



Department of Pesticide Regulation

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MEMORANDUM

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VIA: Shelley DuTeaux, PhD MPH, Chief
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DATE: July 12, 2023

SUBJECT: RISKS FROM HUMAN EXPOSURE TO ATRAZINE AND ITS DEGRADATES
IN GROUNDWATER

On March 15, 2023, the Department of Pesticide Regulation's (DPR) Human Health Assessment Branch (HHA) was notified by the Environmental Monitoring Branch (EMB) that data from routine monitoring conducted by the Groundwater Protection Program (GWPP), and data from other agencies such as the California State Water Resources Control Board (SWRCB) and the United States Geological Survey (USGS) reported detections of atrazine and its degradates in California's groundwater. The highest detected concentrations were atrazine at 8.5 parts-per-billion (ppb), deethylatrazine (DEA) at 2 ppb, deisopropylatrazine/deethylsimazine (ACET) at 6 ppb, desethyldeisopropylatrazine (DACT) at 0.011 ppb, and hydroxyatrazine (OIET) at 0.042 ppb. The well with DEA at concentrations of 2 ppb also contained atrazine at 0.31 ppb, and the well with DACT at concentrations of 0.011 ppb contained ACET at 0.085 ppb. EMB requested that HHA determine if the highest detected concentration of each residue poses health concerns for individuals using the groundwater as a source of drinking water and provide Human Health Reference Levels (HHRLs) for screening detections of atrazine and its degradates in groundwater (see request, Appendix 1). This memorandum is in response to that request.

Conclusions and Recommendations:

1. HHA adopted the previously established Human Health Reference Level (HHRL) for simazine to be used when residues of atrazine and its degradates (deethylatrazine (DEA),

deisopropylatrazine (ACET), desethyldeisopropylatrazine (DACT)) are detected in groundwater. This HHRL is applicable to members of a chlorotriazine common mechanism group (CMG) that also includes simazine and propazine.

2. HHA calculated a HHRL to be used when residues of hydroxyatrazine (OIET) are detected 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 HHA. This HHRL is applicable to members of a hydroxytriazine CMG that includes OIET, hydroxypropazine, and hydroxysimazine, and their metabolites such as ammeline and desethylhydroxyatrazine.
3. Residues for chlorotriazine *or* hydroxytriazine CMG members should be summed and evaluated together using the corresponding HHRL if they co-occur in a well.
4. For chlorotriazines in drinking water, residue levels equal to or less than the DPR HHRL of 17 ppb, alone or in combination if detected in the same well sample, are not expected to pose a risk to human health including for sensitive subpopulations.
5. For hydroxytriazines in drinking water, residue levels equal to or less than the DPR HHRL of 100 ppb, alone or in combination if detected in the same well sample, are not expected to pose a risk to human health, including for sensitive subpopulations.
6. Based on above HHRLs for chlorotriazines and hydroxytriazines, neither the highest detected individual residues of atrazine, DEA, DACT, ACET or OIET nor the combined residues for atrazine and DEA or DACT and ACET co-occurring in wells should be considered acute or chronic health concerns.

Chemical Information

Chlorotriazines

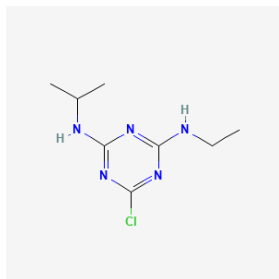
Technical Name: Atrazine

Chemical Name: 6-chloro-4-*N*-ethyl-2-*N*-propan-2-yl-1,3,5-triazine-2,4-diamine

Chemical Abstracts Service Registry Number (CAS): 1912-24-9

Molecular Weight: 215.68 g/mol (NIH, 2023a)

Chemical Structure:



(NIH, 2023a)

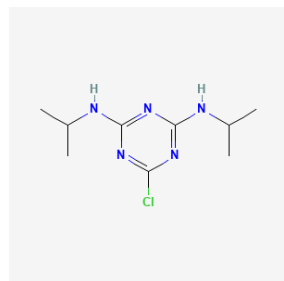
Technical Name: Propazine

Chemical Name: 6-chloro-2-*N*,4-*N*-di(propan-2-yl)-1,3,5-triazine-2,4-diamine

Chemical Abstracts Service Registry Number (CAS): 139-40-2

Molecular Weight: 229.71 g/mol (NIH, 2023b)

Chemical Structure:



(NIH, 2023b)

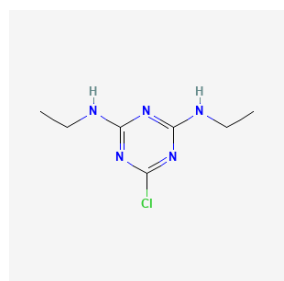
Technical Name: Simazine

Chemical Name: 6-chloro-2-N,4-N-diethyl-1,3,5-triazine-2,4-diamine

Chemical Abstracts Service Registry Number (CAS): 122-34-9

Molecular Weight: 201.66 g/mol (NIH, 2023c)

Chemical Structure:



(NIH, 2023c)

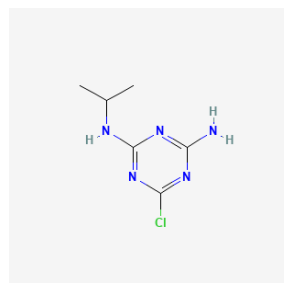
Technical Name: Deethylatrazine (DEA)

Chemical Name: 6-chloro-2-N-propan-2-yl-1,3,5-triazine-2,4-diamine

Chemical Abstracts Service Registry Number (CAS): 6190-65-4

Molecular Weight: 187.63 g/mol (NIH, 2023f)

Chemical Structure:



(NIH, 2023f)

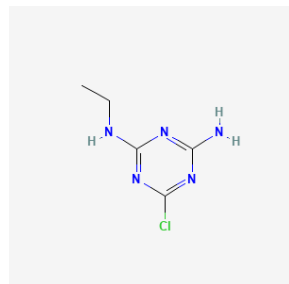
Technical Name: Deisopropylatrazine or Deethylsimazine (ACET)

Chemical Name: 6-chloro-2-N-ethyl-1,3,5-triazine-2,4-diamine

Chemical Abstracts Service Registry Number (CAS): 1007-28-9

Molecular Weight: 173.6 g/mol (NIH, 2023d)

Chemical Structure:



(NIH, 2023d)

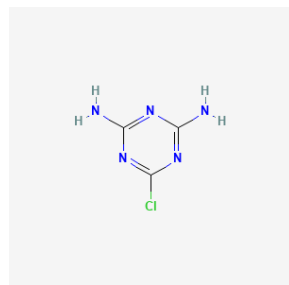
Technical Name: Desethyldeisopropylatrazine (DACT)

Chemical Name: 6-chloro-1,3,5-triazine-2,4-diamine

Chemical Abstracts Service Registry Number (CAS): 3397-62-4

Molecular Weight: 145.55 g/mol (NIH, 2023e)

Chemical Structure:



(NIH, 2023e)

Hydroxytriazines

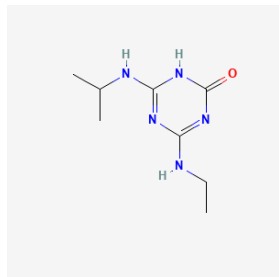
Technical Name: Hydroxyatrazine (OIET)

Chemical Name: 4-(ethylamino)-6-(propan-2-ylamino)-1H-1,3,5-triazin-2-one

Chemical Abstracts Service Registry Number (CAS): 2163-68-0

Molecular Weight: 197.24 g/mol (NIH, 2023g)

Chemical Structure:



(NIH, 2023g)

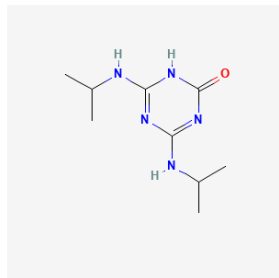
Technical Name: Hydroxypropazine

Chemical Name: 4,6-bis(propan-2-ylamino)-1H-1,3,5-triazin-2-one

Chemical Abstracts Service Registry Number (CAS): 7374-53-0

Molecular Weight: 211.26 g/mol (NIH, 2023k)

Chemical Structure:



(NIH, 2023k)

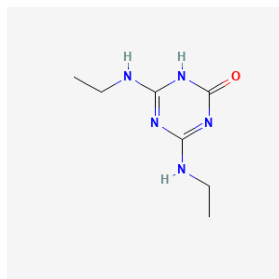
Technical Name: Hydroxysimazine

Chemical Name: 4,6-bis(ethylamino)-1H-1,3,5-triazin-2-one

Chemical Abstracts Service Registry Number (CAS): 2599-11-3

Molecular Weight: 183.21 g/mol (NIH, 2023i)

Chemical Structure:



(NIH, 2023i)

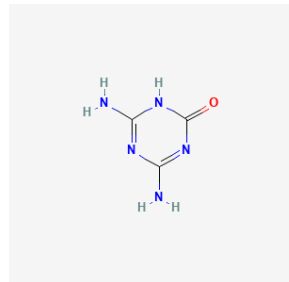
Technical Name: Ammeline

Chemical Name: 4,6-diamino-1H-1,3,5-triazin-2-one

Chemical Abstracts Service Registry Number (CAS): 645-92-1

Molecular Weight: 127.11 g/mol (NIH, 2023j)

Chemical Structure:



(NIH, 2023j)

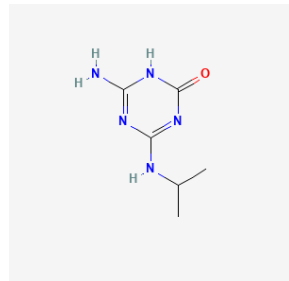
Technical Name: Desethylhydroxyatrazine

Chemical Name: 6-amino-4-(propan-2-ylamino)-1H-1,3,5-triazin-2-one

Chemical Abstracts Service Registry Number (CAS): 19988-24-0

Molecular Weight: 169.19 g/mol (NIH, 2023l)

Chemical Structure:



(NIH, 2023l)

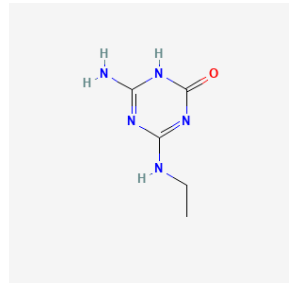
Technical Name: Deisopropylhydroxyatrazine

Chemical Name: 6-amino-4-(ethylamino)-1H-1,3,5-triazin-2-one

Chemical Abstracts Service Registry Number (CAS): 7313-54-4

Molecular Weight: 155.16 g/mol (NIH, 2023h)

Chemical Structure:



(NIH, 2023h)

Background

Atrazine, first registered by the US Environmental Protection Agency (US EPA) in 1958, is a chlorinated triazine herbicide selective against broadleaf and grassy weeds before they emerge (US EPA, 2018b; US EPA, 2020a). Its application includes agricultural uses (corn, sorghum, sugarcane, wheat, macadamia nuts, leafy vegetables, and guava), non-agricultural uses (ornamentals, Christmas trees, sod), and residential and recreational uses on turf in parks, school grounds, home lawns, as well as application to the exterior of some allowable commercial and industrial sites (US EPA, 2018b; US EPA, 2020a). Atrazine was first registered in California in 1982. As of March 2023, there are four products with active registrations in California (DPR, 2023c). According to the most currently available data from the DPR's Pesticide Use Reporting (PUR) database, 21,000 pounds of atrazine and atrazine-associated pesticides were used in 300 California agricultural applications in 2020 (DPR, 2020).

ACET, DACT, DEA and OIET are degradates of atrazine. Metabolically, ACET, DACT and DEA may also be derived from simazine and propazine. Figure 1 depicts the common chlorinated degradation pathways of atrazine, simazine, and propazine (US EPA, 2002). US EPA determined that atrazine, simazine, propazine, and their three major chlorinated metabolites DEA, ACET and DACT, share a common mechanism of toxicity for disruption of the hypothalamic-pituitary-gonadal (HPG) axis to cause neuroendocrine and endocrine-related developmental and reproductive effects (US EPA, 2002; US EPA, 2018b; US EPA, 2018f). These chemicals were evaluated as a CMG through a chlorotriazine cumulative risk assessment for human health (US EPA, 2002; US EPA, 2006; US EPA, 2018f; US EPA, 2020a).

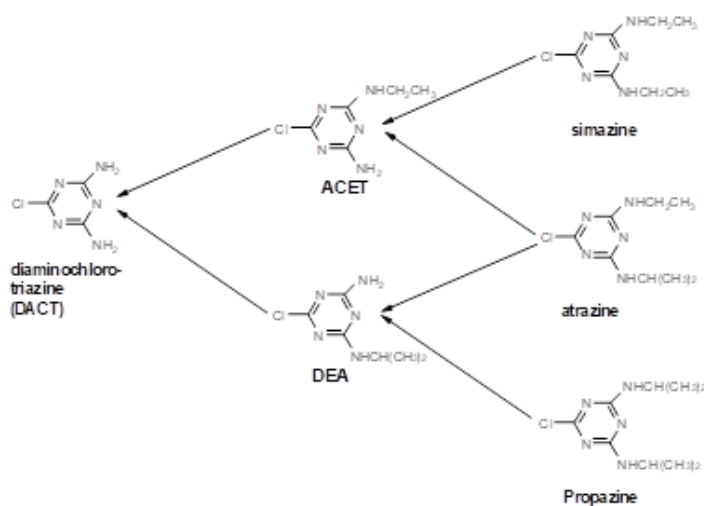


Figure 1. Chlorinated Triazine Herbicides and Their Chlorinated Degradation Products (Modified from (US EPA, 2002)). ACET, deisopropylatrazine; DEA, deethylatrazine.

OIET is a metabolite of atrazine derived from plants or livestock (US EPA, 2018b). Atrazine loses its chlorine atom to form OIET. Through a similar degradation pathway, hydroxypropazine and hydroxysimazine are derived from propazine and simazine, respectively. OIET was excluded from the chlorotriazine CMG because it lacks neuroendocrine-related toxicity (US EPA, 2002; US EPA, 2018f). OIET, as well as hydroxypropazine and hydroxysimazine and their metabolites of concern (e.g., desethylhydroxyatrazine, desisopropylhydroxyatrazine, and ammeline), are members of a hydroxytriazine CMG for human health risk assessment (US EPA, 2018f).

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	1990	Nonoccupational Pesticide Exposure Study NOPES	US EPA, 1990
USGS	1998	Pesticides in Surface and Ground Water of the United States: Summary of Results of the National Water Quality Assessment Program (NAWQA)	USGS, 1998
IARC	1999	Some Chemicals that Cause Tumours of the Kidney or Urinary Bladder in Rodents and Some Other Substances	IARC, 1999
DPR	2001	Atrazine Risk Characterization Document	DPR, 2001a
DPR	2001	Summary of Toxicology Data Atrazine	DPR, 2001b
US EPA	2002	The Grouping of a Series of Triazine Pesticides Based on a Common Mechanism of Toxicity	US EPA, 2002
ADSTR	2003	Toxicological Profile for Atrazine	ADSTR, 2003
US EPA	2003	Assessment of Potential Mitigation Measures for Atrazine	US EPA, 2003a
US EPA	2003	Atrazine: Addendum to Revised Human Health Risk Assessment for the Reregistration Eligibility Decision RED dated April 16, 2002. PC Code: 080803. DP Barcode: D287740	US EPA, 2003b
US EPA	2003	Review of Atrazine Cancer Epidemiology DP Barcode D295200, Chemical #080803	US EPA, 2003c
US EPA	2006	Triazine Cumulative Risk Assessment. HED Human Health Risk Assessment in Support of the Reregistration Eligibility Decisions for Atrazine, Simazine and Propazine. PC Codes: 080808, 080803, 080807. DP 317976	US EPA, 2006
DPR	2009	Guidance for Dietary Exposure Assessment	DPR, 2009
US EPA	2009	Final List of Initial Pesticide Active Ingredients and Pesticide Inert Ingredients to be Screened Under the Federal Food, Drug, and Cosmetic Act	US EPA, 2009a
US EPA	2009	National Primary Drinking Water Regulations	US EPA, 2009b
US EPA	2011	Integrated Risk Information System IRIS Glossary	US EPA, 2011
DPR	2012	Summary of Toxicity Data Simazine	DPR, 2012

Table 1. Review of Regulatory Documents and Databases

Regulatory Agency	Year	Title	Reference(s)
US EPA	2012	Use Characterization for Atrazine	US EPA, 2012
DPR	2013	Simazine Risk Characterization Document	DPR, 2013
US EPA	2013	Atrazine, Propazine, and Simazine. Human Health Risk Scoping Document in Support of Registration Review	US EPA, 2013
OEHHA	2015	Atrazine, Propazine, Simazine and their Chlorometabolites DACT, DEA And DIA Listed as Reproductive Toxicants	OEHHA, 2015
US EPA	2015	EDSP: Weight of Evidence Analysis of Potential Interaction with the Estrogen, Androgen or Thyroid Pathways Chemical: Atrazine	US EPA, 2015a
US EPA	2015	Propazine. Acute and Chronic Dietary Food Only Exposure Assessments for Registration Review	US EPA, 2015b
OEHHA	2016	Chemicals Listed Effective July 16, 2016 as Known to the State of California to Cause Reproductive Toxicity: Atrazine, Propazine, Simazine and their Chlorometabolites DACT, DEA and DIA.	OEHHA, 2016
US EPA	2016	Environmental Fate and Effects Division Review of Environmental Effects Studies for Atrazine	US EPA, 2016a
US EPA	2016	Refined Ecological Risk Assessment for Atrazine	US EPA, 2016b
OEHHA	2017	Amendment to Section 25805 Maximum Allowable Dose Levels (Oral Exposure) for Atrazine, Propazine, Simazine, And Their Chlorometabolites 2,4-Diamino-6-Chloro-S-Triazine (DACT, Des-Ethyl Atrazine (DEA), and Des-Isopropyl Atrazine (DIA)	OEHHA, 2017
US EPA	2017	National Primary Drinking Water Regulations; Announcement of the Results of EPA’s Review of Existing Drinking Water Standards and Request for Public Comment and/or Information on Related Issues	US EPA, 2017
US EPA	2018	2018 Edition of the Drinking Water Standards and Health Advisories Tables	US EPA, 2018a
US EPA	2018	Atrazine. Draft Human Health Risk Assessment for Registration Review	US EPA, 2018b
US EPA	2018	Atrazine. Occupational and Residential Exposure Assessment for the Registration Review Risk Assessment	US EPA, 2018c
US EPA	2018	Atrazine: Tier II Epidemiology Report	US EPA, 2018d
US EPA	2018	Chlorotriazines. Toxicology Systematic Literature Review - Atrazine, Simazine and Propazine	US EPA, 2018e
US EPA	2018	Chlorotriazines: Cumulative Risk Assessment - Atrazine, Propazine, and Simazine	US EPA, 2018f
US EPA	2018	Label Review Manual, Chapter 7: Precautionary Statements	US EPA, 2018g
US EPA	2018	Simazine. Human Health Risk Assessment for Registration Review and to Support the Registration of Proposed Uses on Citrus Fruit (Crop Group 10-10), Pome Fruit (Crop Group 11-10), Stone Fruit (Crop Group 12-12), Tree Nuts (Crop Group 14-12), and Tolerance Amendment for Almond Hulls.	US EPA, 2018h
USGS	2018	Health-Based Screening Levels for Evaluating Water-Quality Data	USGS, 2018a
USGS	2018	Health-Based Screening Levels: Updated 2018 Technical Information	USGS, 2018b

Table 1. Review of Regulatory Documents and Databases

Regulatory Agency	Year	Title	Reference(s)
US EPA	2019	Community Right-to-Know; Corrections to Toxics Release Inventory (TRI) Reporting Requirements.	US EPA, 2019a
US EPA	2019	Draft Human Health Risk Assessment for Registration Review Table 11.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Atrazine	US EPA, 2019b
DPR	2020	2020 Annual Statewide Pesticide Use Report Chemical Totals	DPR, 2020
US EPA	2020	Atrazine: Interim Registration Review Decision Case Number 0062	US EPA, 2020a
US EPA	2020	Simazine: Interim Registration Review Decision Case Number 0070	US EPA, 2020c
US EPA	2020	Propazine Interim Registration Review Decision Case Number 0230	US EPA, 2020b
US EPA	2021	2021 Human Health Benchmarks for Pesticides	US EPA, 2021a
US EPA	2021	Drinking Water Contaminant Candidate List 5—Draft	US EPA, 2021b
US EPA	2021	Human Health Benchmarks for Pesticides: Updated 2021 Technical Document	US EPA, 2021c
DPR	2022	Risks from Human Exposure to Simazine Residues in Groundwater	DPR, 2022
US EPA	2022	Pesticide Tolerance; Exemptions, Petitions, Revocations, etc.: Simazine	US EPA, 2022a
US EPA	2022	Proposed Revisions to the Atrazine Interim Registration Review Decision, Case Number 0062	US EPA, 2022b
DPR	2023	California Code of Regulations Title 3. Food and Agriculture Division 6. Pesticides and Pest Control Operations	DPR, 2023a
DPR	2023	California Pesticide Illness Query CalPIQ	DPR, 2023b
DPR	2023	Search for Chemical Ingredient by Partial Name, Chemical Code or CAS Number	DPR, 2023c
eCFR	2023	Code of Federal Regulation. §180.220 Atrazine; tolerances for residues	eCFR, 2023
OEHHA	2023	The Proposition 65 List.	OEHHA, 2023
US EPA	2023	CompTox Chemicals Dashboard: 2-Hydroxyatrazine	US EPA, 2023a
US EPA	2023	CompTox Chemicals Dashboard: 6-Chloro-1,3,5-triazine-2,4-diamine	US EPA, 2023b
US EPA	2023	CompTox Chemicals Dashboard: Atrazine	US EPA, 2023c
US EPA	2023	CompTox Chemicals Dashboard: Deisopropylatrazine	US EPA, 2023d
US EPA	2023	CompTox Chemicals Dashboard: s-Chloroaminoisopropylaminotriazine	US EPA, 2023e
ADSTR: Agency for Toxic Substances and Disease Registry; DPR: Department of Pesticide Regulation; eCFR: Electronic Code of Federal Regulations; NIH: National Institute of Health; IARC: International Agency for Research on Cancer; US EPA: United States Environmental Protection Agency; USGS: United States Geological Survey; OEHHA: Office of Environmental Health Hazard Assessment			

Summary of Toxicology

Atrazine has an acute Toxicity Category¹ value of III for oral and dermal toxicities and was determined to be Toxicity Category IV for inhalation toxicity based on median lethal doses. It is not a skin sensitizer or an eye or skin irritant (US EPA, 2018b). US EPA classified atrazine as "not likely to be carcinogenic to humans" based on the Mode of Action analysis of differences between rat and human neuroendocrine behaviors (US EPA, 2018b; US EPA, 2020a)

Atrazine has been used as a model compound for characterizing the toxicity for other members of chlorotriazine and hydroxytriazine CMGs (US EPA, 2002; US EPA, 2018f). Neurotoxicity, immunotoxicity, and developmental toxicity have been reported for chlorotriazines with some effects mediated by the perturbation of neuroendocrine system signaling (US EPA, 2018b). Atrazine, propazine and simazine were subject to Tier 1 screening in the Endocrine Disruptor Screening Program (EDSP) to determine if they have the potential to interact with the estrogen, androgen or thyroid signal pathways (US EPA, 2015a). The primary toxicity target for hydroxytriazines (e.g., OIET and others) is the kidney (US EPA, 2002; US EPA, 2018f).

Because of developmental and reproductive toxicity, atrazine, propazine, simazine, ACET, DEA, and DACT were 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, 2016; OEHHA, 2023). OIET is not on the Proposition 65 list (OEHHA, 2023).

In rats and rabbits, exposure to atrazine during pregnancy resulted in delayed ossification in fetuses. Subchronic and chronic oral treatment of laboratory animals with atrazine resulted in reductions of bodyweight (DPR, 2001a; US EPA, 2018b). In rats, hematological abnormalities, renal histopathology, and alterations in the estrus cycle were noted in subchronic studies and oncogenic effects (mammary gland tumors or interstitial cell tumors) were observed in chronic studies (DPR, 2001a; US EPA, 2018b). In dogs, the primary subchronic and chronic effects were related to cardiotoxicity. ACET, DACT and DEA toxicity studies had effects consistent with the above observations (DPR, 2001a; US EPA, 2002; US EPA, 2018b). Hydroxytriazines were associated with kidney toxicity (US EPA, 2018f; US EPA, 2018b).

DPR's Pesticide Illness Surveillance Program (PISP) maintains a database of pesticide-related illnesses and injuries reported in California from 1992 to 2018 (the most recent data available). There were two reported cases involving exposure to atrazine in combination with other active

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, 2018g).

ingredients (DPR, 2023b). No cases were reported for propazine. Among 40 reported cases associated with simazine, only one case involved exposure to simazine alone. Nausea, dizziness, vomiting, and throat redness were reported by the affected worker (DPR, 2023b).

HHA evaluated all required toxicity data submitted for the active ingredient atrazine, propazine, and simazine as part of registration in California. While this evaluation initially focused on atrazine, regulatory endpoints for all members of the chlorotriazine and hydroxytriazine CMGs were considered together because the parent chemicals share metabolites and degradates (see Appendix 2). For this evaluation, HHA adopted points of departure (PODs) established in the Risk Characterization Documents (RCDs) for atrazine and simazine (DPR, 2001a; DPR, 2013; DPR, 2022).

Atrazine, ACET, DACT, DEA and Other Chlorotriazines

The acute reference dose (aRfD²) and chronic reference dose (cRfD) for simazine were chosen to represent members of the chlorotriazine CMG (see Appendix 2). The previously established simazine HHRL was based on the simazine chronic POD (DPR, 2022). The chronic POD was a no observed effect level (NOEL) of 0.52 mg/kg/day based on decreased bodyweight, food intake, and survival rates in females observed at a lowest observed effect level (LOEL) of 5.34 mg/kg/day in a 2-year rat study (DPR, 2013; DPR, 2022). This chronic POD was adopted for chlorotriazines because it resulted in the lowest cRfD evaluated and was therefore protective for all members of the chlorotriazine CMG. The cRfD of 0.0017 mg/kg/day was calculated by dividing the chronic NOEL by the UF_{TOTAL} of 300 (10x each for interspecies and intraspecies extrapolation, and 3x factor for insufficient data relating to the neuroendocrine effects on reproduction and development) (DPR, 2013).

OIET and Other Hydroxytriazines

The hydroxytriazines (e.g., OIET and others) were evaluated separately from chlorotriazines because they belong to a separate CMG. The acute POD was a NOEL of 3.75 mg/kg/day derived from the LOEL of 37.5 mg/kg/day based on kidney degradation and inflammation observed in a 13-week toxicity study of OIET in dogs (DPR, 2001a). The acute POD for OIET was adopted for hydroxytriazines. The aRfD 0.038 mg/kg/day was calculated by dividing the acute POD by the UF_{TOTAL} of 100 (10x each for interspecies and intraspecies extrapolation) (DPR, 2001a). The hydroxytriazine chronic POD was a NOEL of 1.0 mg/kg/day based on chronic nephropathy at a LOEL of 7.8 mg/kg/day in a 2-year study of OIET in rats. The cRfD of 0.010 mg/kg/day was calculated by dividing the chronic POD by the UF_{TOTAL} of 100 (10x each for interspecies and intraspecies extrapolation) (DPR, 2001a).

² A reference dose (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, 2011).

Calculation of Human Health Reference Levels for Chlorotriazines and Hydroxytriazines

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 chlorotriazines and hydroxytriazines as the maximum safe exposure and the acute (95th 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 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).

Human Health Reference Levels for Chlorotriazines

HHA adopted the cRfD and corresponding HHRL for simazine to screen residues of chlorotriazines in groundwater (Table 2) (DPR, 2022). This HHRL is intended to be used for screening maximum detected residue levels. Residue levels of chlorotriazines in groundwater equal to or less than the DPR HHRL of **17 ppb**, alone or in combination if detected in the same well sample, are not expected to pose a risk to human health, including for sensitive subpopulations.

Human Health Reference Levels for Hydroxytriazines

HHA calculated acute and chronic HHRLs for hydroxytriazines in groundwater with the established RfDs for OIET. Based on the results shown in Table 2, the chronic HHRL level of **100 ppb** was selected as the HHRL for hydroxytriazines in groundwater and is intended to be used for screening maximum detected residue levels. Hydroxytriazines in groundwater equal to or less than the DPR HHRL of **100 ppb**, alone or in combination if detected in the same well sample, are not expected to pose a risk to human health, including for sensitive subpopulations.

Other Reference or Regulatory Levels for Drinking Water

US EPA issued enforceable Maximum Contaminant Levels (MCLs³) of 3 ppb for atrazine and 4 ppb for simazine. In addition, US EPA set the Drinking Water Equivalent Level (DWEL) of 700 ppb for both propazine and simazine in Health Advisories (HAs⁴) (US EPA, 2017; US EPA, 2018a) (Table 2). US EPA established a chronic Human Health Benchmark for Pesticides (HHBP⁵) for DACT of 11 ppb and 400 ppb for OIET for the general population (Table 2) (US EPA, 2021a). In addition, Health-Based Screening Levels (HBSLs⁶) database maintained by the US Geological Survey (USGS) noted a noncancer HBSL of 40 ppb for propazine (USGS, 2018a). The DWEL, HHBPs, HBSLs and DPR HHRLs for chlorotriazines or hydroxytriazines differ because they were calculated using different parameters and/or assumptions (e.g., PODs, consumption rates and relative source contribution (RSC) factors). The DPR HHRLs are the only reference level that is specifically intended to be used for screening maximum detected residue levels in groundwater.

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, 2021c).

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, 2018a).

Table 2. Acute and Chronic HHRLs for Chlorotriazines or Hydroxytriazines^a

Residue	Acute or Chronic	Consumption Rates for Non-Nursing Infants ^b (L water/kg BW)	RfD ^c (mg/kg/day)	HHRL ^d (ppb)	US EPA		
					MCL ^e (ppb)	DWEL ^f (ppb)	HHBP ^g (ppb)
Chlorotriazines (including atrazine, propazine, simazine, ACET, DACT, and DEA)	Chronic	0.10	0.0017	17	3	700	11 (for DACT) (General Population)
Hydroxytriazines (including OIET, hydroxypropazine, hydroxysimazine, ammeline, and desethylhydroxy-atrazine.)	Acute	0.19	0.038	200	NA	NA	NA
	Chronic	0.10	0.010	100	NA	NA	400 (General Population)

ACET: deisopropylatrazine; BW: bodyweight; DACT: desethyldeisopropylatrazine; DEA: deethylatrazine; DWEL: Drinking Water Equivalent Level; HHBP: Human Health Benchmark for Pesticides; HHRL: Human Health Reference Level; L: liter; MCL: Maximum Contaminant Level; NA: not applicable; OIET: hydroxyatrazine; RfD: reference dose; ppb: parts-per-billion.

^a Chlorotriazine’s chronic reference dose (cRfD) was based on the cRfD of simazine, which is the same for DPR HHRL of simazine (DPR, 2022). Hydroxytriazine’s RfDs were based on OIET’s RfDs as described in the main text.

^b 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.

^c Acute and chronic RfDs for chlorotriazines and hydroxytriazines were established by HHA as described in the text.

^d HHRL (ppb) = [RfD (mg/kg/day) x 1000 (µg/mg)] / Daily water intake (L/kg/day). Daily water intake is 95th percentile for acute or chronic (mean) water consumption rates for non-nursing infants.

^e A Maximum Contaminant Level (MCL) is the highest level of a contaminant that is allowed in drinking water. MCLs are enforceable standards (US EPA, 2018a).

^f A DWEL is a drinking water lifetime maximum noncarcinogenic safe exposure level when assuming 100% exposure from that medium. DWEL is a parameter of Health Advisories (HAs). An HA, not a legally enforceable Federal standard, serves as a technical guidance to assist Federal, State, and local officials (US EPA, 2018a).

^g An HHBP (ppb) for chronic exposure in general population = [chronic RfD (mg/kg bw/day) x 1000 (µg/mg) x 0.2 RSC / 0.0338 (L/kg/day) DWI-BW ratio]; DWI-BW: daily water intake-bodyweight; RSC: relative source contribution, assumed as 20% (US EPA, 2021a).

The recommended HHRLs for screening chlorotriazine and hydroxytriazine residues in drinking water are **bolded**.

Conclusions

HHA calculated Human Health Reference Levels (HHRLs) to be used when atrazine or its degradates are detected in groundwater or drinking water. Based on mode of action, atrazine, DEA, ACET, DACT, propazine, and simazine were evaluated together under the established chlorotriazine CMG, while OIET, hydroxypropazine, and hydroxysimazine, and their metabolites ammeline, desethylhydroxyatrazine, and desisopropylhydroxyatrazine, were evaluated together under the established hydroxytriazine CMG. For chlorotriazines, residue levels equal to or less than the DPR HHRL of **17 ppb**, alone or in combination if detected in the same well sample, are not expected to pose a risk to human health, including for sensitive subpopulations. Thus, the highest reported detections of atrazine, ACET, DACT, and DEA in groundwater should not be considered to pose an acute or chronic human health concern. For hydroxytriazines, residue levels equal to or less than the DPR HHRL of **100 ppb**, alone or in combination if detected in the same well sample, are not expected to pose a risk to human health, including for sensitive subpopulations. Thus, the highest reported detections of OIET in groundwater should not be considered to pose an acute or chronic human health concern.

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References

- ADSTR 2003. Toxicological Profile for Atrazine. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry. www.atsdr.cdc.gov/ToxProfiles/tp153.pdf.
- DPR 2001a. Atrazine Risk Characterization Document. Medical Toxicology Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.
- DPR 2001b. Summary of Toxicology Data Atrazine. Human Health Assessment Branch. 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 2012. Summary of Toxicology Data Simazine. Human Health Assessment Branch. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.
- DPR 2013. Simazine Risk Characterization Document. Medical Toxicology Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.
- DPR 2020. 2020 Annual Statewide Pesticide Use Report Chemical Totals. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. https://www.cdpr.ca.gov/docs/pur/pur20rep/pur_data/pur2020_subtotals_indexed_by_chemical.pdf.
- DPR 2022. Risks from Human Exposure to Simazine Residues in Groundwater. Human Health Assessment Branch. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. https://www.cdpr.ca.gov/docs/risk/rcd/simazine_risks_exposure_groundwater.pdf
- DPR 2023a. 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 March 23, 2023 from <https://www.cdpr.ca.gov/docs/legbills/calcode/040101.htm>.
- DPR 2023b. California Pesticide Illness Query (CalPIQ). Human Health Assessment Branch. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. Retrieved March 25, 2023 from https://apps.cdpr.ca.gov/calpiq/calpiq_input.cfm.

- DPR 2023c. Search for Chemical Ingredient by Partial Name, Chemical Code or CAS Number. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. Retrieved March 20, 2023 from <https://apps.cdpr.ca.gov/docs/chemical/master2.cfm>.
- eCFR 2023. Code of Federal Regulation. §180.220 Atrazine; tolerances for residues. United States Environmental Protection Agency. Retrieved March 20, 2023 from <https://www.ecfr.gov/current/title-40/chapter-I/subchapter-E/part-180/subpart-C/section-180.220>.
- IARC 1999. Some Chemicals that Cause Tumours of the Kidney or Urinary Bladder in Rodents and Some Other Substances. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 73. International Agency for Research on Cancer, World Health Organization. <https://publications.iarc.fr/91>.
- NIH 2023a. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 2256, Atrazine. Retrieved March 20, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Atrazine>.
- NIH 2023b. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 4937, Propazine. Retrieved June 5, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Propazine>.
- NIH 2023c. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 5216, Simazine. Retrieved June 5, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Simazine>.
- NIH 2023d. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 13878, Deisopropylatrazine. Retrieved March 20, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Deisopropylatrazine>.
- NIH 2023e. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 18831, 6-Chloro-1,3,5-triazine-2,4-diamine. Retrieved March 20, 2023 from https://pubchem.ncbi.nlm.nih.gov/compound/6-Chloro-1_3_5-triazine-2_4-diamine.
- NIH 2023f. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 22563, Deethylatrazine. Retrieved March 20, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Deethylatrazine>.
- NIH 2023g. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 135398733, Hydroxyatrazine. Retrieved March 20, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Hydroxyatrazine>.

- NIH 2023h. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 135398734, Deisopropylhydroxyatrazine. Retrieved June 5, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Deisopropylhydroxyatrazine>.
- NIH 2023i. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 135408659, Hydroxysimazine. Retrieved June 5, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Hydroxysimazine>.
- NIH 2023j. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 135408770, Ammeline. Retrieved June 5, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Ammeline>.
- NIH 2023k. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 135461611, 1,3,5-Triazin-2(1H)-one, 4,6-bis((1-methylethyl)amino)-. Retrieved June 5, 2023 from https://pubchem.ncbi.nlm.nih.gov/compound/4_6-bis_propan-2-ylamino_-1H-1_3_5-triazin-2-one.
- NIH 2023l. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 135510207, Atrazine-desethyl-2-hydroxy. Retrieved June 5, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Atrazine-desethyl-2-hydroxy>.
- OEHHA 2015. Atrazine, Propazine, Simazine and their Chlorometabolites DACT, DEA And DIA Listed as Reproductive Toxicants. The Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA. <https://oehha.ca.gov/proposition-65/cnr/atrazine-propazine-simazine-and-their-chlorometabolites-dact-dea-and-dia-listed>.
- OEHHA 2016. Chemicals Listed Effective July 16, 2016 as Known to the State of California to Cause Reproductive Toxicity: Atrazine, Propazine, Simazine and their Chlorometabolites DACT, DEA and DIA. The Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA. <https://oehha.ca.gov/proposition-65/cnr/atrazine-propazine-simazine-and-their-chlorometabolites-dact-dea-and-dia-0>.
- OEHHA 2017. Amendment to Section 25805 Maximum Allowable Dose Levels (Oral Exposure) for Atrazine, Propazine, Simazine, And Their Chlorometabolites 2,4-Diamino-6-Chloro-S-Triazine (DACT, Des-Ethyl Atrazine (DEA), and Des-Isopropyl Atrazine (DIA). The Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA. <https://oehha.ca.gov/media/downloads/cnr/triazinesmadl05122017.pdf>.
- OEHHA 2023. The Proposition 65 List. The Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA. Retrieved March 19, 2023 from <https://oehha.ca.gov/water/chemicals/atrazine>.

- US EPA 1990. Nonoccupational Pesticide Exposure Study (NOPES). United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPPT-2002-0066-0037>.
- US EPA 2002. The Grouping of a Series of Triazine Pesticides Based on a Common Mechanism of Toxicity. Health Effects Division, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2005-0481-0011>.
- US EPA 2003a. Assessment of Potential Mitigation Measures for Atrazine. Office Of Prevention, Pesticides and Toxic Substance, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2003-0367-0015>.
- US EPA 2003b. Atrazine: Addendum to Revised Human Health Risk Assessment for the Reregistration Eligibility Decision (RED) dated April 16, 2002. PC Code: 080803. DP Barcode: D287740. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2003-0072-0006>.
- US EPA 2003c. Review of Atrazine Cancer Epidemiology DP Barcode D295200, Chemical #080803. Office Of Prevention, Pesticides and Toxic Substance, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2003-0367-0004>.
- US EPA 2006. Triazine Cumulative Risk Assessment. HED Human Health Risk Assessment in Support of the Reregistration Eligibility Decisions for Atrazine, Simazine and Propazine. PC Codes: 080808, 080803, 080807. DP 317976. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2005-0481-0003>.
- US EPA 2009a. Final List of Initial Pesticide Active Ingredients and Pesticide Inert Ingredients to be Screened Under the Federal Food, Drug, and Cosmetic Act. Federal Register, Vol. 74, No. 71. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPPT-2004-0109-0080>.
- US EPA 2009b. National Primary Drinking Water Regulations. Office Of Ground Water and Drinking Water, United States Environmental Protection Agency. https://www.epa.gov/sites/default/files/2016-06/documents/npwdr_complete_table.pdf.
- US EPA 2011. Integrated Risk Information System (IRIS) Glossary. Integrated Risk Information System, United States Environmental Protection Agency. <https://www.epa.gov/iris/iris-glossary>.
- US EPA 2012. Use Characterization for Atrazine. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-0005>.

- US EPA 2013. Atrazine, Propazine and Simazine: Review of Human Incidents. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-0004>.
- US EPA 2014. 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 2015a. EDSP: Weight of Evidence Analysis of Potential Interaction with the Estrogen, Androgen or Thyroid Pathways Chemical: Atrazine. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-0313>.
- US EPA 2015b. Propazine. Acute and Chronic Dietary (Food Only) Exposure Assessments for Registration Review. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0250-0070>.
- US EPA 2016a. Environmental Fate and Effects Division Review of Environmental Effects Studies for Atrazine. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-0349>.
- US EPA 2016b. Refined Ecological Risk Assessment for Atrazine. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-0315>.
- US EPA 2017. National Primary Drinking Water Regulations; Announcement of the Results of EPA's Review of Existing Drinking Water Standards and Request for Public Comment and/or Information on Related Issues. Federal Register, Vol. 82, No. 7. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OW-2016-0627-0001>.
- 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. Atrazine. Draft Human Health Risk Assessment for Registration Review. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-1159>.
- US EPA 2018c. Atrazine. Occupational and Residential Exposure Assessment for the Registration Review Risk Assessment. Office Of Chemical Safety and Pollution

- Prevention, United States Environmental Protection Agency.
<https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-1155>.
- US EPA 2018d. Atrazine: Tier II Epidemiology Report. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency.
<https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-1266>.
- US EPA 2018e. Chlorotriazines. Toxicology Systematic Literature Review - Atrazine, Simazine and Propazine. Office Of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency.
<https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-1157>.
- US EPA 2018f. Chlorotriazines: Cumulative Risk Assessment - Atrazine, Propazine, and Simazine. Office Of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-1160>.
- US EPA 2018g. Label Review Manual, Chapter 7: Precautionary Statements. Office of Pesticide Programs, United States Environmental Protection Agency.
<https://www.epa.gov/sites/production/files/2018-04/documents/chap-07-mar-2018.pdf>.
- US EPA 2018h. Simazine. Human Health Risk Assessment for Registration Review and to Support the Registration of Proposed Uses on Citrus Fruit (Crop Group 10-10), Pome Fruit (Crop Group 11-10), Stone Fruit (Crop Group 12-12), Tree Nuts (Crop Group 14-12), and Tolerance Amendment for Almond Hulls. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency.
<https://www.regulations.gov/document/EPA-HQ-OPP-2012-0301-0006>.
- US EPA 2019a. Community Right-to-Know; Corrections to Toxics Release Inventory (TRI) Reporting Requirements. Federal Register. Vol. 84, No. 230. United States Environmental Protection Agency.
<https://www.federalregister.gov/documents/2019/11/29/2019-25356/community-right-to-know-corrections-to-toxics-release-inventory-tri-reporting-requirements>
- US EPA 2019b. Draft Human Health Risk Assessment for Registration Review Table 11.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Atrazine. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-1256>.
- US EPA 2020a. Atrazine: Interim Registration Review Decision Case Number 0062. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-1605>.

US EPA 2020b. Propazine Interim Registration Review Decision Case Number 0230. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0250-0112>.

US EPA 2020c. Simazine: Interim Registration Review Decision Case Number 0070. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0251-0174>.

US EPA 2021a. 2021 Human Health Benchmarks for Pesticides. Office Of Ground Water and Drinking Water, United States Environmental Protection Agency. Retrived October 24, 2022 from <https://www.epa.gov/sdwa/2021-human-health-benchmarks-pesticides>.

US EPA 2021b. Drinking Water Contaminant Candidate List 5—Draft. Federal Register. Vol. 86, No. 135. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OW-2018-0594-0031>.

US EPA 2021c. 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. Pesticide Tolerance; Exemptions, Petitions, Revocations, etc.: Simazine. United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2012-0301-0005>.

US EPA 2022b. Proposed Revisions to the Atrazine Interim Registration Review Decision, Case Number 0062. Office Of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0266-1625>.

US EPA 2023a. CompTox Chemicals Dashboard: 2-Hydroxyatrazine. United States Environmental Protection Agency. Retrieved March 20, 2023 from <https://comptox.epa.gov/dashboard/chemical/details/DTXSID6037807>.

US EPA 2023b. CompTox Chemicals Dashboard: 6-Chloro-1,3,5-triazine-2,4-diamine. United States Environmental Protection Agency. Retrieved March 20, 2023 from <https://comptox.epa.gov/dashboard/chemical/details/DTXSID1037806>.

US EPA 2023c. CompTox Chemicals Dashboard: Atrazine. United States Environmental Protection Agency. Retrieved March 20, 2023 from <https://comptox.epa.gov/dashboard/chemical/details/DTXSID9020112>.

US EPA 2023d. CompTox Chemicals Dashboard: Deisopropylatrazine. United States Environmental Protection Agency. Retrieved March 20, 2023 from <https://comptox.epa.gov/dashboard/chemical/details/DTXSID0037495>.

US EPA 2023e. CompTox Chemicals Dashboard: s-Chloroaminoisopropylaminotriazine. United States Environmental Protection Agency. Retrieved March 20, 2023 from <https://comptox.epa.gov/dashboard/chemical/details/DTXSID5037494>.

USGS 1998. Pesticides in Surface and Ground Water of the United States: Summary of Results of the National Water Quality Assessment Program (NAWQA). Pesticides National Synthesis Project, National Water-Quality Assessment, United States Geological Survey. <https://www.regulations.gov/document/EPA-HQ-OW-2008-0465-0037>

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

USGS 2018b. Health-Based Screening Levels: Updated 2018 Technical Information. United States Geological Survey. <https://water.usgs.gov/water-resources/hbsl/methods-guidance.html>.

Minh Pham
July 12, 2023
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Appendix 1: DPR Memo: Human Health Reference Level Request for Atrazine and Its Degradates in Groundwater 15 March 2023 (2 pages)



Julie Henderson
Director

Yana Garcia
Secretary for
Environmental Protection

MEMORANDUM

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

VIA: Minh Pham
Environmental Program Manager II
Environmental Monitoring Branch

Original Signed 3/16/23

FROM: Joy Dias
Environmental Program Manager I
Environmental Monitoring Branch

Original Signed 3/16/23

DATE: March 15, 2023

SUBJECT: HUMAN HEALTH REFERENCE LEVEL REQUEST FOR ATRAZINE AND ITS 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 atrazine and its degradates, DEA (deethyl-atrazine) and ACET (deethyl-simazine or deisopropyl-atrazine), due to their occurrence in groundwater and atrazine’s status as a 3CCR 6800(a) pesticide. 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). Groundwater monitoring data from other agencies, such as the California State Water Resources Control Board (SWRCB) and the United States Geological Survey (USGS), includes the atrazine degradates OIET (2-hydroxyatrazine) and desisopropyl desethyl atrazine. Table 1 lists the highest reported concentration of atrazine and its degradates. If the parent or a degradate of atrazine was also detected in that sample, the analyte and concentration are shown in the footnotes.

EMB requests the assistance of the Human Health Assessment Branch (HHA) in determining whether these detections pose a significant risk to human health and to provide human health reference levels for atrazine and its degradates to use for screening detections. ACET, a degradate of atrazine and simazine, is included in this request for completeness but was previously evaluated by HHA as part of the simazine request in 2022.

Table 1. Summary of the highest reported detections of atrazine and degradates from the Well Inventory Database.

Chemical	DPR Chemical Code	CAS Number	Sampling Agency	Maximum Concentration Reported (ppb)	Year
Atrazine	45	1912-24-9	DPR	8.5	1986
DEA	4051	6190-65-4	DPR	2*	1996
ACET	4096	1007-28-9	DPR	6	1994
OIET	6087	2163-68-0	SWRCB	0.042	2005
Desisopropyl desethyl atrazine	99904	3397-62-4	USGS	0.011**	2015

* Atrazine was also detected in this sample at 0.31 ppb

** ACET was also detected in this sample at 0.085 ppb

cc: Carissa Ganapathy, Senior Environmental Scientist (Supervisory)

Appendix 2. Summaries of Toxicological Endpoints for Atrazine, Propazine and Simazine based on regulatory documents of DPR or US EPA (2 Pages)

Table A1. Summary of Toxicological Endpoints for Atrazine, Propazine, Simazine or Chlorotriazines

Source	^a NOEL or NOAEL (mg/kg/day)	^b LOEL or LOAEL (mg/kg/day)	Uncertainty Factors (UF)	^c RfD (mg/kg/day)	Study Effects
Acute Endpoints					
Atrazine Risk Characterization Document (DPR, 2001a)	NOEL = 5	LOEL = 75	UF _A = 10x UF _H = 10x ^d FQPA SF = 1x	aRfD = 0.05	Developmental study in rabbits: maternal bodyweight loss and delayed fetus ossification
Atrazine by US EPA (US EPA, 2018b)	NOAEL = 10	LOAEL = 70	UF _A = 10x UF _H = 10x FQPA SF = 1x	aRfD = 0.1	Developmental studies in rats and rabbits: delayed fetus ossification
Propazine by US EPA (US EPA, 2015b)	NOAEL = 10	LOAEL = 100	UF _A = 10x UF _H = 10x FQPA SF = 1x	aRfD = 0.1	Developmental study in rats: delayed fetus ossification
Simazine Risk Characterization (Document DPR, 2013)	NOEL = 5	LOEL = 75	UF _A = 10x UF _H = 10x FQPA SF = 3x	aRfD = 0.016	Developmental study in rabbits: maternal bodyweight loss and delayed fetus ossification
Simazine by US EPA (US EPA, 2018h)	NOAEL = 30	LOAEL = 300	UF _A = 10x UF _H = 10x FQPA SF = 1x	aRfD = 0.3	Developmental study rats: delayed fetus ossification
Chlorotriazine by US EPA (US EPA, 2018f)	An acute cumulative dietary POD was not selected				
Chronic Endpoints					
Atrazine Risk Characterization Document (DPR, 2001a)	NOEL = 0.5	LOEL = 5	UF _A = 10x UF _H = 10x FQPA SF = 1x	cRfD = 0.005	1-Year study in dogs: abnormal cardiac activity and heart weight; extramedullary hematopoiesis in spleen
Atrazine by US EPA (US EPA, 2018b)	BMDL _{1SD} = 2.42	BMDL _{1SD} = 4.92	UF _A = 10x UF _H = 10x FQPA SF = 1x	cRfD = 0.024	^e 4-Day repeated exposures in rats: attenuation of LH surge
Propazine by US EPA (US EPA, 2015b)	Based on chronic toxicological endpoints established by atrazine				
Simazine Risk Characterization Document (DPR, 2013)	NOEL = 0.52	LOEL = 5.34	UF _A = 10x UF _H = 10x FQPA SF = 3x	cRfD = 0.0017	2-Year study in rats: decreased bodyweight, food intake and survival rates in females
Simazine by US EPA (US EPA, 2018h)	Based on chronic toxicological endpoints established by atrazine				
Chlorotriazine by US EPA (US EPA, 2018f)	Based on chronic toxicological endpoints established by atrazine				
aRfD: acute reference dose; BMDL _{1SD} : benchmark dose one standard deviation); BMDL _{1SD} : benchmark dose lower confidence limit one standard deviation); cRfD: chronic reference dose; DPR: Department of Pesticide Regulation; FQPA SF: Food Quality Protection Act safety factor; LH: luteinizing hormone; LOAEL: lowest observed adverse effect level; LOEL: lowest observed effect level; NOAEL: no observed adverse effect level; NOEL: no observed effect level; POD: point of departure; UF _A : interspecies uncertainty factor; UF _H : intraspecies uncertainty factor; US EPA: United States Environmental Protection Agency.					

^a NOEL is the highest dose where the effects observed in the treated group do not imply an effect. NOAEL is the highest dose where the effects observed in the treated group do not imply an adverse effect. These endpoints are often used as PODs.

^b LOEL is the lowest dose where the effects are observed in the treated group. LOAEL is the lowest dose where adverse effects are observed in the treated group.

^c aRfD and cRfD are the maximum acceptable oral dose of a toxic substance calculated by dividing the acute POD and chronic POD, respectively, by the total number of uncertainty factors.

^d The FQPA Amendments to FIFRA require, among other things, that US EPA consider the special susceptibility of children to pesticides by using an additional tenfold (10X) safety factor when setting and reassessing tolerances unless adequate data are available to support a different factor. The law allows a different FQPA SF if US EPA has reliable data supporting a conclusion that the revised safety factor would protect infants and children.

^e 4-Day repeated exposures were used to estimate steady-state exposures. A physiologically based pharmacokinetic (PBPK) model was used to estimate human equivalent doses and PODs for repeated dose exposures for specific subpopulations. These PODs are applicable to exposures of four days or longer since that is the time required to attenuate the luteinizing hormone surge in rats (US EPA, 2018f).

Table A2. Summary of Toxicological Endpoints for Hydroxyatrazine or Hydroxytriazines

Source	^a NOEL or NOAEL (mg/kg/day)	^b LOEL or LOAEL (mg/kg/day)	Uncertainty Factors	^c RfD (mg/kg/day)	Study Effects
Acute Endpoints					
Atrazine Risk Characterization Document (DPR, 2001a)	NOEL = 3.75	LOEL = 37.5	UF _A = 10x UF _H = 10x FQPA SF = 1x	aRfD = 0.038	13-Week study in dogs: kidney degeneration and inflammation
Atrazine by US EPA (US EPA, 2018b)	An acute endpoint was not identified and no risk is expected from this exposure scenario				
Hydroxytriazine by US EPA (US EPA, 2018f)	An acute endpoint was not identified and no risk is expected from this exposure scenario				
Chronic Endpoints					
Atrazine Risk Characterization Document (DPR, 2001a)	NOEL = 1.0	LOEL = 7.8	UF _A = 10x UF _H = 10x FQPA SF = 1x	cRfD = 0.005	2-Year study in rats: histopathological lesions of the kidney
Atrazine by US EPA (US EPA, 2018b)	BMDL ₁₀ = 6.76	BMD ₁₀ = 7.72	UF _A = 10x UF _H = 10x FQPA SF = 1x	cRfD = 0.0676	The same study as the above
Hydroxytriazine by US EPA (US EPA, 2018f)	The same as the atrazine US EPA assessment				
aRfD: acute reference dose; BMD ₁₀ : benchmark dose associated with a benchmark response of 10%; BMDL ₁₀ : lower 95% confidence limit on the benchmark dose benchmark response of 10%; cRfD: chronic reference dose; DPR: Department of Pesticide Regulation; FQPA SF: Food Quality Protection Act safety factor; LOAEL: lowest observed adverse effect level; LOEL: lowest observed effect level; NOAEL: no observed adverse effect level; NOEL: no observed effect level; UF _A : interspecies uncertainty factor; UF _H : intraspecies uncertainty factor; US EPA: United States Environmental Protection Agency.					

^a NOEL is the highest dose where the effects observed in the treated group do not imply an effect. NOAEL is the highest dose where the effects observed in the treated group do not imply an adverse effect. These endpoints are often used as points of departure (PODs).

^b LOEL is the lowest dose where the effects are observed in the treated group. LOAEL is the lowest dose where adverse effects are observed in the treated group.

^c aRfD and cRfD are the maximum acceptable oral dose of a toxic substance calculated by dividing the acute and chronic PODs, respectively, by the total number of uncertainty factors.

^d The FQPA Amendments to FIFRA require, among other things, that US EPA consider the special susceptibility of children to pesticides by using an additional tenfold (10X) safety factor when setting and reassessing tolerances unless adequate data are available to support a different factor. The law allows a different FQPA SF if US EPA has reliable data supporting a conclusion that the revised safety factor would protect infants and children.