

Julie Henderson Director

MEMORANDUM

Jared Blumenfeld Secretary for Environmental Protection

TO:	Minh Pham
	Environmental Program Manager II
	Environmental Monitoring Branch
VIA:	Shelley DuTeaux, PhD MPH, Chief
	Human Health Assessment Branch
FROM:	Brandon M. Brown, PhD, Staff Toxicologist
	Pete Lohstroh, PhD, Senior Toxicologist
	Toxicology and Dose Response Assessment Section
	Svetlana Koshlukova, PhD, Senior Toxicologist
	Risk Assessment Section

DATE: May 10, 2022

SUBJECT: RISKS FROM HUMAN EXPOSURE TO SIMAZINE RESIDUES IN GROUNDWATER

On November 22, 2021, the Department of Pesticide Regulation's (DPR) Human Health Assessment (HHA) Branch was notified by the Environmental Monitoring (EM) Branch that the Groundwater Protection Program (GWPP) detected simazine residues in wells in California. Between 1982 and 2020, GWPP sampled a total of 19,019 wells, of which 1,381 tested positive for simazine with concentrations ranging from 0.001 to 3.5 ppb. The highest concentration of 3.5 ppb was detected in a domestic well in 1982. GWPP also monitors for the simazine degradates ACET (deethyl-simazine or deisopropyl-atrazine) and DACT (diaminochlorotriazine). From 1993 to 2020, ACET was detected in 610 out of 2,896 monitored wells. Between 1993 and 2020, ACET concentrations ranged from 0.003 to 6 ppb, with the maximum concentration of 6 ppb detected in a domestic well in 1994. DACT was detected in 447 out of 1,685 monitored wells. DACT concentrations ranged from 0.001 to 8.89 ppb between 1993 and 2020, with the maximum concentration of 8.89 ppb detected in a domestic well in 2016. EM requested that HHA determine if there is a health concern for individuals using these wells as a source of drinking water (see request, Appendix 1). This memorandum is in response to that request.

Conclusions and Recommendations:

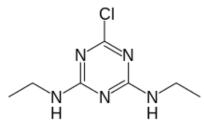
 HHA evaluated the human health risk from exposure to simazine in California well water using (1) acute and chronic dietary exposure estimates based on consumption rates for drinking water from the National Health and Nutrition Examination Survey (NHANES) 2005-2010 database and (2) toxicological endpoints established by DPR.

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- 2. The results indicate that detected simazine concentrations in California well water, including the highest measured residue in a domestic well (3.5 ppb), do not pose an acute or chronic health risk to humans. Note: this applies if simazine was the only residue detected in the sample.
- 3. The results also indicate that detected ACET and DACT concentrations in California well water, including the highest measured residues (6 and 8.89 ppb, respectively), do not pose acute or chronic health risks to humans. Note: this applies if only ACET or only DACT residue was detected in the sample.
- 4. HHA calculated a human health reference level of 17.4 ppb to be used as a screening level for the parent simazine and its chlorinated degradates ACET and DACT. If two or more residues of simazine, ACET, and DACT are detected in the same groundwater sample, the values should be summed and compared to the HHRL (17.4 ppb). Individual or summed maximum detected residues measured in groundwater exceeding this reference level would indicate a health concern.

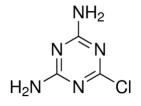
Background

Technical Name: Simazine Chemical Name: 6-Chloro- N^2 , N^4 -diethyl-1,3,5-triazine-2,4-diamine Chemical Abstracts Service Registry Number (CASRN): 122-34-9 (NIH, 2022d) Chemical Structure:

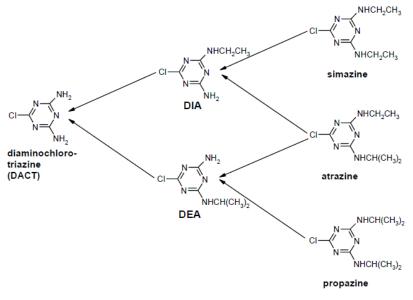


Technical Name: De(s)isopropylatrazine (ACET) Chemical Name: 6-Chloro-N-ethyl-1,3,5-triazine-2,4-diamine Chemical Abstracts Service Registry Number (CASRN): 1007-28-9 (NIH, 2022b) Chemical Structure:

Technical Name: Diaminochlorotriazine (DACT) **Chemical Name:** 2-Chloro-4,6-diamino-1,3,5-triazine **Chemical Abstracts Service Registry Number (CASRN)**: 3397-62-4 (NIH, 2022a) **Chemical Structure:**



Simazine is a chlorinated triazine herbicide used to control annual grasses and broadleaf weeds (USEPA, 2006a). ACET and DACT are chlorotriazine degradates of simazine. ACET and DACT are also degradation products of the chlorinated triazine herbicide atrazine; and DACT is a degradate of the chlorinated triazine herbicide propazine (USEPA, 2002; USEPA, 2018a). DPR uses the abbreviation DIPA for de(s)isopropylatrazine while the US Environmental Protection Agency (US EPA) uses DIA (USEPA, 2005; DPR, 2013; USEPA, 2018c; USEPA, 2018b). However, to be consistent with the request for evaluation, this memorandum will use the abbreviation ACET to denote this simazine degradate. The common degradation pathway for simazine and atrazine is depicted in Figure 1.



[Figure adapted from Hanioka et al., 1999]

Figure 1. Degradation of Simazine (USEPA, 2002). DIA or DIPA are abbreviations for the degradation product de(s)isopropylatrazine, referred to as ACET in this document. ACET is a degradation product of simazine and also of the chlorinated triazine herbicide atrazine (USEPA, 2018a). DACT, diaminochlorotriazine, is a degradation product of simazine, atrazine and the chlorinated triazine herbicide propazine (NIH, 2022c). DEA, deethylatrazine, is a degradation product of atrazine, and propazine (USEPA, 2018a; NIH, 2022c).

Simazine is registered for use on a variety of food and feed crops including apples, oranges, almonds, and corn. Uses also include nonselective weed control on non-agricultural land (USEPA, 2006a). Additionally, simazine is registered for residential use on turfgrass including both commercial use on recreational lawns and homeowner use on home lawns (USEPA, 2006a). Simazine was first registered in California in 1981 and there are currently nine products with active registrations (DPR, 2022b). Simazine has also been detected in surface water and agricultural products, which may contribute to dietary exposure (DPR, 2013).

Review of Regulatory Documents

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

Agency	Year	Title	Reference(s)
US EPA	2005	Overview of Simazine Risk Assessments	(USEPA, 2005)
US EPA	2006	Reregistration Eligibility Decision for Simazine	(USEPA, 2006a)
US EPA	2006	Triazine Cumulative Risk Assessment	(USEPA, 2006b)
DPR	2013	Simazine Risk Characterization Document	(DPR, 2013)
US EPA	2018	Simazine. Human Health Risk Assessment	(USEPA, 2018c)
US EPA	2018	Chlorotriazines Cumulative Risk Assessment	(USEPA, 2018b)

Table 1. Review of Regulatory Documents

Summary of Toxicology

Simazine was placed in Toxicity Category IV.^a for acute oral and dermal toxicity based on the median lethal doses, and Toxicity Category III for inhalation based on its median lethal concentration (USEPA, 2018c). It is not an eye or dermal irritant or dermal sensitizer (Toxicity Category IV). US EPA classified simazine as "not likely to be carcinogenic to humans" (USEPA, 2006a; USEPA, 2018c). In 2016, simazine was listed as a developmental and female reproductive toxicant under Proposition 65, the California Safe Drinking Water and Toxic Enforcement Act of 1986 (OEHHA, 2022).

^a 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. <u>https://www.epa.gov/sites/production/files/2018-04/documents/chap-07-mar-2018.pdf</u>

Simazine, atrazine, propazine and the chlorinated degradates ACET, DACT, and DEA all share a neuroendocrine mode of action for reproductive and developmental effects by targeting the hypothalamus and effecting down-stream hormonal responses in the pituitary gland, ovaries, and mammary glands (USEPA, 2018c). Oral exposure to simazine causes attenuation of luteinizing hormone (LH) surge, disruption of estrous cycle and vaginal cytology, and delays in vaginal opening and pubertal separation in rats (USEPA, 2006b). Cases of possible human exposures to simazine have reported clinical signs such as nausea, dizziness, and throat redness (DPR, 2022a).

US EPA grouped simazine and its chlorinated degradates with the chlorotriazine herbicides atrazine, propazine, and DEA in a common mechanism group (CMG). This grouping was based on the ability of these compounds to cause neuroendocrine and endocrine-related developmental and reproductive effects (USEPA, 2018b). As a CMG, these chemicals were evaluated for risks resulting from cumulative toxicity (USEPA, 2006b; USEPA, 2018c). Simazine, ACET, and DACT have equivalent toxicity with respect to their common neuroendocrine mechanism (USEPA, 2006b; DPR, 2013). Therefore, if more than one of these chemicals are detected in a sample, their residues can be summed to evaluate toxicity.

In 2013, DPR completed a risk characterization document (RCD) for simazine that evaluated risks for the general population and workers (DPR, 2013). This RCD was the primary source of toxicity data used for this evaluation.

The critical acute point of departure (POD) was a no observed effect level (NOEL) of 5 mg/kg/day from a developmental toxicity study in rabbits (Arthur, 1984; DPR, 2013). It was based on reduced body weight and body weight gain, anorexia, abnormal stools and tremors seen at the lowest observed effect level (LOEL) (75 mg/kg/day). The acute NOEL was divided by a total uncertainty factor (UF_{TOTAL}) of 300 to calculate an acute reference dose.^b (aRfD) of 0.016 mg/kg/day. The UF_{TOTAL} included 10x for interspecies extrapolation (UF_A), 10x for intraspecies variation (UF_H), and a 3x database uncertainty factor (UF_{DB}) to address concerns for neuroendocrine effects in developing fetuses.

The critical chronic POD was a NOEL of 0.52 mg/kg/day from a chronic toxicity/carcinogenicity study in rats (DPR, 2013). It was based on decreases in body weight, body weight gain, food consumption, and reduced survival seen at the LOEL (5.34 mg/kg/day). The chronic RfD (cRfD)

^b 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 (USEPA 2011. Integrated Risk Information System (IRIS) Glossary.

 $https://ofmpub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do; jsession id=VlwqcwYyLhUo1oDvgiO0TvQRBc0DnFfnaT0N8nvQPdtRKQaPCtCF!1236830639?details=&vocabName=IRI S%20Glossary&filterTerm=reference%20dose&checkedAcronym=false&checkedTerm=false&hasDefinitions=false &filterTerm=reference%20dose&filterMatchCriteria=Contains.<u>https://sor.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&vocabName=IRIS%20Glossary)</u>$

of 0.0017 mg/kg/day was calculated by dividing the NOEL by the UF_{TOTAL} of 300 as described above. These critical PODs were considered protective of any other effects, including endocrine effects.

Simazine, ACET, and DACT were evaluated using the critical PODs of the parent simazine because they were members of a CMG. DPR conducted a search for published US EPA human health risk assessments, including the US EPA Human Health Benchmarks for Pesticides (HHBPs) for simazine, atrazine, propazine, ACET, DACT, and DEA that were available as of May 2022 to ensure that any toxicological data used was current and relevant. Because of the complex nature of the evaluations herein, a comparison of the DPR's critical PODs, UFs and RfDs with US EPA counterparts for simazine was included in Appendix 2.

Risk Evaluation of Simazine Residues in Well Water

Groundwater Exposure Analysis

HHA estimated the acute and chronic exposures to simazine in drinking water using the Dietary Exposure Evaluation Model - Food Commodity Intake Database (DEEM-FCID, version 4.02, 5-10c) and the What We Eat in America (WWEIA) database (see DEEM-FCID outputs, Appendices 3 through 6). 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 (USEPA, 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). The maximum detected levels of residues in well water were used for both the acute and chronic analyses: 3.5 ppb (simazine), 6 ppb (ACET), and 8.89 ppb (DACT). Based on the request from EM (Appendix 1), this evaluation assumed that the maximum detections were for a single chemical species (e.g., simazine or ACET or DACT). HHA suggests summing the coincident residue levels of simazine, ACET, and DACT when detected in the same well.

The acute POD of 5 mg/kg/day, based on effects in the developmental study in rabbits, was used to calculate the acute risk for simazine, ACET, and DACT. The exposure estimates were calculated for the US population and sensitive subpopulations including infants, children aged 1 -2, and women of childbearing age (13 -49 years old). The chronic POD of 0.52 mg/kg/day based on effects in a chronic toxicity study in rats was used to evaluate chronic risk in the same manner.

Risks were calculated in terms of margins of exposure (MOE), a quantitative tool used by HHA to determine the potential risk arising from exposure to a pesticide. An MOE is defined as the ratio of the POD to anticipated exposure. The resulting value is compared to a target MOE. The target MOE for both analyses was equivalent to the UF_{TOTAL} of 300. A calculated MOE lower than the target MOE (300) would indicate a potential health concern. A summary of values for simazine is found in Table 2, below.

Simazine

- <u>Acute Exposure</u>: At the 95th exposure percentile, the estimated acute exposures to simazine ranged from 0.153 µg/kg/day for seniors 55+ years of age to 0.681 µg/kg/day for non-nursing infants.
- <u>Chronic Exposure:</u> Estimates for chronic exposure to simazine residues in drinking water ranged from 0.046 µg/kg/day for males 13 to 19 years of age to 0.348 µg/kg/day for non-nursing infants.
- <u>Acute Risk:</u> Acute MOEs at the 95th percentile exposure were greater than 7300 for all population subgroups, thereby exceeding the target MOE of 300 and indicating no risk.
- <u>Chronic Risk:</u> Chronic MOEs were greater than 1400 for all population subgroups, thereby exceeding the target MOE of 300 and indicating no risk.

ACET

- <u>Acute Exposure:</u> At the 95th exposure percentile, the estimated acute exposures to ACET ranged from 0.262 µg/kg/day for seniors 55+ years of age to 1.167 µg/kg/day for non-nursing infants.
- <u>Chronic Exposure</u>: Estimates for chronic exposure to ACET residues in drinking water ranged from 0.08 µg/kg/day for males 13 to 19 years of age to 0.597 µg/kg/day for non-nursing infants.
- <u>Acute Risk:</u> Acute MOEs at the 95th percentile exposure were greater than 4,000 for all population subgroups, thereby exceeding the target MOE of 300 and indicating no risk.
- <u>Chronic Risk:</u> Chronic MOEs were greater than 800 for all population subgroups, thereby exceeding the target MOE of 300 and indicating no risk.

DACT

- <u>Acute Exposure</u>: At the 95th exposure percentile, the estimated acute exposures to DACT ranged from 0.389 µg/kg/day for seniors 55+ years of age to 1.730 µg/kg/day for non-nursing infants.
- <u>Chronic Exposure</u>: Estimates for chronic exposure to DACT residues in drinking water ranged from 0.118 µg/kg/day for males 13 to 19 years of age to 0.885 µg/kg/day for non-nursing infants.
- <u>Acute Risk:</u> Acute MOEs at the 95th percentile exposure were greater than 2000 for all population subgroups, thereby exceeding the target MOE of 300 and indicating no risk.
- <u>Chronic Risk:</u> Chronic MOEs were greater than 500 for all population subgroups, thereby exceeding the target MOE of 300 and indicating no risk.

Calculation of DPR Human Health Reference Levels for Simazine

HHA calculated acute and chronic screening levels (human health reference levels or HHRLs) for simazine and proposes that the lower of the two values (the chronic HHRL of 17.4 ppb) be used by EM as a guide when residues of simazine and its degradates ACET and DACT are detected in groundwater. This HHRL should be used for screening maximum detected residue levels in groundwater and should be compared to the sum of simazine, ACET and DACT if they are present in the same sample (i.e., from the same well).

An HHRL is the threshold pesticide residue for a maximum water intake that results in the maximum safe oral exposure. The reference levels were calculated using the acute and chronic RfDs for simazine 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 (see Appendices 2 and 3). Non-nursing infants are the population identified as having the highest consumption of drinking water among the standard populations that HHA evaluates, including the general US population and sensitive subpopulations such as infants, children aged 1 - 2, and women of childbearing age (13 - 49 years old). The water consumption rates were from the NHANES/WWEIA dietary survey as mentioned above.

The HHRLs for simazine in drinking water are summarized below (Table 2). The lowest reference value (chronic level 17.4 ppb) was selected as the HHRL for residues of simazine ACET and DACT in groundwater and is intended to be used for screening maximum detected residue levels. For comparison, US EPA issued acute and chronic HHBPs for DACT of 300 ppb (acute or 1-day) and 11 ppb (chronic or lifetime) (USEPA, 2003; USEPA, 2022a). It should be

noted that US EPA uses chronic HHBPs to screen mean residue levels. Simazine is one of the few pesticides for which an enforceable drinking water standard (maximum contaminant level, MCL)^c was established. US EPA's MCLs are used for protection of public drinking water systems and do not apply to privately owned wells or any other individual water system. The MCL for simazine is 0.004 mg/L (4 ppb) (USEPA, 2022b).

 Table 2. Acute and chronic reference levels for simazine and its chlorinated degradates in drinking water

Residue	Acute or Chronic	Residue Level (ppb)	Subpopulation with Highest Water Intake per Bodyweight	Exposure Estimate	Calculated MOE ^a	Target MOE ^b	DPR HHRL ° (ppb)
Simazine, ACET,	Acute	3.5	Non-Nursing Infants	95 th Percentile	7,342	300	85.7
and DACT	Chronic	3.5	Non-Nursing Infants	Average	1,492	300	17.4

a) Simazine MOE (Margin of Exposure) for non-nursing infants.

b) Target MOE is equal to the total uncertainty factor (UF_{TOTAL}) of 300 that accounts for interspecies sensitivity (10x) and intraspecies variability (10x) and 3x database factor

c) The Human Health Reference Level (HHRL) is the Residue Level (pesticide concentration) that will result in a MOE at the Target MOE; HHRL (ppb) = (DEEM MOE/Target MOE) x (Residue Level at DEEM MOE (ppb). The HHRL recommended for evaluating corresponding residues in drinking water is bolded.

^eMaximum Contaminant Level (MCL) is the highest level of a contaminant that is allowed in drinking water. MCLs are set as close to Maximum Contaminant Level Goals (MCLG) as feasible using the best available treatment technology and taking cost into consideration MCLs are legally enforceable standards that apply to public water systems. (<u>National Primary Drinking Water Regulations | US EPA</u>), US EPA regulations that protect public drinking water systems do not apply to privately owned wells or any other individual water system (<u>Private Drinking Water Wells | US EPA</u>)

Conclusions

- 1. The detected simazine residues in California well water ranging from 0.001 to 3.5 ppb should not be considered an acute or chronic health concern to residents that use the well for drinking water. Note: this applies if simazine is the only residue detected in the sample.
- 2. The results also indicate that the detected ACET and DACT concentrations in California well water, including the highest measured residues (6 and 8.89 ppb, respectively), do not pose acute or chronic health risks to humans. Note: this applies if the sample contained only ACET or only DACT residues.
- 3. HHA also calculated a human health reference level of 17.4 ppb to be used as a screening level for maximum residues of simazine, ACET and DACT detected in groundwater. If residues of the parent simazine and the degradates ACET and DACT are detected in the same groundwater sample, the values should be summed and compared to the HHRL (17.4 ppb). Individual or summed maximum detected residues measured in groundwater exceeding this reference level would indicate a health concern.

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- USEPA. 2018c. Simazine. Human Health Risk Assessment.
- USEPA 2022a. Human Health Benchmarks for Pesticides.
- USEPA 2022b. National Primary Drinking Water Regulations. In 40 CFR Part 141.

Appendices

Appendix 1. DPR Memo: Potential Health Effects of Simazine and Degradates in Groundwater 22 November 2021 (2 pages)

Sepr.	Department of Pestic	ide Regulation	Gavin Newsom Governor
Julie Henderson Director	M E M O R A N I	DUM	Jared Blumenfeld Secretary for Environmental Protection
TO:	Shelley DuTeaux Environmental Program Manager II Human Health Assessment Branch		
VIA:	Minh Pham Environmental Program Manager II Environmental Monitoring Branch	Original Signed by 1/3/22	
FROM:	Joy Dias Environmental Program Manager I Environmental Monitoring Branch	Original Signed by 1/3/22	
DATE:	January 3, 2022		

SUBJECT: POTENTIAL HEALTH EFFECTS OF SIMAZINE AND DEGRADATES IN GROUNDWATER

The Environmental Monitoring Branch (EMB) monitors the environment to determine the fate of pesticides, protecting the public and the environment from pesticide contamination through analyzing hazards and developing pollution prevention strategies. Consistent with EMB's mission, the Groundwater Protection Program (GWPP) routinely monitors for simazine and its degradates ACET (deethyl-simazine or deisopropyl-atrazine) and DACT (diaminochlorotriazine) due to their occurrence in groundwater and simazine'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 compiles the data into the Well Inventory Database (WIDB). Based on these records, 19 public agencies¹ have reported sampling results for simazine and 4 public agencies² have reported sampling results for ACET and DACT. The data reviewed for this memorandum include data from the WIDB up to December 31, 2020 (Table 1).

Based on the WIDB, 19,017 unique wells have been sampled for simazine in California, totaling 68,750 samples (Table 1). Of these wells, 1,381 wells have tested positive for simazine. Between 1982 and 2020, simazine concentrations have ranged from 0.001 to 49.2 ppb. The maximum concentration of simazine detected across all wells sampled in the state (49.2 ppb) was detected

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¹ California Department of Pesticide Regulation (DPR), California Department of Public Health, California Department of Water Resources, California Regional Water Quality Control Board (Region 1), California Regional Water Quality Control Board (Region 2), California Regional Water Quality Control Board (Region 5), California State Water Resources Control Board (SWRCB), SWRCB Drinking Water Program, Ciba-Geigy, City of San Francisco, Lake County, Sacramento County, Santa Barbara County, Santa Clara County, Stockton-E. San Joaquin Water Conservation District, United States Environmental Protection Agency, United States Geological Survey (USGS), Yolo County, and Yuba County

² DPR, SWRCB, Ciba-Geigy, and USGS

Shelley DuTeaux January 3, 2022 Page 2

in a monitoring well in 1982. This well was not resampled but nearby wells were sampled and no residues were detected. The maximum concentration detected in a domestic well was 3.5 ppb in 1982.

Similarly, 2,896 unique wells have been sampled for ACET in California, totaling 4,977 samples (Table 1). Of these wells, 610 wells have tested positive for ACET. Between 1993 and 2020, ACET concentrations have ranged from 0.003 to 6 ppb. The maximum concentration of ACET detected across all wells sampled in the state (6 ppb) was detected in a domestic well sampled in 1994. This well was resampled and a concentration of 4.63 ppb was reported.

Lastly, 1,685 unique wells have been sampled for DACT in California, totaling 3,422 samples (Table 1). Of these wells, 447 wells have tested positive for DACT. Between 1993 and 2020, DACT concentrations have ranged from 0.001 to 8.89 ppb. The maximum concentration of DACT detected across all wells sampled in the state (8.89 ppb) was detected in a domestic well sampled in 2016 as part of DPR's Well Monitoring Network. This domestic well has been sampled 25 times with DACT concentrations ranging from 0.778 to 8.89 ppb.

Table 1. Summary of groundwater	monitoring data from the Well Inventory Database for
simazine and its degradates.	

Chemical	CAS	Unique	Total	Unique	Concentration	Maximum
	Number	Wells	Samples	Wells	Range (ppb)	Concentration
		Sampled	Analyzed	with		Detected in a
		_		Detections		Domestic Well (ppb)
Simazine	122-34-9	19,017	68,750	1,381	0.001 - 49.2	3.5
ACET	1007-28-9	2,896	4,977	610	0.003 - 6	6
DACT	3397-62-4	1,685	3,422	447	0.001 - 8.89	8.89

EMB requests the assistance of the Human Health Assessment Branch in determining whether these detections pose a significant risk to human health. The full dataset reviewed for this memorandum is available upon request.

cc: Carissa Ganapathy, Senior Environmental Scientist (Supervisory)

Appendix 2. Summary of Toxicological Doses and Endpoints for Simazine (1 Page)

Source	Exposure	POD	Uncertainty	RfD, PAD	Study Effects
	Scenario		Factors		
Simazine	Acute Oral	NOEL = 5	UF _A 10x	aRfD =	Developmental Toxicity
(DPR, 2013)		mg/kg/day	$UF_{\rm H}$ 10x	0.016	Study in Rabbits; LOEL =
			UF _{DB} 3x	mg/kg/day	75 mg/kg/day based on
					reduced body weight and
					body weight gain,
					anorexia, abnormal stools
					and tremors
	Chronic	NOEL = 0.52	UF _A 10x	cRfD =	Chronic
	Oral	mg/kg/day	$UF_{\rm H}$ 10x	0.0017	Toxicity/Carcinogenicity
			UF _{DB} 3x	mg/kg/day	Study in Rats; LOEL =
					5.34 mg/kg/day based on
					decreases in body weight,
					life span, and increase in
					mammary tumors
Simazine (USEPA,	Acute	NOAEL = 30	UF _A 10x	aRfD = 0.30	Developmental Study in
2018c)	Dietary	mg/kg/day	UF _H 10x	mg/kg/day	Rats; $LOAEL = 300$
	(Females				mg/kg/day based on
	13-49)				increased incidence of
					unossified teeth, head,
					centra vertebrae,
					sternabrae, and
					rudimentary ribs
	4-Day	2.32	UF _A 3x	4-Day PAD	4-Day Atrazine Study in
	(Females	mg/kg/day	UF_{H} 10x	= 0.073	Rats; $BMDL_{1SD} = 2.42$
	13-49)			mg/kg/day	mg/kg/day based on
					reduced LH surge

Table A1. Summary of Toxicological Doses and Endpoints for Simazine and Atrazine

a) 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 points of departure (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 (LH) surge in rats (USEPA, 2018c; USEPA, 2018a)

Reference Dose (RfD) is the maximum acceptable oral dose of a toxic substance; calculated by dividing the POD by the total number of uncertainty factors.

Population Adjusted Dose (PAD) is an RfD that has been divided by an additional uncertainty factor that only applies to certain population.

No observed adverse effect level (NOAEL) is the highest dose where the effects observed in the treated group do not imply an adverse effect.

Lowest observed adverse effect level (LOAEL) is the lowest dose where adverse effects are observed in the treated group.

Appendix 3. Acute Drinking Water Exposure Analysis for Simazine (Users Only) (2 pages)

Ver. 4.02, 05-10-c DEEM-FCID ACUTE Analysis for SIMAZINE NHANES 2005-2010 2-Day Residue file: Simazine21DEC2021.R10 Adjustment factor #2 NOT used. Analysis Date: 12-21-2021/12:01:30 Residue file dated: 12-21-2021/10:19:56 NOEL (Acute) = 5.000000 mg/kg body-wt/day RAC/FF intake summed over 24 hours Run Comment: ""

Summary calculations--users:

	95th Percen Exposure	tile MOE	99th Percen Exposure	MOE	99.9th Perce Exposure	MOE
Total US Populatio	n: 0.000189	26401	0.000335	14917	0.000638	7830
Hispanic:	0.000199	25115	0.000409	12213	0.000714	7004
Non-Hisp-White:	0.000188	26545	0.000318	15729	0.000592	8446
Non-Hisp-Black:	0.000160	31245	0.000351	14233	0.000790	6327
Non-Hisp-Other:	0.000220	22763	0.000361	13866	0.000612	8165
Nursing Infants:	0.000420	11899	0.000737	6785	0.001266	3948
Non-Nursing Infant	s: 0.000681	7342	0.000899	5564	0.001191	4199
Female 13+ PREG: Children 1-6:	0.000179	27910	0.000224	22313	0.000319	15655
Children 7-12:	0.000233	21450	0.000369	13534	0.000626	7988
Male 13-19:	0.000163	30601	0.000271	18458	0.000418	11961
Female 13-19/NP:	0.000154	32542	0.000239	20880	0.000547	9148
Seniors 55+:	0.000170	29463	0.000250	19982	0.000369	13560
All Infants:	0.000153	32664	0.000238	21043	0.000361	13846
Children 1-2:	0.000659	7581	0.000886	5643	0.001194	4188
Children 3-5:	0.000273	18304	0.000407	12270	0.001054	4742
Children 6-12:	0.000217	22991	0.000337	14822	0.000583	8574
Youth 13-19:	0.000171	29286	0.000278	18002	0.000458	10906
Adults 20-49:	0.000161	31151	0.000249	20108	0.000369	13549
Adults 50-99:	0.000185	27020	0.000277	18019	0.000388	12878
Female 13-49:	0.000159	31396	0.000252	19838	0.000397	12605
	0.000186	26868	0.000270	18516	0.000405	12351

 Ver. 4.02, 05-10-c

 DEEM-FCID Acute analysis for SIMAZINE

 Residue file name: C:\Program Files\DeemFCID40\Simazine21DEC2021.R10

 Analysis Date 12-21-2021
 Residue file dated: 12-21-2021/10:19:56

 Reference dose (NOEL) = 5 mg/kg bw/day

 EPA
 Crop

 Code
 Grp Food Name

 (ppm)
 #1

 8601000000
 86A Water, direct, all sources
 0.003500

 8602000000
 86B Water, indirect, all sources
 0.003500

Appendix 4. Chronic Drinking Water Exposure Analysis for Simazine (2 pages)

Evaluation Copy Ver. 4.02, 05-10-c DEEM-FCID Chronic analysis for SIMAZINE NHANES 2005-2010 2-day Residue file name: C:\Program Files\DeemFCID40\Simazine21DEC2021.R10 Adjustment factor #2 NOT used. Analysis Date 12-21-2021/10:56:40 Residue file dated: 12-21-2021/10:19:56 NOEL (Chronic) = .52 mg/kg bw/day Total exposure by population subgroup

	Total Exposure					
Population Subgroup	mg/kg body wt/day	Percent of NOEL				
Total US Population	0.000071	0.01%	7,353			
Hispanic	0.000069	0.01%	7,537			
Non-Hisp-White	0.000073	0.01%	7,168			
Non-Hisp-Black	0.000057	0.01%	9,150			
Non-Hisp-Other	0.00083	0.02%	6,255			
Nursing Infants	0.00080	0.02%	6,464			
Non-Nursing Infants	0.000348	0.07%	1,492			
Female 13+ PREG	0.000074	0.01%	7,055			
Children 1-6	0.00085	0.02%	6,131			
Children 7-12	0.000056	0.01%	9,273			
Male 13-19	0.000046	0.01%	11,191			
Female 13-19/NP	0.000053	0.01%	9,804			
Male 20+	0.000066	0.01%	7,917			
Female 20+/NP	0.000073	0.01%	7,150			
Seniors 55+	0.000066	0.01%	7,860			
All Infants	0.000264	0.05%	1,969			
Female 13-50	0.000069	0.01%	7,491			
Children 1-2	0.000097	0.02%	5,347			
Children 3-5	0.000079	0.02%	6,571			
Children 6-12	0.000059	0.01%	8,838			
Youth 13-19	0.000050	0.01%	10,431			
Adults 20-49	0.000070	0.01%	7,401			
Adults 50-99	0.000068	0.01%	7,610			
Female 13-49	0.000069	0.01%	7,529			

Evaluation Copy Ver. 4.02, 05-10-c DEEM-FCID Chronic analysis for SIMAZINE Residue file: C:\Program Files\DeemFCID40\Simazine21DEC2021.R10 Adjust. #2 NOT used Analysis Date 12-21-2021 Residue file dated: 12-21-2021/10:19:56 Reference dose (NOEL) = 0.52 mg/kg bw/day

Food	Crop	Food Name	Residue	Adj.Fa	actors
EPA Code	Grp		(ppm)	#1	#2
		Water, direct, all sources Water, indirect, all sources	0.003500 0.003500	1.000 1.000	1.000

Appendix 5. Acute Drinking Water Exposure Analysis for de(s)isopropylatrazine (Users Only) (2 pages)

Ver. 4.02, 05-10-c DEEM-FCID ACUTE Analysis for ACET NHANES 2005-2010 2-Day Residue file: ACET10DEC2021.R10 Adjustment factor #2 NOT used. Analysis Date: 12-10-2021/17:12:25 Residue file dated: 12-10-2021/16:46:25 NOEL (Acute) = 5.000000 mg/kg body-wt/day RAC/FF intake summed over 24 hours Run Comment: ""

Summary calculations--users:

	95th Percer Exposure	MOE	99th Percen Exposure	MOE	99.9th Perce Exposure	MOE
Total US Population						
	0.000325	15400	0.000575	8702	0.001095	4568
Hispanic:	0.000341	14650	0.000702	7124	0.001224	4086
Non-Hisp-White:	0 000000	1 5 4 9 5		0155	0 001015	4007
Non-Hisp-Black:	0.000323	15485	0.000545	9175	0.001015	4927
New Wire Others	0.000274	18226	0.000602	8302	0.001355	3691
Non-Hisp-Other:	0.000377	13278	0.000618	8088	0.001050	4763
Nursing Infants:	0 000700	CO 41	0 001060	2050	0 000171	0.202
Non-Nursing Infant	0.000720 s:	6941	0.001263	3958	0.002171	2303
Esmale 12, DEC.	0.001167	4283	0.001540	3245	0.002041	2449
Female 13+ PREG:	0.000307	16281	0.000384	13016	0.000547	9132
Children 1-6:	0 000400	10510	0 000633	7005	0 001073	4650
Children 7-12:	0.000400	12512	0.000633	7895	0.001073	4659
Mala 12 10.	0.000280	17850	0.000464	10767	0.000717	6977
Male 13-19:	0.000263	18983	0.000411	12180	0.000937	5336
Female 13-19/NP:	0 000201	17187	0 000420	11656	0.000632	7910
Seniors 55+:	0.000291	1/10/	0.000429	11030	0.000632	7910
All Infants:	0.000262	19054	0.000407	12275	0.000619	8077
All infants.	0.001131	4422	0.001519	3292	0.002046	2443
Children 1-2:	0.000468	10677	0.000699	7157	0.001807	2766
Children 3-5:	0.000408	10677	0.000099	/15/	0.001807	2700
Children 6-12:	0.000373	13411	0.000578	8646	0.001000	5001
children 0-12.	0.000293	17083	0.000476	10501	0.000786	6362
Youth 13-19:	0.000275	18171	0.000426	11729	0.000633	7903
Adults 20-49:	0.000275	101/1				1905
Adults 50-99:	0.000317	15761	0.000476	10511	0.000666	7512
	0.000273	18314	0.000432	11572	0.000680	7353
Female 13-49:	0.000319	15673	0.000463	10801	0.000694	7204

Ver. 4.02, 05-10-c DEEM-FCID Acute analysis for ACET Residue file name: C:\Program Files\DeemFCID40\ACET10DEC2021.R10 Analysis Date 12-10-2021 Residue file dated: 12-10-2021/16:46:25 Reference dose (NOEL) = 5 mg/kg bw/day EPA Crop Def Res Adj.Factors Comment Code Grp Food Name (ppm) #1 #2 8601000000 86A Water, direct, all sources 0.006000 1.000 1.000 8602000000 86B Water, indirect, all sources 0.006000 1.000 1.000

Appendix 6. Chronic Drinking Water Exposure Analysis for de(s)isopropylatrazine (2 pages)

	Total Exposure				
Population Subgroup	mg/kg body wt/day	Percent of NOEL	2		
Total US Population	0.000121	0.02%	4,290		
Hispanic	0.000118	0.02%	4,396		
Non-Hisp-White	0.000124	0.02%	4,182		
Non-Hisp-Black	0.000097	0.02%	5,338		
Non-Hisp-Other	0.000143	0.03%	3,649		
Nursing Infants	0.000138	0.03%	3,771		
Non-Nursing Infants	0.000597	0.11%	871		
Female 13+ PREG	0.000126	0.02%	4,115		
Children 1-6	0.000145	0.03%	3,576		
Children 7-12	0.000096	0.02%	5,409		
Male 13-19	0.000080	0.02%	6,528		
Female 13-19/NP	0.000091	0.02%	5,719		
Male 20+	0.000113	0.02%	4,618		
Female 20+/NP	0.000125	0.02%	4,171		
Seniors 55+	0.000113	0.02%	4,585		
All Infants	0.000453	0.09%	1,148		
Female 13-50	0.000119	0.02%	4,370		
Children 1-2	0.000167	0.03%	3,119		
Children 3-5	0.000136	0.03%	3,833		
Children 6-12	0.000101	0.02%	5,155		
Youth 13-19	0.000085	0.02%	6,085		
Adults 20-49	0.000120	0.02%	4,318		
Adults 50-99	0.000117	0.02%	4,439		
Female 13-49	0.000118	0.02%	4,392		

Evaluation Copy Ver. 4.02, 05-10-c DEEM-FCID Chronic analysis for ACET Residue file: C:\Program Files\DeemFCID40\ACET10DEC2021.R10Adjust. #2 NOT used Analysis Date 12-10-2021 Residue file dated: 12-10-2021/16:46:25 Reference dose (NOEL) = 0.52 mg/kg bw/day

Food C		Crop		Residue	Adj.Factors	
	EPA Code	Grp	Food Name	(ppm)	#1	#2
	860100000	86A	Water, direct, all sources	0.006000	1.000	1.000
	860200000	86B	Water, indirect, all sources	0.006000	1.000	1.000

Appendix 7. Acute Drinking Water Exposure Analysis for DACT (Users Only) (2 pages)

Ver. 4.02, 05-10-c DEEM-FCID ACUTE Analysis for DACT NHANES 2005-2010 2-Day Residue file: DACT10DEC2021.R10 Adjustment factor #2 NOT used. Analysis Date: 12-10-2021/17:28:13 Residue file dated: 12-10-2021/16:48:02 NOEL (Acute) = 5.000000 mg/kg body-wt/day RAC/FF intake summed over 24 hours Run Comment: ""

Summary calculations--users:

	95th Percentile Exposure MOE		99th Percentile Exposure MOE		99.9th Percentile Exposure MOE	
Total US Population						
Hispanic:	0.000481	10394	0.000851	5873	0.001622	3083
hispanic.	0.000506	9887	0.001040	4808	0.001813	2757
Non-Hisp-White:	0.000478	10451	0.000807	6192	0.001504	3325
Non-Hisp-Black:						
Non-Hisp-Other: Nursing Infants:	0.000406	12301	0.000892	5603	0.002007	2491
	0.000558	8961	0.000916	5459	0.001555	3214
	0.001067	4684	0.001872	2671	0.003217	1554
Non-Nursing Infant	s: 0.001730	2890	0.002282	2190	0.003024	1653
Female 13+ PREG:						
Children 1-6:	0.000455	10988	0.000569	8785	0.000811	6163
	0.000592	8444	0.000938	5328	0.001590	3144
Children 7-12:	0.000415	12047	0.000688	7267	0.001062	4709
Male 13-19:	0.000390	12812	0.000608	8220	0.001388	3601
Female 13-19/NP:						
Seniors 55+:	0.000431	11599	0.000636	7867	0.000937	5338
All Infants:	0.000389	12859	0.000604	8284	0.000917	5451
	0.001675	2984	0.002250	2221	0.003032	1649
Children 1-2:	0.000694	7206	0.001035	4830	0.002678	1067
Children 3-5:	0.000694	1200	0.001035	4030	0.002678	1867
Children 6-12:	0.000552	9051	0.000857	5835	0.001481	3375
	0.000434	11530	0.000705	7087	0.001164	4293
Youth 13-19:	0.000408	12264	0.000632	7916	0.000937	5334
Adults 20-49:	0.000470	10637	0.000705	7094	0.000986	5070
Adults 50-99:		T0031		1094		5070
Female 13-49:	0.000405	12360	0.000640	7810	0.001008	4962
10	0.000473	10578	0.000686	7290	0.001028	4862

Ver. 4.02, 05-10-c DEEM-FCID Acute analysis for DACT Residue file name: C:\Program Files\DeemFCID40\DACT10DEC2021.R10 Analysis Date 12-10-2021 Residue file dated: 12-10-2021/16:48:02 Reference dose (NOEL) = 5 mg/kg bw/day EPA Crop Def Res Adj.Factors Comment Code Grp Food Name (ppm) #1 #2 8601000000 86A Water, direct, all sources 0.008890 1.000 1.000 8602000000 86B Water, indirect, all sources 0.008890 1.000 1.000

Appendix 8. Chronic Drinking Water Exposure Analysis for DACT (2 pages)

	Total Exposure				
Population Subgroup	mg/kg body wt/day	Percent of NOEL	2		
Total US Population	0.000180	0.03%	2,895		
Hispanic	0.000175	0.03%	2,967		
Non-Hisp-White	0.000184	0.04%	2,822		
Non-Hisp-Black	0.000144	0.03%	3,602		
Non-Hisp-Other	0.000211	0.04%	2,463		
Nursing Infants	0.000204	0.04%	2,545		
Non-Nursing Infants	0.000885	0.17%	588		
Female 13+ PREG	0.000187	0.04%	2,778		
Children 1-6	0.000215	0.04%	2,414		
Children 7-12	0.000142	0.03%	3,651		
Male 13-19	0.000118	0.02%	4,406		
Female 13-19/NP	0.000135	0.03%	3,860		
Male 20+	0.000167	0.03%	3,117		
Female 20+/NP	0.000185	0.04%	2,815		
Seniors 55+	0.000168	0.03%	3,094		
All Infants	0.000671	0.13%	775		
Female 13-50	0.000176	0.03%	2,949		
Children 1-2	0.000247	0.05%	2,105		
Children 3-5	0.000201	0.04%	2,587		
Children 6-12	0.000149	0.03%	3,479		
Youth 13-19	0.000127	0.02%	4,107		
Adults 20-49	0.000178	0.03%	2,914		
Adults 50-99	0.000174	0.03%	2,996		
Female 13-49	0.000175	0.03%	2,964		

Evaluation Copy Ver. 4.02, 05-10-c DEEM-FCID Chronic analysis for DACT Residue file: C:\Program Files\DeemFCID40\DACT10DEC2021.R10Adjust. #2 NOT used Analysis Date 12-10-2021 Residue file dated: 12-10-2021/16:48:02 Reference dose (NOEL) = 0.52 mg/kg bw/day

Food Crop	Residue	Adj.Factors	
EPA Code Grp Food Name	(mqq)	#1	#2
·			
8601000000 86A Water, direct, all sources	0.008890	1.000	1.000
8602000000 86B Water, indirect, all sources	0.008890	1.000	1.000