oral range-finding study in rats, which established the same short-term NOAEL (17 mg/kg/day) based on thyroid hypertrophy and hyperplasia at the LOAEL of 69.3 mg/kg/day (US EPA, 2015b).

The acute RfD (aRfD) of 0.17 mg/kg/day for methoxyfenozide was calculated by dividing the aPOD (16.8 mg/kg/day) by a total uncertainty factor ( $UF_{TOTAL}$ ) of 100 (US EPA, 2023a). The  $UF_{TOTAL}$  includes 10x for interspecies extrapolation ( $UF_A$ ) and 10x for intraspecies variation ( $UF_H$ ) (US EPA, 2023a). HHA also uses this methoxyfenozide aRfD for evaluating risk from illegal residues on fresh produce for the California Pesticide Residue Monitoring Program (DPR, 2021). The chronic POD (cPOD) was a NOAEL of 10.2 mg/kg/day based on observed hematological effects at the LOAEL of 411 mg/kg/day in a 24-month chronic/carcinogenicity toxicity study in rats (DPR, 2000; US EPA, 2023a). The cPOD was considered to be co-critical with a NOAEL of 9.8 mg/kg/day based on hematological and clinical chemistry effects at the LOAEL of 106.1 mg/kg/day in a 1-year chronic toxicity study in dogs (US EPA, 2023a). The chronic RfD (cRfD) of 0.10 mg/kg/day (all populations) was calculated by dividing the NOAEL by the  $UF_{TOTAL}$  of 100 (10x each for interspecies and intraspecies extrapolation) (US EPA, 2023a).

### **Calculation of Human Health Reference Levels**

An HHRL is the threshold pesticide residue level for a maximum water intake that results in the maximum safe oral exposure. HHRLs are calculated using the acute (95<sup>th</sup> percentile) and chronic (mean) drinking water intake rates for non-nursing infants as the high-end water intake rates. Non-nursing infants are the population identified as having the highest consumption of drinking water per kilogram of body weight 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 95<sup>th</sup> percentile 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).

### ***Formulae Used to Calculate Acute and Chronic Surface Water HHRLs***

$$\text{Acute Surface Water HHRL (ppb)} = \frac{\text{acute RfD}}{\text{acute DWI}} \times 1000$$

$$\text{Chronic Surface Water HHRL (ppb)} = \frac{\text{chronic RfD}}{\text{chronic DWI}} \times 1000 \times \text{RSC}$$

DWI, drinking water intake, is 95<sup>th</sup> percentile (acute) or mean (chronic) water consumption rates for non-nursing infants as described above. When a residue level of 1 ppm consumption defaults to the consumption rates by dimensional analysis, the acute DWI for non-nursing infants were 0.194566 L water/kg body weight and the chronic DWI 0.099559 L water/kg body weight (US EPA, 2014a). The values were rounded to two decimal points for the calculation of HHRLs (Table 2).

DPR Chronic Surface Water HHRLs incorporate a relative source contribution (RSC) factor of 0.2. The RSC factor accounts for the possibility that exposure to a pesticide residue may come from sources other than drinking water (*i.e.*, food and air). A default RSC of 0.2 assumes that the exposure from water sources will be 20% of the total exposure while other intakes will make up the remainder (80%). The RSC is routinely used by regulatory agencies for deriving chronic drinking water screening levels (US EPA, 2000; US EPA, 2015a; US EPA, 2024c)

### ***DPR Acute Surface Water HHRL for Methoxyfenozide***

DPR Acute Surface Water HHRLs are for screening detections of pesticide maximum residue concentrations in surface water. The DPR Acute Surface Water HHRL for methoxyfenozide in surface water is **895** ppb (Table 2). Maximum residue concentrations of methoxyfenozide in surface water equal to or less than 895 ppb are not expected to pose an acute risk to human health, including for sensitive subpopulations. This DPR Acute Surface Water HHRL of 895 ppb supersedes the previous issued level of 504 ppb (DPR, 2023).



### ***DPR Chronic Surface Water HHRL for Methoxyfenozide***

A DPR Chronic Surface Water HHRL applies to the evaluation of average pesticide residue levels in a surface water body. HHA calculated a DPR Chronic Surface Water HHRL of **200** ppb for screening average methoxyfenozide residue levels in a surface water body (Table 2). Average residue levels of methoxyfenozide equal to or less than the DPR Chronic Surface Water HHRL of 200 ppb are not expected to pose a chronic risk to human health, including for sensitive subpopulations. This DPR Chronic Surface Water HHRL of 200 ppb supersedes a corresponding HHRL (205 ppb) previously issued in 2023 (DPR, 2023).

### ***Formulae Used to Calculate Groundwater HHRLs***

A DPR Groundwater HHRL is for screening maximum pesticide residue concentrations in groundwater and is protective for single or repeated exposures from groundwater sources. A Groundwater HHRL is the lower value of the following two calculations and the selected data set is listed in Table 2:

$$\text{acute HHRL (ppb)} = \frac{\text{acute RfD}}{\text{acute DWI}} \times 1000$$

$$\text{chronic HHRL (ppb)} = \frac{\text{chronic RfD}}{\text{chronic DWI}} \times 1000$$

### ***DPR Groundwater HHRL for Methoxyfenozide***

As shown in Table 2, the DPR Groundwater HHRL for methoxyfenozide is **895** ppb. Maximum residue levels of methoxyfenozide in groundwater equal to or less than 895 ppb are not expected to pose an acute or chronic risk to human health, including for sensitive subpopulations. This DPR Groundwater HHRL of 895 ppb supersedes the previous issued level of 504 ppb (DPR, 2022b; DPR, 2023).

### **Other Reference or Regulatory Levels for Methoxyfenozide 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<sup>4</sup>), non-legally enforceable Health

---

<sup>4</sup> 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).

Advisories (HAs<sup>5</sup>) and Human Health Benchmark for Pesticides (HHBPs<sup>6</sup>), and United States Geological Survey (USGS) Health-Based Screening Levels (HBSLs<sup>7</sup>) (US EPA, 2018a; USGS, 2018; US EPA, 2021a). For methoxyfenozide, US EPA did not issue MCLs or HAs but have a chronic HHBP of 600 ppb for the general population (US EPA, 2021a). Although the chronic HHBP and the DPR Chronic Surface Water HHRL for methoxyfenozide are both based on the same cPOD, their values differ because they were calculated using different parameters and/or assumptions such as water consumption rates.

---

<sup>5</sup> 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).

<sup>6</sup> 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 advisories (HAs). Available at <https://www.epa.gov/system/files/documents/2021-07/hh-benchmarks-technical-document-2021.pdf> (US EPA, 2021b).

<sup>7</sup> 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).

**Table 2. DPR’s HHRLs<sup>a</sup> for Methoxyfenozide**

Sources	Duration of Exposure	Water Consumption Rates for Non-Nursing Infants (L water/kg BW)	RfD (mg/kg/day)	HHRL (ppb)	US EPA Chronic HHBP <sup>b</sup> (ppb)
Surface Water HHRLs	Acute (maximum residues)	0.19	0.17 <sup>c</sup>	<b>895<sup>d</sup></b>	600 (General Population)
	Chronic (average residues)	0.10	0.10	<b>200<sup>d</sup></b>	
Groundwater HHRL	Single or Repeat Exposures (maximum residues)	0.19	0.17 <sup>c</sup>	<b>895<sup>d</sup></b>	

BW: body weight; DPR: Department of Pesticide Regulation; HHBP: Human Health Benchmark for Pesticides; HHRL: Human Health Reference Level; L: liter; RfD: reference dose; ppb: parts-per-billion.

<sup>a</sup> Surface water and groundwater HHRL calculation methods are described in the text.

<sup>b</sup> In 2021, US EPA provided Human Health Benchmark for Pesticides (HHBPs) containing 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 advisories (US EPA, 2021a). Chronic HHBP for General Population (ppb) = [chronic RfD (mg/kg/day) x 1000 x 0.2 (RSC)] / [0.0338 (L/kg/day) of Drinking Water Intake-Body Weight ratio].

<sup>c</sup> Acute and chronic RfDs for methoxyfenozide were based on toxicological endpoints established by US EPA (US EPA, 2023a) as described in the text. Please note that the acute RfD is updated and different from that used in previous issued methoxyfenozide HHRLs for surface water and groundwater (DPR, 2022b; DPR, 2023).

<sup>d</sup> The updated DPR Acute Surface Water HHRL of 895 ppb and the DPR Chronic Surface Water HHRL of 200 ppb supersedes the previous issued levels of 504 and 205 ppb, respectively (DPR, 2023). The updated DPR Groundwater HHRL of 895 ppb overwrites the previous issued level of 504 ppb (DPR, 2022b; DPR, 2023).

The recommended HHRLs for screening methoxyfenozide residues in drinking water are **bolded**.

## **Conclusions**

HHA calculated DPR's Human Health Reference Levels (HHRLs) to be used for methoxyfenozide in drinking water from surface water and groundwater sources.

### ***Surface Water Sources***

Maximum residue concentrations of methoxyfenozide equal to or less than the DPR Acute Surface Water HHRL (895 ppb), or average residue levels equal to or less than the DPR Chronic Surface Water HHRL (200 ppb) are not expected to pose a risk to human health, including for sensitive subpopulations. These HHRLs supersede previously issued HHRLs (504 and 205 ppb, respectively) (DPR, 2023).

### ***Groundwater Sources***

Maximum residue concentrations of methoxyfenozide equal to or less than the DPR Groundwater HHRL (895 ppb) are not expected to pose a risk to human health, including for sensitive subpopulations. This HHRL supersedes a previously issued HHRL (504 ppb) for methoxyfenozide (DPR, 2022b; DPR, 2023).

*Chunbo Zhang*

---

**Chunbo Zhang, PhD**  
**Staff Toxicologist, Toxicology and Dose Response 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 2000. Summary of Toxicology Data Methoxyfenozide. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.
- DPR 2009. Guidance for Dietary Exposure Assessment. Human Health Assessment Branch. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA
- DPR 2021. Evaluating Risk from Exposure to Illegal Pesticides on Fresh Agricultural Commodities. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.
- DPR 2022a. 2022 Annual Statewide Pesticide Use Report Chemical Totals. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. [www.cdpr.ca.gov/docs/pur/pur22rep/pur\\_data/pur2022\\_subtotals\\_indexed\\_by\\_chemical.pdf](https://www.cdpr.ca.gov/docs/pur/pur22rep/pur_data/pur2022_subtotals_indexed_by_chemical.pdf).
- DPR 2022b. Risks from Human Exposure to Methoxyfenozide Residues in Groundwater. Human Health Assessment Branch. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. [https://www.cdpr.ca.gov/docs/whs/active\\_ingredient/methoxyfenozide.htm](https://www.cdpr.ca.gov/docs/whs/active_ingredient/methoxyfenozide.htm).
- DPR 2023. Risks from Human Exposure to Methoxyfenozide in Surface Water. Human Health Assessment Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. [https://www.cdpr.ca.gov/docs/risk/rcd/methoxyfenozide\\_surface\\_water\\_2023\\_2\\_6.pdf](https://www.cdpr.ca.gov/docs/risk/rcd/methoxyfenozide_surface_water_2023_2_6.pdf).
- DPR 2024a. California Code of Regulations (Title 3. Food and Agriculture) Division 6. Pesticides and Pest Control Operations. Retrieved July 4, 2024 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 July 6, 2024 from [https://apps.cdpr.ca.gov/calpiq/calpiq\\_input.cfm](https://apps.cdpr.ca.gov/calpiq/calpiq_input.cfm).
- DPR 2024c. Environmental Monitoring Programs and Projects. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. Retrieved July 5, 2024 from <https://www.cdpr.ca.gov/docs/emon/ehap.htm>.
- DPR 2024d. Search for Chemical Ingredient by Partial Name, Chemical Code or CAS Number. Department of Pesticide Regulation, California Environmental Protection Agency,

- Sacramento, CA. Retrieved July 17, 2024 from <https://apps.cdpr.ca.gov/docs/chemical/master2.cfm>.
- DPR 2024e. Surface Water Database (SURF). Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. Retrieved July 17, 2024 from <https://www.cdpr.ca.gov/docs/emon/surfwtr/surfcont.htm>.
- eCFR 2024. Code of Federal Regulation. § 180.544 Methoxyfenozide; Tolerances for Residues. United States Environmental Protection Agency. Retrieved July 11, 2024 from <https://www.ecfr.gov/current/title-40/chapter-I/subchapter-E/part-180/subpart-C/section-180.544>.
- EFSA 2017. Peer Review of the Pesticide Risk Assessment of the Active Substance Methoxyfenozide. EFSA Journal 15:4978. <https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2017.4978>.
- EFSA 2020. Focussed Assessment of Certain Existing MRLs of Concern for Methoxyfenozide. EFSA Journal 2020;18: 6330. <https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2020.6330>.
- NIH 2024. National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 105010, Methoxyfenozide. Retrieved July 14, 2024 from <https://pubchem.ncbi.nlm.nih.gov/compound/Methoxyfenozide>.
- OEHHA 2023. The Proposition 65 List. The Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA. Retrieved March 6, 2024 from <https://oehha.ca.gov/proposition-65/proposition-65-list>.
- OEHHA 2024. Public Health Goals (PHGs). The Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA. Retrieved July 17, 2024 from <https://oehha.ca.gov/water/public-health-goals-phgs>.
- US EPA 2000. Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000). Office of Water, United States Environmental Protection Agency. <https://www.epa.gov/sites/default/files/2018-10/documents/methodology-wqc-protection-hh-2000.pdf>.
- US EPA 2007. Ecological Risk Assessment for the Methoxyfenozide Section 3 New Uses (Variety of Uses). Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2007-0495-0009>.
- 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. Methoxyfenozide. Revised Human Health Risk Assessment to Support Proposed New Section 3 Use on Pineapple. Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency.  
<https://www.regulations.gov/document/EPA-HQ-OPP-2013-0476-0008>.

US EPA 2015a. 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 2015b. Methoxyfenozide. Human Health Draft Risk Assessment for Registration Review and New Use Risk Assessment to Support the Registration of Proposed Use on Chives, and Crop Group Expansions for Stone Fruit and Tree Nuts. Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency.  
<https://www.regulations.gov/document/EPA-HQ-OPP-2014-0591-0008>.

US EPA 2016. Diacylhydrazines Cumulative Screening Risk Assessment: Methoxyfenozide and Tebufenozide. Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2008-0824-0078>.

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. Methoxyfenozide. Human Health Risk Assessment to Support the Proposed Establishment of a Tolerance (without Section 3 Registration) on Imported Tea. Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2017-0494-0007>.

US EPA 2021a. 2021 Human Health Benchmarks for Pesticides. Office of Ground Water and Drinking Water, United States Environmental Protection Agency.  
<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 2022a. Methoxyfenozide. Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessment for the Section 3 Regional Registration on Rice. Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2020-0336-0012>.

US EPA 2022b. Methoxyfenozide. Human Health Risk Assessment for the Petition to Establish Permanent Tolerances, and Associated Section 3 Registration, for Residues Resulting from Use of the Insecticide on Rice, and Crop Group Conversions and Expansions. Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2020-0336-0013>.

US EPA 2023a. Methoxyfenozide. Human Health Risk Assessment for the Petition to Establish Permanent Tolerances without a U.S. Registration on Coffee Beans and Sugar Cane. Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2022-0139-0006>.

US EPA 2023b. Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2023-0474-0001>.

US EPA 2024a. CompTox Chemicals Dashboard: Methoxyfenozide. United States Environmental Protection Agency. Retrieved July 5, 2024 from <https://comptox.epa.gov/dashboard/chemical/details/DTXSID3032628>.

US EPA 2024b. Endocrine Disruptor Screening Program (EDSP) Estrogen Receptor Bioactivity. United States Environmental Protection Agency. <https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-estrogen-receptor-bioactivity>.

US EPA 2024c. Human Health Water Quality Criteria and Methods for Toxics. United States Environmental Protection Agency. Retrieved July 16, 2024 from <https://www.epa.gov/wqc/human-health-water-quality-criteria-and-methods-toxics>

US EPA 2024d. Incident Data System (IDS) - All Aggregate Summary Incidents: Methoxyfenozide. United States Environmental Protection Agency. Retrieved July 6, 2024 from <https://ordspub.epa.gov/ords/pesticides/f?p=359:4>.



US EPA 2024e. Integrated Risk Information System (IRIS) Glossary. Integrated Risk Information System, United States Environmental Protection Agency.  
<https://www.epa.gov/iris/iris-glossary>

US EPA 2024f. Methoxyfenozide; Pesticide Tolerances; Correction. Federal Register 89: 3891. United States Environmental Protection Agency.  
<https://www.regulations.gov/document/EPA-HQ-OPP-2020-0336-0016>.

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