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SUBJECT: HUMAN HEALTH REFERENCE LEVELS FOR BENZOBICYCLON AND ITS DEGRADATE METABOLITE B IN SURFACE WATER

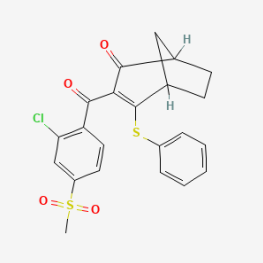
On November 16, 2020 the Department of Pesticide Regulation's (DPR) Pesticide Registration Branch requested that the Human Health Assessment Branch (HHA) provide Human Health Reference Levels (HHRLs) for DPR's Surface Water Protection Program (SWPP) of the Environmental Monitoring Branch (EMB) for benzobicyclon and its degradate, metabolite B [3-(2-chloro-4-methylsulfonylbenzoyl)bicyclo[3.2.1]octane-2,4-dione]. These HHRLs were applicable for screening when the parent and/or degradates were detected in surface water following reduced holding time in rice fields north (upstream) of the greater Sacramento area. Subsequently, on July 26, 2023, the SWPP requested that HHA provide HHRLs for screening model-estimated concentrations of benzobicyclon and metabolite B in surface water to determine whether then proposed expanded use for rice crops would pose a significant risk to human health through drinking water exposure (DPR, 2023). Registration for these uses was approved in November 2023 for the 2024 rice growing season (DPR, 2024e). The updated DPR HHRLs for benzobicyclon and metabolite B in surface water supersede the corresponding HHRLs established in 2021, 2023, and 2024 (DPR, 2021b; DPR, 2023; DPR, 2024d). The updated HHRLs reflect HHA's revised approach which now establishes separate acute and chronic HHRLs for surface water.

Human Health Reference Levels (HHRLs) in Surface Water:

1. HHA calculated Human Health Reference Levels (HHRLs) to be used for detected or model-estimated residues of benzobicyclon and its degradate, metabolite B (3-(2-chloro-4-methylsulfonylbenzoyl) bicyclo[3.2.1]octane-2,4-dione), in surface water 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. DPR Acute Surface Water HHRLs for benzobicyclon and metabolite B at 3368 and 1421 parts-per-billion (ppb), respectively, apply to the evaluation of **maximum** residue concentrations in drinking water from surface water sources. Benzobicyclon and metabolite B residue concentrations equal to or less than their corresponding DPR Acute Surface Water HHRLs are not expected to pose a risk to human health, including for sensitive subpopulations. The DPR Acute Surface Water HHRL for benzobicyclon (3368 ppb) supersedes the corresponding HHRL of 3269 ppb issued in 2021 (DPR, 2021b). The DPR Acute Surface Water HHRL of 1421 ppb for metabolite B supersedes corresponding HHRLs (0.4 and 40 ppb) issued in 2021, 2023, and 2024 (DPR, 2021b; DPR, 2023; DPR, 2024d).
3. DPR Chronic Surface Water HHRLs for benzobicyclon and metabolite B at 1280 and 8 ppb, respectively, apply to the evaluation of **average** residue concentrations in surface water sources. Average residue concentrations of benzobicyclon and metabolite B in surface water equal to or less than their corresponding DPR Chronic Surface Water HHRLs are not expected to pose a chronic risk to human health, including for sensitive subpopulations.

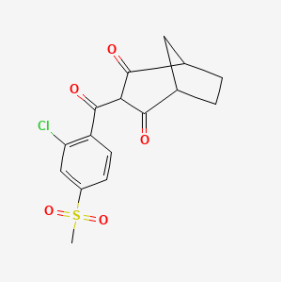
Background

Technical Name: Benzobicyclon
Chemical Name: 3-(2-chloro-4-methylsulfonylbenzoyl)-4-phenylsulfanylbicyclo[3.2.1]oct-3-en-2-one
Chemical Abstracts Service Registry Number (CAS #): 156963-66-5
Molecular Weight: 447.0 g/mol (NIH, 2024b)
Chemical Structure:



(NIH, 2024b)

Technical Name: Metabolite B
Chemical Name: 3-(2-chloro-4-methylsulfonylbenzoyl)bicyclo[3.2.1]octane-2,4-dione
Chemical Abstracts Service Registry Number (CAS #): 126656-88-0
Molecular Weight: 354.8 g/mol (NIH, 2024a)
Chemical Structure:



(NIH, 2024a)

Benzobicyclon is used for selective pre- and post-emergence control of susceptible grasses and broadleaf and sedge weeds for water-seeded rice (US EPA, 2021d). It is also used on wheat, barley, and corn (US EPA, 2021g). Benzobicyclon was first registered by US EPA in 2017 and was subsequently registered for use in California in the same year (US EPA, 2017h; DPR, 2024e). As of May 2024, there are two products actively registered for use in California (DPR, 2024e). According to the most recent available data from the DPR's Pesticide Use Reporting (PUR) database, 41,000 pounds of benzobicyclon-associated pesticides were used in 2450 California agricultural applications in 2021 (DPR, 2021a).

Benzobicyclon functions as a pro-pesticide. It undergoes hydrolysis or photolysis of the thiophenyl group to generate the active herbicidal metabolite B, an inhibitor of p-hydroxylphenyl-pyruvate dioxygenase (HPPD) that blocks prenylquinone biosynthesis (carotenoid synthesis) in plants (US EPA, 2017e; US EPA, 2020b; US EPA, 2021g). As of 2021, there were eight HPPD inhibitors, forming the HPPD common mechanism group (CMG), registered for use as herbicides by US EPA: isoxaflutole, mesotrione, tembotrione, pyrasulfotole,

topramezone, bicyclopyrone, tolpyralate, and benzobicyclon (producing metabolite B) (US EPA, 2020b; US EPA, 2021g). Unlike benzobicyclon, metabolite B is persistent in the aquatic environment and is a residue of concern in drinking water (US EPA, 2017e; US EPA, 2021b). Benzobicyclon does not induce effects in mammals commonly seen after inhibition of the HPPD enzyme, and therefore, is not assessed together with the HPPD CMG (US EPA, 2021g).

Recent human health risk assessments conducted by US EPA reevaluated the human health toxicity of benzobicyclon, metabolite B, and cumulative risk of HPPD inhibitors on mammalian systems (US EPA, 2016a; US EPA, 2017e; US EPA, 2017a; US EPA, 2020d; US EPA, 2020a; US EPA, 2020b; US EPA, 2020c; US EPA, 2021d; US EPA, 2021b; US EPA, 2021g). In this evaluation, HHA used the most recent toxicological endpoints for benzobicyclon and tembotrione (a member of the HPPD inhibitor CMG whose database was used as a surrogate for metabolite B) to establish HHRLs for benzobicyclon and metabolite B in drinking water. US EPA's cumulative screening-level analyses concluded that cumulative risk of HPPD inhibitors is not of concern (US EPA, 2021g).

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	2000	Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)	US EPA, 2000
US EPA	2007	PP#5F7009: Tembotrione. Human-Health Risk Assessment for Proposed Uses on Field Corn, Sweet Corn and Popcorn. PC Code 012808. DP# 325935. Decision # 362526.	US EPA, 2007
DPR	2009	Guidance for Dietary Exposure Assessment	DPR, 2009
EFSA	2013	Conclusion on the Peer Review of the Pesticide Risk Assessment of the Active Substance Tembotrione	EFSA, 2013
US EPA	2013	Environmental Protection Agency [EPA–HQ–OPP–2013–0026; FRL–9383–8] Pesticide Products; Registration Applications for New Active Ingredients	US EPA, 2013
DPR	2014	Summary of Toxicology Data Benzobicyclon	DPR, 2014
US EPA	2014	Dietary Exposure Evaluation Model User's Guide	US EPA, 2014
US EPA	2015	Human Health Ambient Water Quality Criteria: 2015 Update.	US EPA, 2015
DPR	2016	Summary of Toxicology Data Tembotrione	DPR, 2016

Table 1. Review of Regulatory Documents and Databases

Regulatory Agency	Year	Title	Reference(s)
US EPA	2016	Tembotrione. Human Health Assessment Scoping Document in Support of Registration Review	US EPA, 2016a
US EPA	2016	Tembotrione: Tier I (Scoping) Review of Human Incidents and Epidemiology	US EPA, 2016b
US EPA	2017	Benzobicyclon and Metabolite B. Acute and Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessment to Support the Section 3 Registration Request for Use on Rice.	US EPA, 2017a
US EPA	2017	Benzobicyclon Technical Notice of Unconditional Registration No. 10163-333	US EPA, 2017b
US EPA	2017	Benzobicyclon. Occupational and Residential Exposure Assessment to Support Registration of the New Active Ingredient on Water Seeded Rice in California	US EPA, 2017c
US EPA	2017	Benzobicyclon. Revised Human Health Risk Assessment for the Section 3 Registration Action on Rice and the Establishment of Permanent Tolerances for Residues in/on Rice	US EPA, 2017e
US EPA	2017	Benzobicyclon. Petition for the Establishment of Permanent Tolerances for Residues in/on Rice. Summary of Analytical Chemistry and Residue Data	US EPA, 2017d
US EPA	2017	Drinking Water Assessment for the Proposed Use of Benzobicyclon on Rice in California	US EPA, 2017f
US EPA	2017	Environmental Fate and Ecological Risk Assessment for Use of the New Herbicide Benzobicyclon for Weed Control in California Rice	US EPA, 2017g
US EPA	2017	Final Registration Decision of the New Active Ingredient Benzobicyclon	US EPA, 2017h
US EPA	2017	Proposed Registration Decision of the New Active Ingredient Benzobicyclon	US EPA, 2017i
US EPA	2017	Review of Benefits of the Registration of Benzobicyclon on California Rice	US EPA, 2017j
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
USGS	2018	Health-Based Screening Levels for Evaluating Water-Quality Data	USGS, 2018
US EPA	2020	Drinking Water Assessment in Support of Registration Review of Tembotrione	US EPA, 2020a
US EPA	2020	HPPD Inhibiting Herbicides: State of the Science	US EPA, 2020b
US EPA	2020	Tembotrione Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessment to Support the Human Health Risk Assessment for Registration Review	US EPA, 2020c
US EPA	2020	Tembotrione. Draft Human Health Risk Assessment in Support of Registration Review	US EPA, 2020d

Table 1. Review of Regulatory Documents and Databases

Regulatory Agency	Year	Title	Reference(s)
US EPA	2020	Tembotrione: Data Evaluation Records for Mammalian Toxicity Studies	US EPA, 2020e
US EPA	2020	Tembotrione: Data Evaluation Records for Mammalian Toxicity Studies	US EPA, 2020f
DPR	2021	2021 Annual Statewide Pesticide Use Report Chemical Totals	DPR, 2021a
DPR	2021	Evaluation Report - Pesticide: Benzobicyclon	DPR, 2021b
US EPA	2021	2021 Human Health Benchmarks for Pesticides	US EPA, 2021a
US EPA	2021	Benzobicyclon and Metabolite B. Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessment to Support the New National Expansion Use Request on Rice	US EPA, 2021b
US EPA	2021	Benzobicyclon. Submission to Extend the Regional Registration Use on Rice and Increase the Established Tolerance. Summary of Analytical Chemistry and Residue Data	US EPA, 2021c
US EPA	2021	Benzobicyclon: Section 3 Risk Assessment for Proposed New Formulation, Increase to the Established Tolerance, and National Use Expansion on Rice	US EPA, 2021d
US EPA	2021	Environmental Protection Agency 40 CFR Part 180 [EPA–HQ–OPP–2020–0391; FRL–8991–01–OCSPP] Pesticide Tolerances: Benzobicyclon	US EPA, 2021e
US EPA	2021	Human Health Benchmarks for Pesticides: Updated 2021 Technical Document	US EPA, 2021f
US EPA	2021	P-Hydroxyphenyl-Pyruvate Dioxygenase (HPPD) Inhibitors Cumulative Risk Assessment: Benzobicyclon, Bicyclopyrone, Isoxaflutole, Mesotrione, Pyrasulfotole, Tembotrione, Tolpyralate, and Topramezone	US EPA, 2021g
US EPA	2021	Tembotrione. Interim Registration Review Decision Case Number 7273	US EPA, 2021h
US EPA	2021	Tembotrione: Response to Comments on the Draft Human Health Risk Assessment for Registration Review	US EPA, 2021i
OEHHA	2023	The Proposition 65 List.	OEHHA, 2023
US EPA	2023	Integrated Risk Information System (IRIS) Glossary	US EPA, 2023a
US EPA	2023	Provisional Peer-Reviewed Toxicity Values (PPRTVs) Assessments	US EPA, 2023b
US EPA	2023	Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions	US EPA, 2023c
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	Human Health Reference Levels for Benzobicyclon and Its Degradate Metabolite B in Groundwater and Surface Water	DPR, 2024d

Table 1. Review of Regulatory Documents and Databases

Regulatory Agency	Year	Title	Reference(s)
DPR	2024	Search for Chemical Ingredient by Partial Name, Chemical Code or CAS Number	DPR, 2024e
eCFR	2024	Code of Federal Regulation. § 180.693 Benzobicyclon; tolerances for residues	eCFR, 2024
OEHHA	2024	Public Health Goals (PHGs)	OEHHA, 2024
US EPA	2024	CompTox Chemicals Dashboard: Benzobicyclon	US EPA, 2024a
US EPA	2024	CompTox Chemicals Dashboard: Bicyclo[3.2.1]octane-2,4-dione, 3-[2-chloro-4-(methylsulfonyl)benzoyl]-	US EPA, 2024b
US EPA	2024	CompTox Chemicals Dashboard: Tembotrione	US EPA, 2024c
US EPA	2024	Human Health Water Quality Criteria and Methods for Toxics	US EPA, 2024d
US EPA	2024	Incident Data System (IDS) - Incidents Submitted in Aggregate	US EPA, 2024e

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

Benzobicyclon has an acute Toxicity Category[1] value of IV for oral and inhalation hazards and was determined to be Toxicity Category III for dermal hazards based on median lethal doses. It is not a skin sensitizer or skin irritant, and is considered minimally irritating to eyes (Category IV) (US EPA, 2021d). US EPA classified benzobicyclon as "Not likely to be Carcinogenic to Humans" based on no evidence of treatment-related tumors in carcinogenicity studies in mice and rats (US EPA, 2021d).

Benzobicyclon and metabolite B are 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).

Effects reported after subchronic and chronic exposure of rats to benzobicyclon included hydropic degeneration in basophilic cells of pituitaries in F1 generation males and tubular cytotoxicity secondary to α2u-globulin nephropathy (US EPA, 2017e; US EPA, 2021d).

[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).

Unlike the parent benzobicyclon, metabolite B induced toxicity similar to the other HPPD inhibitors, specifically ocular toxicity in rats and abnormal skeletal ossification in fetuses of rats, rabbits and mice (US EPA, 2020d; US EPA, 2021d). These effects are consistent with the established adverse outcome pathway (AOP) for HPPD inhibitors, in which inhibition of HPPD prevents the formation of homogentisate (HGA), an intermediate in the catabolism of tyrosine, leading to accumulation of tyrosine in the body (US EPA, 2020b). The ocular and developmental effects correlate with elevated systemic tyrosine levels. Studies showed that humans and mice, but not rats, have alternative pathways to catabolize tyrosine through the tyrosine aminotransferase (TAT) pathway to reduce toxicity (US EPA, 2020b; US EPA, 2021g). Although dogs and rabbits had similar TAT activity as rats, tyrosine accumulation in dogs was lower than in rats but higher than mice, whereas rabbits had developmental toxicity close to rats by exhibiting skeletal effects at low doses (US EPA, 2020b). US EPA determined that mice and dogs are the most relevant surrogates for human health risk assessment of HPPD inhibitors (US EPA, 2020b; US EPA, 2021d).

HHA evaluated all required toxicity data submitted as part of registration for benzobicyclon in California but has not conducted a human health risk assessment (DPR, 2014; DPR, 2016). For purposes of this evaluation, HHA reviewed relevant regulatory documents (Table 1) and adopted toxicological endpoints established by US EPA (US EPA, 2020d; US EPA, 2021d; US EPA, 2021b; US EPA, 2021g)

Benzobicyclon

US EPA has not established an acute point of departure (POD) for benzobicyclon but did establish a chronic POD of 63.6 mg/kg/day that was a no observed adverse effect level (NOAEL) based on hydropic degeneration of basophilic cells in the pituitaries of F1 generation males reported at the lowest observed adverse effect level (LOAEL) of 1320 mg/kg/day in a reproductive study in rats (US EPA, 2017e; US EPA, 2021d). This NOAEL was divided by a total uncertainty factor (UF_{TOTAL}) of 100 to calculate a chronic reference dose (cRfD[2]) of 0.64 mg/kg/day. The UF_{TOTAL} is comprised of a factor of 10x for interspecies extrapolation (UF_A) and 10x for intraspecies variation (UF_H) (US EPA, 2007; US EPA, 2021d; US EPA, 2021b). US EPA considered this cRfD to be applicable for incidental oral short-term exposures (1–30 days), so it was used to calculate both acute and chronic HHRLs for benzobicyclon (US EPA, 2021d; US EPA, 2021b).

[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, 2023a).

Metabolite B

The toxicology database for metabolite B was limited. The PODs established by US EPA for the related chemical tembotrione were used as surrogates for metabolite B (US EPA, 2017e; US EPA, 2021d). US EPA did not establish an acute POD for tembotrione but did establish a short-term (1–30 days) incidental oral POD. This POD was derived from a NOAEL of 27 mg/kg/day based on effects on hematology parameters and lesions in the liver, adrenal glands, eyes, and peripheral nerves observed at the LOAEL of 111 mg/kg/day in a subchronic oral study in dogs (DPR, 2016; US EPA, 2020d; US EPA, 2021h). The aRfD was 0.27 mg/kg/day after dividing the acute POD by a UF_{TOTAL} of 100 (10x for UF_A and 10x for UF_H) (US EPA, 2020d; US EPA, 2021h). The chronic POD was derived from a LOAEL of 4 mg/kg/day based on effects on the gallbladder, liver, kidneys, and hematological parameters in a chronic/carcinogenicity study in mice. The POD (0.4 mg/kg/day) was calculated by dividing the LOAEL by a 10x LOAEL-to-NOAEL extrapolation factor. The resulting NOAEL was then divided by a 10x for UF_A and a 10x for UF_H to calculate a cRfD of 0.004 mg/kg/day for tembotrione (US EPA, 2007; US EPA, 2021h; US EPA, 2021d; US EPA, 2021b).

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 benzobicyclon and metabolite B as the maximum safe exposure and the acute (95^{th} percentile) 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, 2014). HHA uses the 95^{th} 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).

Acute Surface Water Human Health Reference Levels for Benzobicyclon and Metabolite B
DPR Acute Surface Water HHRLs are for screening maximum pesticide residue concentrations in drinking water from a surface water body. As shown in Table 2, the DPR Acute Surface Water HHRLs for benzobicyclon and metabolite B in surface water was **3368** ppb and **1421** ppb, respectively. Maximum residue concentrations of benzobicyclon and metabolite B in surface water equal to, or less than, their respective DPR Acute Surface Water HHRLs (3368 and 1421 ppb) are not expected to pose an acute risk to human health, including for sensitive subpopulations.

Chronic Surface Water Human Health Reference Levels for Benzobicyclon and Metabolite B
DPR Chronic Surface Water HHRLs are for screening average pesticide residue concentrations in a surface water body and 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 make up the remainder (80%). RSCs are routinely used by regulatory agencies for deriving chronic screening levels for drinking water (US EPA, 2000; US EPA, 2015; US EPA, 2024d). DPR Chronic Surface Water HHRLs that incorporate RSCs are only appropriate for the evaluation of averaged (*i.e.*, mean) residue concentrations in surface water. As shown in Table 2, average residue concentrations of benzobicyclon and metabolite B in surface water equal to or less than the DPR Chronic Surface Water HHRLs of **1280** ppb and **8** ppb, respectively, are not expected to pose a risk to human health, including for sensitive subpopulations.

Other Reference or Regulatory Levels for Benzobicyclon and Metabolite B 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 regulatory levels for drinking water include US EPA enforceable Maximum Contaminant Levels (MCLs[3]), non-legally enforceable Health

[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).

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 issued a chronic HHBP of 3760 ppb for benzobicyclon (general population), and acute and chronic HHBPs for metabolite B with the acute HHBP of 1.8 ppb (children) and chronic HHBP of 0.2 ppb (general population) (US EPA, 2021a). It should be noted that the toxicological data used for the HHBPs for metabolite B had not been updated to be consistent with the most recent US EPA human health risk assessments (US EPA, 2021d; US EPA, 2021b). Although the chronic HHBP and the DPR Chronic Surface Water HHRL for benzobicyclon are both based on the same chronic POD, the US EPA chronic HHBP and DPR Chronic Surface Water HHRL for benzobicyclon differ because they were calculated using different parameters/assumptions (*e.g.* water consumption rates).

[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, 2021f).

[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).

Table 2. DPR Acute and Chronic Surface Water HHRLs[a] for Benzobicyclon and Metabolite B[b]

Residue	Acute or Chronic	Water Consumption Rates for Non-Nursing Infants[c] (L water/kg BW)	RfD[d] (mg/kg/day)	HHRL (ppb)	US EPA HHBP[e] (ppb)
Benzobicyclon	Acute (maximum residues)	0.19	0.64	**3368**[f]	NA
	Chronic (average residues)	0.10	0.64	**1280**	3760 (General Population)
Metabolite B	Acute (maximum residues)	0.19	0.27	**1421**[f]	1.8[g] (Children)
	Chronic (average residues)	0.10	0.004	**8**	0.2[g] (General Population)

BW: bodyweight; DPR: Department of Pesticide Regulation; HHBP: Human Health Benchmark for Pesticides; HHRL: Human Health Reference Level; L: liter; NA: not applicable; RfD: reference dose; ppb: parts-per-billion.

[a] A DPR Acute Surface Water HHRL is calculated for screening maximum pesticide residue concentrations in a surface water body, DPR Acute Surface Water HHRLs (ppb) = [acute RfD (mg/kg/day) x 1000] / [acute DWI]; A DPR Chronic Surface Water HHRL is applied for screening average pesticide concentrations in a surface water body, DPR Chronic Surface Water HHRLs (ppb) = [chronic RfD (mg/kg/day) x 1000 x RSC] / [chronic DWI]. DWI, daily water intake, is the acute (95th percentile) or chronic (mean) water consumption rates for non-nursing infants (see Note c); RSC: relative source contribution, assumed as 20% (US EPA, 2015).

[b] Metabolite B, 3-(2-chloro-4-methylsulfonylbenzoyl)bicyclo[3.2.1]octane-2,4-dione, is a degradate of benzobicyclon.

[c] Water consumption rates for non-nursing infants were 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 concentration 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 for benzobicyclon and metabolite B were established based on toxicology endpoints issued by US EPA as described in the text (US EPA, 2021d; US EPA, 2021b; US EPA, 2021h).

[e] 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). Acute HHBP for Children (ppb) = [acute RfD (mg/kg/day) x 1000] / [0.15 (L/kg/day) of DWI-BW ratio]; Chronic HHBP for General Population (ppb) = [chronic RfD (mg/kg/day) x 1000 x 0.2 RSC] / [0.0338 (L/kg/day) of DWI-BW ratio].

[f] The DPR Acute Surface Water HHRL for benzobicyclon (3368 ppb) supersedes the corresponding HHRL of 3269 ppb issued in 2021 (DPR, 2021b). The DPR Acute Surface Water HHRL for metabolite B (1421 ppb) supersedes the corresponding HHRLs (0.4 or 40 ppb) issued in 2021, 2023, and 2024 (DPR, 2021b; DPR, 2023; DPR, 2024d).

[g] US EPA HHBPs for metabolite B were based on outdated risk assessments for benzobicyclon and tembotrione.

The recommended HHRLs for screening benzobicyclon and metabolite B residues in surface water are **bolded**.

Conclusions

HHA calculated Human Health Reference Levels (HHRLs) to be used for benzobicyclon and its degradate, metabolite B, in drinking water from surface water sources. Maximum residue concentrations of benzobicyclon and metabolite B equal to or less than the DPR Acute Surface Water HHRLs of 3368 ppb and 1421 ppb, respectively, or average residue concentrations equal to or less than the DPR Chronic Surface Water HHRLs (1280 ppb and 8 ppb, respectively), are not expected to pose a risk to human health, including for sensitive subpopulations. The DPR Acute Surface Water HHRL for benzobicyclon (3368 ppb) supersedes the corresponding HHRL (3269 ppb) issued in 2021 (DPR, 2021b), and the DPR Acute Surface Water HHRL of 1421 ppb for metabolite B supersedes corresponding HHRLs (0.4 or 40 ppb) issued in 2021, 2023, and 2004 for surface water (DPR, 2021b; DPR, 2023; DPR, 2024d).

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