

Julie Henderson Director

MEMORANDUM

Jared Blumenfeld Secretary for Environmental Protection

| TO: | Minh Pham |
|-------|---|
| | Environmental Program Manager II |
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| VIA: | Shelley DuTeaux, PhD MPH, Chief |
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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:

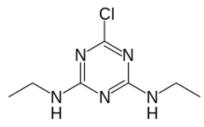
 HHA evaluated the human health risk from exposure to simazine in California well water using (1) acute and chronic dietary exposure estimates based on consumption rates for drinking water from the National Health and Nutrition Examination Survey (NHANES) 2005-2010 database and (2) toxicological endpoints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

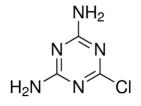
Background

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:

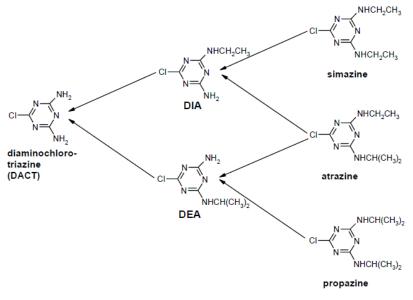


Technical Name: De(s)isopropylatrazine (ACET) Chemical Name: 6-Chloro-N-ethyl-1,3,5-triazine-2,4-diamine Chemical Abstracts Service Registry Number (CASRN): 1007-28-9 (NIH, 2022b) Chemical Structure:

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 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 |
|-----------------------------|---|---------------------------|---|
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| 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

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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 |