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October 21, 2026

Dr. Kristina Thayer
Director
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

Re: Comment on September 2026 Vinyl Acetate Pre-Regulatory Workshop

Dear Dr. Thayer:

RHP Risk Management Inc. appreciates the opportunity to comment on the proposed no significant risk level (NSRL) of 11 µg/day for vinyl acetate monomer (VAM; CAS No. 108-05-4) and the accompanying proposal concerning analytical testing. We support development of a scientifically supported safe harbor and clarification of methods used to evaluate exposure to the listed monomer. Our comments focus on the quantitative suitability of the principal study, documentation of study selection, the treatment of uncertainty, and the applicability of the value across exposure routes. [1, 2]

We have independently evaluated the carcinogenicity studies described in OEHHA's 2024 Evidence on the Carcinogenicity of Vinyl Acetate report. Our analysis, described in a manuscript currently under review, suggests candidate NSRLs of 750 µg/day for oral exposure and 398 µg/day for inhalation exposure. We used benchmark dose modeling with a benchmark response of 10% extra risk, probabilistic analyses for selected parameters, and model-averaging approaches to account for uncertainty associated with model selection. Both values retain linear low-dose extrapolation to a lifetime excess cancer risk of 10^{-5}. We offer this work as additional context for OEHHA's evaluation. Our principal request is that the final assessment more fully explain how the available studies and alternative analytical choices were evaluated. [2, 3]

Quantitative suitability of the principal study

The proposed value is based on multisite tumor findings in female F344 rats from Lijinsky and Reuber (1983), incorporating the EPL (1982) pathology review. This study's suitability for estimating a specific human cancer potency nevertheless warrants further discussion. The study included 20 animals per sex per group, two nonzero concentrations, and exposure through drinking water five days per week for 100 weeks. Tissue-specific denominators differed, and an independent pathology review included additional examination of previously unexamined tissues. [1, 2, 4, 5]

There are several concerns with this study including instability of vinyl acetate in drinking water with weekly preparations of the drinking water solution, small group sizes, uncertain test-material purity, We recommend that OEHHA explain how these limitations were considered in determining that this study is of sufficient quality for quantitative risk assessment. The calculation should clearly identify the basis for the water intake and body weight assumptions, the handling of the five-day dosing schedule and follow-up period, and the effect of uncertainty in the delivered dose. Solution degradation does not necessarily imply that the proposed NSRL should increase; it introduces uncertainty in both the VAM dose and the composition of the administered solution.

Documentation of study and endpoint selection

The explanatory document identifies higher tumor incidences, tumors across more sites, and findings at lower or multiple administered concentrations as reasons for selecting studies. These features are relevant to sensitivity, but they do not fully describe how study quality and quantitative suitability were weighed. A concise comparison of the available bioassays would help explain the selection, including group sizes, concentration verification, dose estimation, pathology coverage, exposure duration, and route.

The oral bioassays have differing strengths and limitations, and dose-estimation concerns are not confined to the selected study. We recommend that OEHHA apply and document consistent criteria across the available oral studies, explaining which limitations affect their use for hazard identification and which affect their use for quantitative potency estimation. This comparison would help establish whether the selected study provides a reliable quantitative basis despite its limitations.

For the selected female F344 study, the final assessment should also explain the inclusion and contribution of each tumor type to the multisite potency. The biological rationale for including benign lesions, combining or separating lesions, and estimating cumulative risk across sites should be documented. Site-specific potency estimates and sensitivity analyses would show whether the result is broadly supported or depends strongly on particular endpoints. The same endpoint-selection criteria should be applied when evaluating alternative datasets.

Combined effect of conservative assumptions

Health-protective assumptions are appropriate when developing an NSRL. However, choices that are reasonable individually can collectively produce a substantially more protective estimate. The assessment selects the highest estimated potency among the retained studies, incorporates several tumor types, uses a lower-bound dose estimate, and applies linear extrapolation to low exposures. Some of these choices reflect regulatory defaults; others depend on the data and the analytical implementation. Their combined effect should be explained.

We recommend that OEHHA distinguish requirements and defaults from study-specific judgments, then show how reasonable alternatives affect the estimate. Relevant comparisons include alternative studies and endpoint groupings, model selection or averaging, and benchmark responses of 5% and 10% using otherwise consistent assumptions. Neither a lower benchmark response nor model averaging necessarily produces a more protective result in every dataset. The purpose of these comparisons is to identify the decisions that materially influence potency and whether the combined assumptions are appropriately supported.

This evaluation would preserve the 10^{-5} lifetime risk criterion while making the treatment of uncertainty more transparent. We are not recommending removal of protective assumptions solely because they lower the NSRL. Rather, the assessment should explain why the overall combination is appropriate for VAM and how much each consequential choice contributes to the result.

Exposure route and target tissue dosimetry

VAM follows a predominantly portal-of-entry tumor pattern, with respiratory tumors following inhalation and oral or upper gastrointestinal tumors following ingestion, while recognizing limited evidence of tumors at distant sites. This pattern supports explicit consideration of route and local tissue dosimetry. Rapid metabolism does not establish that systemic exposure or carcinogenic effects are absent, but it makes the location and magnitude of reactive-metabolite formation relevant to extrapolation between routes. [6]

OEHHA's pre-regulatory workshop slide 13 states that no route-specific pharmacokinetic differences were identified, citing absorption, distribution, and excretion of radiolabeled products. [7] OEHHA's 2024 review also reports high nasal-tissue radioactivity after inhalation but not oral administration and identifies carbon dioxide as a major exhaled product. Similar elimination of radiolabeled carbon does not by itself establish equivalent target-tissue exposure or cancer potency across routes. We recommend that OEHHA explain how these findings, together with the route-specific tumor data, support the intended applicability of the proposed value.

The regulatory entry does not specify an exposure route. We recommend that OEHHA clarify its intended scope and evaluate a separate inhalation NSRL using the available chronic inhalation study by Bogdanffy et al. (1994) and appropriate respiratory dosimetry. [8]

VAM's volatility makes this relevant to assessments of products that can release residual monomer during use. Oral exposure remains relevant for other product uses. The appropriate route should follow the exposure scenario rather than be assumed from the product's polymer content.

Mechanistic information should inform this evaluation without requiring a definitive threshold conclusion. OEHHA's report describes both genotoxicity and tissue responses associated with local metabolism. The final assessment should explain how that evidence supports the selected dose metric and low-dose extrapolation.

Application to consumer products

We support the substance of proposed section 25901, which distinguishes exposure to residual VAM from monomer generated by analytical breakdown of a polymer under conditions that would not occur during consumer product exposure. Accompanying guidance should address method suitability for the product matrix and reasonably foreseeable use, including analytical recovery, reporting limits, and conditions that could generate VAM during testing. Releases that can occur during reasonably foreseeable use should remain part of the exposure assessment.

Companies will use the NSRL to inform testing, supplier specifications, exposure assessments, and warning decisions. Clear guidance should distinguish product concentration from daily exposure and explain the role of migration, emission, or use-based measurements. We also support retaining OEHHA's explanation that the NSRL is an optional safe harbor and that other scientifically supported assessments may establish no significant risk.

We request that OEHHA expand the documentation of study and endpoint selection, explain the handling of dose uncertainty in the principal study, characterize the combined effect of consequential assumptions, and clarify route applicability. These additions would provide a clearer scientific basis for the final value and support consistent application by the regulated community.

We appreciate OEHHA's consideration of these comments.

Sincerely,

Melanie C. Buser

Melanie C. Buser, PhD, DABT, MPH
RHP Risk Management Inc.

References

[1] OEHHA. September 2026. Possible amendments to section 25705(b) and Article 9. Draft explanatory information and associated draft regulatory text. https://oehha.ca.gov/proposition-65/crnr/proposition-65-vinyl-acetate-pre-regulatory-workshop

[2] OEHHA. October 2024. Evidence on the Carcinogenicity of Vinyl Acetate. https://oehha.ca.gov/sites/default/files/media/downloads/crnr/vinylacetatehid100424.pdf

[3] Buser MC, Jachak A, Persky J. Derivation of Candidate No Significant Risk Levels for Vinyl Acetate Using Probabilistic Benchmark Dose Modeling. Manuscript under review at Regulatory Toxicology and Pharmacology.

[4] Lijinsky W and Reuber MD. 1983. Chronic toxicity studies of vinyl acetate in Fischer rats. *Toxicology and Applied Pharmacology*, *68*(1), 43–53. https://doi.org/10.1016/0041-008x(83)90353-8

[5] Experimental Pathology Laboratories (EPL). 1982. Bioassay of Vinyl Acetate in F344 Rats Pathology Report Addendum.

[6] ATSDR. January 2025. Toxicological Profile for Vinyl Acetate. https://www.atsdr.cdc.gov/toxprofiles/tp59.pdf

[7] OEHHA. September 30, 2026. Proposed Proposition 65 No Significant Risk Level for Vinyl Acetate. Workshop presentation, available with the materials in reference 1.

[8] Bogdanffy MS et al. 1994. Chronic toxicity and oncogenicity inhalation study with vinyl acetate in the rat and mouse. Fundamental and Applied Toxicology 23:215–229. https://doi.org/10.1006/faat.1994.1100

[9] Umeda Y et al. 2004. Carcinogenicity and chronic toxicity in mice and rats administered vinyl acetate monomer in drinking water. Journal of Occupational Health 46:87–99. https://doi.org/10.1539/joh.46.87