



Department of Pesticide Regulation

Gov. Gavin Newsom
Governor

Jared Blumenfeld
Secretary for
Environmental Protection

MEMORANDUM

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TO: Minh Pham
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VIA: Shelley DuTeaux, PhD MPH, Chief
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DATE: September 29, 2021

SUBJECT: RISKS FROM HUMAN EXPOSURE TO BROMACIL RESIDUES IN
GROUNDWATER

On July 26, 2021, the Department of Pesticide Regulation's (DPR) Human Health Assessment (HHA) Branch was notified by the Environmental Monitoring (EM) Branch that bromacil residues were detected in 349 of 39,304 groundwater samples collected from a total of 12,938 monitored wells. In 2020, the DPR's Groundwater Protection Program (GWPP) detected a bromacil concentration of 10.3 parts per billion (ppb) in a single sample collected from a well located in Fresno County, section 10M13S23E32. Previous samples collected from this well between 1996 and 2019 had bromacil concentrations ranging from 0.051 to 6.69 ppb, with an analytical reporting limit (RL) of 0.05 ppb. The maximum concentration of bromacil (23 ppb) was detected in a single well sampled in 1994. No subsequent samples were taken from this well. 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:

1. HHA evaluated the human health risk from exposure to bromacil 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 United States Environmental Protection Agency (US EPA).

2. The results indicate that the detected bromacil concentrations in California well water, including the highest measured residue (23 ppb), do not pose acute or chronic health risks to humans.
3. HHA also calculated a human health reference level of 197 ppb to be used as a screening level for bromacil residues. Residues measured in groundwater exceeding this reference level should be sent to HHA for further evaluation.

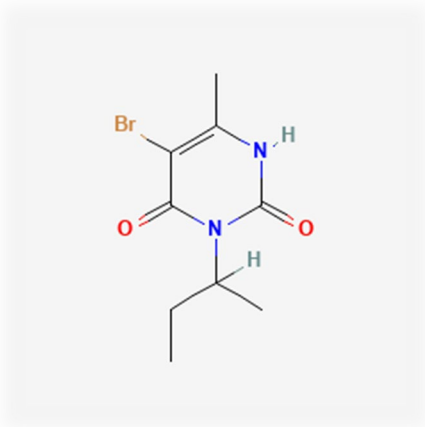
Background

Technical Name: Bromacil

Chemical Name: 5-bromo-3-butyl-6-methyl-1H-pyrimidine-2,4-dione;

Chemical Abstracts Service Registry Number (CAS) 314-40-9 (NIH, 2021)

Chemical Structure:



Bromacil is a non-selective, broad spectrum herbicide that belongs to the uracil class of pesticides used for control of grasses and broadleaf weeds in agricultural and non-agricultural lands (USEPA, 2012). Agricultural uses of bromacil include soil treatment for the protection of citrus and pineapple crops; non-agricultural uses include weed and brush control (USEPA, 2016a). Dietary exposure to bromacil residues may occur through the consumption of crops and drinking water (USEPA, 2016a). Based on the frequencies of detection in both surface and groundwater, US EPA concluded that “bromacil may contaminate both surface water and groundwater resulting from use of the compound” (USEPA, 2016b). Formulated products containing bromacil acid (pK_a = 9.1) or its lithium salt are registered federally and at the state level. In California the first product containing bromacil was registered 1981 and there are currently 19 products with active registrations (DPR, 2021). Residues from formulations of either the acid or salt form are considered equivalent because the lithium salt rapidly disassociates in water to form the acid (USEPA, 2016b).

Bromacil was placed in Toxicity Category IV (low) for acute oral, dermal (including irritation and sensitization), and inhalation toxicity¹ based on its median lethal oral, dermal, and inhalation doses in mice. It is not a dermal irritant or sensitizer (Toxicity Category IV) and is a mild eye irritant (Toxicity Category III) (USEPA, 2016a). US EPA classified bromacil as a “Group C – Possible Human Carcinogen” based on an increased incidence of liver tumors in male mice and thyroid tumors in male rats (USEPA, 2016a). US EPA concluded that bromacil does not represent a mutagenic concern and evaluated cancer risk by using the chronic reference dose (RfD²) approach (USEPA, 2016a).

Summary of Toxicology

Although HHA has evaluated all required toxicity data that were submitted as part of registration in California, HHA has not conducted a human health risk assessment for bromacil. For purposes of this evaluation, HHA adopted the toxicological endpoints and points of departure (PODs) established by US EPA (USEPA, 2016a). The acute POD was a no observed adverse effect level (NOAEL) of 100 mg/kg/day based on an increase in the number of litters containing early resorptions in females seen at the lowest observed adverse effect level (LOAEL) (300 mg/kg/day) in a developmental toxicity study in rabbits (USEPA, 2016a). The acute NOAEL was divided by a total uncertainty factor (UF_{TOTAL}) of 100 to calculate an acute RfD (aRfD) of 1 mg/kg/day for women 13 to 49 years. The UF_{TOTAL} included a 10x for interspecies extrapolation (UF_A) and a 10x for intraspecies variation (UF_H). The chronic POD for estimating the chronic dietary risks to all populations was a NOAEL of 1.96 mg/kg/day based on decreases in mean absolute bodyweight and decreased food efficiency seen at the LOAEL (9.82 mg/kg/day) in a combined chronic toxicity/carcinogenicity study in rats (USEPA, 2016a). The chronic RfD (cRfD) of 0.0196 mg/kg/day was calculated by dividing the NOAEL by a UF_{TOTAL} of 100 that included a 10X UF_A and a 10X UF_H.

Risk Evaluation of Bromacil Residues in Well Water

Groundwater Exposure Analysis

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

² An RfD is an estimate of a daily oral exposure for specific duration (acute or chronic) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (USEPA 2011. Integrated Risk Information System (IRIS) Glossary. https://ofmpub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do;jsessionid=VlwqewYyLhUo1oDvgiO0TvQRBc0DnFfnaT0N8nvQPdtRKQaPCtCF!1236830639?details=&vocabName=IRIS%20Glossary&filterTerm=reference%20dose&checkedAcronym=false&checkedTerm=false&hasDefinitions=false&filterTerm=reference%20dose&filterMatchCriteria=Contains.)

HHA estimated the acute and chronic exposures to bromacil in drinking water using the Dietary Exposure Evaluation Model - Food Commodity Intake Database (DEEM-FCID, version 4.02, 5-10c) and the NHANES/“What We Eat in America” (WWEIA) (see DEEM-FCID outputs, Appendices 2 and 3). The NHANES/WWEIA 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). The 95th percentile exposures were used for the acute analysis, while 2-day average exposures were used for the chronic analysis (DPR, 2009). The information on 2-day, nonconsecutive food intake is used as a surrogate for chronic consumption patterns in a population. HHA uses the 95th percentile of the exposure levels for each population subgroup as the default upper bound of acute exposures. The maximum detected level of bromacil in well water (23 ppb) was used for both the acute and chronic analyses.

The acute POD of 100 mg/kg/day based on effects in the developmental study in rabbits was used to calculate the acute risk in terms of the MOE. 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 1.96 mg/kg/day based on effects in a combined chronic toxicity/carcinogenicity study in rats was used to evaluate chronic risk in the same manner.

The margin of exposure (MOE) is 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 the anticipated human exposure. The resulting value is compared to the acceptable or target MOE. Values at or above the target MOE are generally considered as having no health concern. The target MOE for both analyses was 100, assuming that humans are 10 times more sensitive than rats or dogs and that there is a 10-fold variation in the sensitivity of humans. A calculated MOE lower than the target (100) would indicate a potential health concern.

Acute Exposure: At the 95th exposure percentile, the estimated acute exposures to bromacil ranged from 1.006 µg/kg/day for seniors 55+ years of age to 4.475 µg/kg/day for non-nursing infants.

Chronic Exposure: Estimates for chronic exposure to bromacil residues in drinking water ranged from 0.305 µg/kg/day for male 13 to 19 years of age to 2.290 µg/kg/day for non-nursing infants.

Acute Risk: Acute MOEs at the 95th percentile exposure were greater than 22,000 for all population subgroups, thereby exceeding the target MOE of 100 and indicating no risk.

Chronic Risk: Chronic MOEs were greater than 800 for all population subgroups, thereby exceeding the target MOE of 100 and indicating no risk.

Calculation of DPR Human Health Reference Levels for bromacil

DPR calculated acute and chronic screening levels (human health reference levels or HHRLs) and selected the lower of the two values to be used by EM as a guide when bromacil residues are detected in groundwater. An HHRL is the threshold pesticide residue for a maximum water intake that results in a maximum oral exposure that is considered to be without risk. The reference levels were calculated using the acute and chronic RfDs for bromacil as the maximum 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 intake rates were from the National Health and Nutrition Examination Survey)/“What We Eat in America” (NHANES/WWEIA) dietary survey for the years 2005-2010.

The HHRLs for bromacil in drinking water are summarized below (Table 1). The lowest reference value (chronic level 197 ppb) was selected as the HHRL for bromacil residues in drinking water. (Table 1).

Table 1. Acute and chronic reference levels for bromacil in drinking water

Acute or Chronic	Residue Level (ppb)	Subpopulation with Highest Water Intake per Bodyweight	Exposure Estimate	Calculated MOE ^a	Target MOE ^b	DPR HHRL ^c (ppb)
Acute	23	Non-Nursing Infants	95 th Percentile	22,346	100	5140
Chronic	23	Non-Nursing Infants	Average	856	100	197

- a) MOE (Margin of Exposure) for non-nursing infants.
- b) Target MOE is equal to the total uncertainty factors (UF_{TOTAL}) of 100 that accounts for interspecies sensitivity (10x) and intraspecies variability (10x).
- 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.

Conclusions

1. The detected bromacil residues in California well water ranging from 0.051 to 23 ppb should not be considered an acute or chronic health concern to residents that use the well for drinking water.
2. We recommend that bromacil detections in California wells be compared to a reference level of 197 ppb. Detected residues higher than this level should be sent to HHA for further evaluation.

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<https://www.regulations.gov/document/EPA-HQ-OPP-2012-0445-0020>.

USEPA. 2016b. Bromacil and Bromacil Lithium Salt - Registration Review Preliminary Drinking Water Assessment for All Registered Uses.

<https://www.regulations.gov/document/EPA-HQ-OPP-2012-0445-0019>.

Appendices

Appendix 1. DPR Memo: Potential Health Effects of Bromacil in Groundwater 26 July 2021 (2 pages)



Department of Pesticide Regulation

Gov. Gavin Newsom
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Jared Blumenfeld
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Julie Henderson
Acting Director

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

FROM: Minh Pham
Environmental Program Manager II
Environmental Monitoring Branch

Minh Pham

DATE: July 26, 2021

SUBJECT: POTENTIAL HEALTH EFFECTS OF BROMACIL 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 bromacil due to its occurrence in groundwater and its status as a 3CCR 6800(a) pesticide. 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, eleven public agencies¹ (including DPR) have reported sampling results for bromacil in groundwater. The data reviewed for this memorandum include data from the WIDB up to December 31, 2019 and GWPP sampling data through December 31, 2020.

Based on the WIDB, approximately 12,938 unique wells have been sampled for bromacil in California, totaling 39,304 samples. Of these wells, 349 wells have tested positive for bromacil. The first recorded sample for bromacil in the WIDB was collected in 1984, and the first recorded detection occurred in 1986.

In 2020, GWPP detected a bromacil concentration of 10.3 ppb in a single sample in a well with previously recorded bromacil contamination. This well is located in Fresno County, section 10M13S23E32, and has been sampled annually since 1999 as part of DPR's Well Monitoring Network. In 1994, bromacil was not detected in this well above the method detection limit of 0.05 ppb. Between 1996 and 2019, bromacil concentrations in this well have ranged from 0.051 to 6.69 ppb.

The maximum concentration of bromacil detected across all wells sampled in the state is 23 ppb, which was detected in a single well sampled in 1994; this well was not resampled.

¹ California Department of Pesticide Regulation, California Department of Public Health, California Department of Water Resources, Santa Clara County, California Regional Water Quality Control Board (Region 2), Yolo County, Santa Barbara County, United States Environmental Protection Agency, United States Geological Survey, California State Water Resources Control Board (SWRCB), and the SWRCB Drinking Water Program

Shelly DuTeaux
July 26, 2021
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Based on the increase in the bromacil concentration, 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: Joy Dias, CDPR Environmental Program Manager I
Carissa Ganapathy, CDPR, Senior Environmental Scientist (Supervisory)
Tiffany Kocis, CDPR Senior Environmental Scientist

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

Ver. 4.02, 05-10-c
 NHANES 2005-2010 2-Day
 Adjustment factor #2 NOT used.
 DEEM-FCID ACUTE Analysis for BROMACIL
 Residue file: Bromacil7SEPT2021.R10
 Analysis Date: 09-07-2021/11:42:42 Residue file dated: 09-07-2021/09:18:57
 NOEL (Acute) = 100.000000 mg/kg body-wt/day
 RAC/FF intake summed over 24 hours
 Run Comment: ""

Summary calculations--users:

	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure	MOE	Exposure	MOE	Exposure	MOE
Total US Population:	0.001245	80351	0.002203	45402	0.004196	23833
Hispanic:	0.001308	76438	0.002690	37172	0.004691	21318
Non-Hisp-White:	0.001238	80791	0.002089	47872	0.003890	25707
Non-Hisp-Black:	0.001052	95095	0.002308	43319	0.005193	19258
Non-Hisp-Other:	0.001443	69280	0.002370	42201	0.004024	24851
Nursing Infants:	0.002761	36214	0.004842	20651	0.008322	12016
Non-Nursing Infants:	0.004475	22346	0.005905	16934	0.007824	12781
Female 13+ PREG:	0.001177	84946	0.001472	67911	0.002099	47648
Children 1-6:	0.001532	65283	0.002428	41192	0.004113	24311
Children 7-12:	0.001074	93134	0.001780	56178	0.002747	36404
Male 13-19:	0.001010	99042	0.001574	63547	0.003591	27844
Female 13-19/NP:	0.001115	89672	0.001644	60817	0.002423	41269
Seniors 55+:	0.001006	99413	0.001561	64045	0.002373	42142
All Infants:	0.004334	23074	0.005822	17176	0.007844	12748
Children 1-2:	0.001795	55710	0.002678	37344	0.006928	14433
Children 3-5:	0.001429	69972	0.002217	45113	0.003832	26097
Children 6-12:	0.001122	89133	0.001825	54790	0.003013	33193
Youth 13-19:	0.001055	94808	0.001634	61199	0.002425	41237
Adults 20-49:	0.001216	82236	0.001823	54841	0.002551	39196
Adults 50-99:	0.001047	95553	0.001656	60379	0.002607	38364
Female 13-49:	0.001223	81772	0.001774	56354	0.002660	37591

Ver. 4.02, 05-10-c

DEEM-FCID Acute analysis for BROMACIL

Residue file name: C:\Program Files\DeemFCID40\Bromacil7SEPT2021.R10

Analysis Date 09-07-2021

Residue file dated: 09-07-2021/09:18:57

Reference dose (NOEL) = 100 mg/kg bw/day

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	Adj.Factors #2	Comment
8601000000	86A	Water, direct, all sources	0.023000	1.000	1.000	
8602000000	86B	Water, indirect, all sources	0.023000	1.000	1.000	

Appendix 3. Chronic Drinking Water Exposure Analysis (2 pages)

Evaluation Copy
 DEEM-FCID Chronic analysis for BROMACIL
 Residue file name: C:\Program Files\DeemFCID40\Bromacil27AUG2021.R10
 Ver. 4.02, 05-10-c
 NHANES 2005-2010 2-day
 Adjustment factor #2 NOT used.
 Analysis Date 08-27-2021/10:08:29 Residue file dated: 08-27-2021/09:56:56
 NOEL (Chronic) = 1.96 mg/kg bw/day

=====
 Total exposure by population subgroup

Population Subgroup	Total Exposure		
	mg/kg body wt/day	Percent of NOEL	Margin of Exposure
Total US Population	0.000465	0.02%	4,218
Hispanic	0.000453	0.02%	4,323
Non-Hisp-White	0.000477	0.02%	4,112
Non-Hisp-Black	0.000373	0.02%	5,248
Non-Hisp-Other	0.000546	0.03%	3,588
Nursing Infants	0.000529	0.03%	3,708
Non-Nursing Infants	0.002290	0.12%	856
Female 13+ PREG	0.000484	0.02%	4,047
Children 1-6	0.000557	0.03%	3,517
Children 7-12	0.000369	0.02%	5,319
Male 13-19	0.000305	0.02%	6,419
Female 13-19/NP	0.000349	0.02%	5,624
Male 20+	0.000432	0.02%	4,541
Female 20+/NP	0.000478	0.02%	4,101
Seniors 55+	0.000435	0.02%	4,508
All Infants	0.001736	0.09%	1,129
Female 13-50	0.000456	0.02%	4,297
Children 1-2	0.000639	0.03%	3,067
Children 3-5	0.000520	0.03%	3,769
Children 6-12	0.000387	0.02%	5,069
Youth 13-19	0.000328	0.02%	5,983
Adults 20-49	0.000462	0.02%	4,245
Adults 50-99	0.000449	0.02%	4,365
Female 13-49	0.000454	0.02%	4,318

Evaluation Copy

Ver. 4.02, 05-10-c

DEEM-FCID Chronic analysis for BROMACIL

Residue file: C:\Program Files\DeemFCID40\Bromacil27AUG2021.R10

Adjust. #2 NOT used

Analysis Date 08-27-2021

Residue file dated: 08-27-2021/09:56:56

Reference dose (NOEL) = 1.96 mg/kg bw/day

Food EPA Code	Crop Grp	Food Name	Residue (ppm)	Adj.Factors #1	#2
8601000000	86A	Water, direct, all sources	0.023000	1.000	1.000
8602000000	86B	Water, indirect, all sources	0.023000	1.000	1.000