PCPA Imidacloprid Comment
Pesticide Registration Branch
Calif. Department of Pesticide Registration
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EWG comments calling for an immediate end to imidacloprid pollution of California groundwater

The Environmental Working Group, or EWG, a nonprofit research and advocacy organization with offices in Sacramento, Minneapolis and Washington, D.C., objects to the pollution of California’s groundwater with imidacloprid that continues due to the lack of adequate regulation by the California Department of Pesticide Regulation, or CDPR.

Imidacloprid is a neonicotinoid insecticide harmful to the nervous system. The detection of imidacloprid above the reporting limit of 0.05 parts per billion, or ppb, in 15 wells in Fresno, Santa Barbara and Tulare counties at concentrations ranging from 0.051 to 5.97 ppb¹ demonstrates the threat imidacloprid poses to California’s precious groundwater supply, which is a source of drinking water for millions of people.

In this comment letter, EWG presents three key findings and recommendations:
1. The human health reference value used by CDPR disregards numerous studies showing imidacloprid toxicity at much lower concentrations.
2. The health-protective guideline value for groundwater should be developed based on the most sensitive studies and should include a tenfold children’s health safety factor.
3. Imidacloprid pollution of California’s ground water must stop immediately.

Details for these recommendations are listed below.

1. The human health reference value used by CDPR disregards numerous studies showing imidacloprid toxicity at much lower concentrations.

Following the detection of imidacloprid in water wells in Fresno, Santa Barbara and Tulare, a subcommittee of the CDPR’s Pesticide Registration and Evaluation Committee held a public hearing in March and April 2022 to determine whether these detections meet the definition of pollution and whether the registration and use of imidacloprid as an agricultural pesticide should be allowed to continue.

Critical to the determination about whether imidacloprid pollutes California groundwater is whether the detected levels are a concern for human health. Therefore, it is critical that a human health reference level be determined based on the currently available science reflecting the most sensitive toxicological endpoint, as well as current and appropriate risk assessment guidelines.

EWG contends that a human health reference level of 283 ppb is not a health-protective value, and that it should not be used in the Pesticide Registration and Evaluation Committee’s determination. The human health reference level set by CDPR in 2021 is based on a risk characterization document from 2006, which used a 2001 developmental neurotoxicity study with a point of departure of 5.5 mg/kg per day. There are many toxicological assessments of imidacloprid in the peer-reviewed literature showing that doses far lower can cause harm in laboratory animals. This human health reference level is based on outdated science, and more recent publications on the toxicity of imidacloprid support use a much lower value to assess harm to human health.

2. A health-protective guideline value for groundwater should be developed based on the most sensitive studies and should include a tenfold children’s health safety factor.

As reviewed by OEHHA and supported by additional studies, and presented in Figure 1, peer-reviewed studies identified that imidacloprid exposure can cause

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4 OEHHA, 2021. Memorandum: OEHHA’s findings on the health effects of imidacloprid relevant to its identification as a potential groundwater contaminant. Sutherland-Ashley, K. February 18, 2022. Pesticide and Environmental Toxicology Branch, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency.
developmental neurotoxicity, immunotoxicity and glucose homeostasis, and its impact on the reproductive system, particularly the male reproductive system, affecting several parameters associated with sperm function.

Epidemiological studies of real-world exposure to imidacloprid show harm, particularly to children. A systematic review published in 2017 indicated that imidacloprid exposure is associated with increased risk of autism spectrum disorder and adverse birth outcomes, such as birth defects of the brain.

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Figure 1. Toxicological findings from studies in the peer-reviewed literature and associated potential public health-protective concentrations compared to CDPRs’ human health reference level. Figure and table information are adapted and modified (to include an additional children’s health safety factor) from OEHHA’s findings on the health effects of imidacloprid relevant to its identification as a potential groundwater contaminant.

<table>
<thead>
<tr>
<th>Study Author and Year</th>
<th>Toxicological Health Effect</th>
<th>Public Health Protective Concentrations from OEHHA with additional 10X Children’s Health Safety Factor</th>
</tr>
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<tbody>
<tr>
<td>DPR, 2021</td>
<td>Developmental neurotoxicity</td>
<td>28.3</td>
</tr>
<tr>
<td>Kara et al., 2015</td>
<td>Developmental neurotoxicity</td>
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</tr>
<tr>
<td>Badgujar et al., 2013</td>
<td>Immunotoxicity</td>
<td>1.0</td>
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<tr>
<td>Abdel-Rahman et al., 2017</td>
<td>Reproductive toxicity</td>
<td>1.9</td>
</tr>
<tr>
<td>Bal et al., 2012a</td>
<td>Reproductive toxicity</td>
<td>2.3</td>
</tr>
<tr>
<td>Bal et al., 2012b</td>
<td>Reproductive and developmental toxicity</td>
<td>2.3</td>
</tr>
<tr>
<td>Bagri et al., 2015</td>
<td>Reproductive toxicity</td>
<td>2.3</td>
</tr>
<tr>
<td>Zhao et al., 2021</td>
<td>Neurotoxicity and glucose homeostasis</td>
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</tr>
<tr>
<td>Khall et al., 2017</td>
<td>Glucose homeostasis</td>
<td>0.2</td>
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<tr>
<td>Sun et al., 2016</td>
<td>Glucose homeostasis</td>
<td>0.2</td>
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<td>Sun et al., 2017</td>
<td>Glucose homeostasis</td>
<td>0.2</td>
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Figure legend: BMDL (blue data points); ENEL (grey data points); NOAEL (green data points). The blue box denotes the lowest derived value.

In presentations from the registrant during the hearing, the registrant inappropriately dismissed findings from these peer-review studies, which indicate harm from imidacloprid at doses lower than the current point of departure. Inclusion of these studies is extremely important, since toxicological effects at high and low doses may be different; low-dose exposures often represent real world exposure scenarios for humans; and the peer-review studies often investigated health effects not assessed in registrant-submitted studies.

Furthermore, there is the precedent of regulatory agencies using the studies presented in Figure 1 for assessing the risk of imidacloprid in water, namely by the
Wisconsin Department of Health Services\textsuperscript{19} and Minnesota Department of Public Health.\textsuperscript{20} For example, the Wisconsin Department of Health Services has proposed an enforcement standard of 0.2 ppb for imidacloprid based on the Sun et al. 2016 study that identified the impacts on metabolic parameters. This value would be in line with the public health concentration values derived by OEHHA for the Khalil et al. 2017 study, with an additional safety factor for children’s health. Additionally, other studies support the idea that that imidacloprid can act as a metabolic disruptor, promoting lipid accumulation in cells,\textsuperscript{21} and exposure in humans has been associated with being overweight or obese in adults.\textsuperscript{22}

Therefore, a value no higher than 0.2 ppb should be used a screening value, a level more than 1,000 times lower than the value proposed by CDPR and supported by the registrant.

3. Imidacloprid pollution of California’s ground water must end immediately.

The detection of imidacloprid in groundwater wells at levels that may cause harm to human health meets the definition of pollution put forth by the Pesticide Contamination Prevention Act. This calls for such pollution to be stopped immediately.

Although the CDPR’s Pesticide Registration and Evaluation Committee hearing was specific to imidacloprid, it is a member of a group of pesticides known as neonicotinoids, which have a common mechanism of action for their insecticidal use and have toxicological effects that are similar in mammals and other species. In 2020, the National Toxicology Program published a review of neonicotinoid toxicity, reporting neurological and developmental effects as the most studied outcomes.\textsuperscript{23}

\textsuperscript{20} Minnesota Department of Health (MDH, 2020). Toxicological Summary for: Imidacloprid. Available at: https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/imidasumm.pdf
Since 2020, animal studies continue to show neonicotinoids harm the reproductive system, as well as affecting memory and behavior.\textsuperscript{24, 25, 26}

Analyses of neonicotinoid residue data from the U.S. Department of Agriculture Pesticide Data Program indicated that neonicotinoids are widely detected in foods, and multiple residues from different neonicotinoids are often present on the same sample. Additionally, nearly 50 percent of the U.S. population has detectable levels of neonicotinoids, as measured in their urine, with children having higher levels of exposure.

Given the documented exposure to multiple neonicotinoids and shared toxicological properties of these insecticides, additional exposure to imidacloprid through water is a risk to human health.

In conclusion, it is essential that the subcommittee use the best available science to ensure that public health is protected from imidacloprid pollution of ground water. The committee must recognize the low dose effects of imidacloprid in its determination, and pollution of California’s groundwater by imidacloprid must end. To protect Californians from unintended and damaging health impacts, we urge the branch and department to consider EWG’s findings and recommendations seriously.

Submitted on behalf of the Environmental Working Group,

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Toxicologist

Bill Allayaud
California Director of Government Affairs

\textsuperscript{26} Maeda M, Kitauchi A, Hirano T et al. (2021). Fetal and lactational exposure to the no-observed-adverse-effect level (NOAEL) dose of the neonicotinoid pesticide clothianidin inhibits neurogenesis and induces different behavioral abnormalities at the developmental stages in male mice. J Vet Med Sci. 2021 Apr 3;83(3):542-548