Esther Barajas-Ochoa
Office of Environmental Health Hazard Assessment
1001 I Street
P. O. Box 4010
Sacramento, California 95812-4010

Dear Ms. Barajas-Ochoa:

Thank you for the opportunity to comment on the proposed No Significant Risk Level (NSRL) for 1,3-dichloropropene. We strongly support the proposed NSRL and believe that it is consistent with the Safe Drinking Water and Toxic Enforcement Act as well as the regulations that have been enacted to implement the law.

We support the approaches used to calculate the proposed NSRL for the following reasons:

1. **The NSRL is based on tumor frequency at two sites: the lungs and the lacrimal glands.** Combining tumor from multiple sites to estimate cancer potency is recommended by several authoritative agencies. The U.S. Environmental Protection Agency cancer guidelines state that tumors at multiple sites strengthen the evidence for carcinogenicity of a substance, and that risk estimates from different tumor sites should be added.[1] The National Research Council also supports this approach.[2] OEHHA has used tumors at multiple sites to calculate cancer potency and NSRLs at least ten times in the last two decades (p-chloroaniline, p-chloroanilinehydrochloride, chlorothalonil, dibenzo[a,i]pyrene, dibromoacetic acid, diisononyl phthalate, glycidol, s-methylchrysene, nitromethane, and tris(1,3-dichloro-2-propyl) phosphate).

2. **The NSRL is based on cancer potency calculated from the frequency of the combination of adenomas and carcinomas**. Summing adenomas and carcinomas is supported by the World Health Organization (International Agency for Research on Cancer)[3] and the U.S. Environmental Protection Agency[1] when scientifically appropriate. OEHHA has used a combination of adenomas and carcinomas to calculate cancer potency at least nine times in the last two decades (p-chloroaniline, p-chloroaniline hydrochloride, chlorothalonil, p-chloro-α,α,α-trifluorotoluene, dibromoacetic acid, diisononyl phthalate (DINP), glycidol, nitromethane , tris(1,3-dichloro-2-propyl) phosphate).

3. **Tumor frequencies in unexposed (control) animals from the study used to calculate cancer potency are consistent with historical control values.** Charles River states that the historical control values for the strain of mice used in the 1,3-dichloropropene cancer study are 0.5% (range 0 – 7.0%) for lacrimal gland cystadenomas, 8.3% (range 0 - 24.6% for bronchiolar/alveolar adenomas, and 1.9% (range 0 - 5.8%) for bronchiolar/alveolar carcinoma.[4] Control frequencies in the 1,3-dichloropropene study were 2% for lacrimal gland tumors and 18% for bronchiolar/alveolar tumors. In addition, in both cases, frequencies in the animals exposed to the highest doses of 1,3-

dichloropropene (12% for lacrimal gland tumors and 44% for bronchiolar/alveolar tumors) were above the historical control range.

4. **Decreased tumor frequencies are not uncommon in animals exposed to the high dose in carcinogenicity studies if those animals have a decreased body weight.**[5] In the 1,3-dichloropropene study, high-dose males had fewer lacrimal gland tumors than mid-dose males. The body weight of the high-dose males was about 4% less than control animals, potentially masking carcinogenic effects.

Thank you for your work to protect the health of all Californians.

Sincerely,

(affiliations for identification purposes)

Jane Sellen and Sarah Aird
Californians for Pesticide Reform

Anne Katten
California Rural Legal Assistance Foundation

Nathan Donley
Center for Biological Diversity

Caroline Cox
retired

Bill Allayaud
Environmental Working Group

Jennifer Kay and Ruthann Rudel
Silent Spring Institute

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[1] U.S. Environmental Protection Agency. Risk Assessment Forum. 2005. Guidelines for Carcinogen Risk Assessment. https://www.epa.gov/sites/default/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf.

[2] National Research Council (US) Committee on Risk Assessment of Hazardous Air Pollutants. Science and Judgment in Risk Assessment. Washington (DC): National Academies Press (US); 1994. http://www.nap.edu/catalog/2125.html.

[3] World Health Organization. International Agency for Research on Cancer. IARC Monographs on the Identification of Carcinogenic Hazards to Humans Preamble. 2019. https://monographs.iarc.who.int/wp-content/uploads/2019/07/Preamble-2019.pdf

[4] Charles River. Spontaneous Neoplastic Lesions in the B6C3F1 / CrlBR Mouse. 1989. https://www.criver.com/sites/default/files/resources/rm_rm_r_lesions_b6c3f1_crlbr_mouse.pdf.

[5] Haseman JK, Young E, Eustis SL, Hailey JR. Body weight-tumor incidence correlations in long-term rodent carcinogenicity studies. Toxicol Pathol. 1997 May-Jun;25(3):256-63. https://journals.sagepub.com/doi/abs/10.1177/019262339702500302