



July 1, 2024

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

Submitted via the website <https://oehha.ca.gov/comments>

Re: Proposed Proposition 65 No Significant Risk Level (NSRL) for titanium dioxide (airborne, unbound particles of respirable size)

Dear Ms. Barajas-Ochoa:

The American Chemistry Council's Titanium Dioxide Stewardship Council (TDSC)¹ welcomes the opportunity to provide these comments in response to the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) regarding the proposal to adopt a Proposition 65 NSRL for titanium dioxide (airborne, unbound particles of respirable size) by amending Title 27, California Code of Regulations, section 25705(c)(2). TDSC members are manufacturers of titanium dioxide, and TDSC promotes the safe use of titanium dioxide through research, product stewardship, advocacy, and outreach.

OEHHA is proposing an NSRL of 440 micrograms per day for airborne, unbound titanium dioxide particles with diameters of 10 micrometers or less, and an NSRL of 44 micrograms per day for airborne, unbound titanium dioxide particles with diameters of 0.8 micrometers or less. Both parts of the NSRL would have to be met before it applies. We appreciate OEHHA's action to propose an NSRL that can help both plaintiffs and defendants evaluate the significance of an exposure and potentially reduce the need for litigation.

We understand and appreciate that Title 27 of the California code of Regulations, Section 2705(c) gives OEHHA the authority to base an NSRL on a state or federal risk assessment. OEHHA has chosen to base the proposed NSRL on the National Institute of Occupational Safety and Health's (NIOSH) 2011 risk assessment for titanium dioxide.²

We would like to take this opportunity to provide information on the Heinrich et al. (1995)³ study cited by NIOSH in its 2011 risk assessment, as well as the International Agency

¹ <https://www.americanchemistry.com/industry-groups/titanium-dioxide-stewardship-council-tdsc>

² NIOSH. 2011. Current Intelligence Bulletin 63: Occupational Exposure to Titanium Dioxide. Publication No. 2011-160. Available at <https://www.cdc.gov/niosh/docs/2011-160/default.html>.

³ Heinrich U, Fuhst R, Rittinghausen S, Creutzenberg O, Bellmann B, Koch W, Levsen K. 1995. Chronic inhalation exposure of Wistar rats and two different strains of mice to diesel-engine exhaust, carbon black, and titanium dioxide. *Inhalation Toxicology* 7(4):533-556. <https://doi.org/10.3109/08958379509015211>.

for Research on Cancer's (IARC) 2010 monograph on titanium dioxide.⁴ In the Heinrich study, which focused on diesel engine exhaust, titanium dioxide was used as a control, and the female rats exposed to titanium dioxide represented a "satellite control group" exposed to varying concentrations of an ultrafine form of titanium dioxide. Approximately 98% of the titanium dioxide placed on the market is pigmentary, non-ultrafine particle sized titanium dioxide, used as an ingredient in other products. The ultrafine form of titanium dioxide used in the Heinrich study represents a tiny fraction of titanium dioxide sold into the global market designed and used as an ingredient in specialized industrial purposes only.

The Heinrich study subjected the satellite control group of female rats for a nonstandard duration of 18 hrs/day throughout the study. The female rats represented a single "series" of exposure concentrations. They were exposed for 24 months and subsequently held for an additional 6 months prior to sacrifice. Given that this was a single satellite group of female rats and not part of a dose response study and/or gender complete (male + female) set of rats, the study would not qualify as an acceptable study under Good Laboratory Practices and does not meet OECD guidelines. Severely reduced lung clearance (clearance half times exceeding one year after only 12 months of exposure), impaired breathing patterns (reduced tidal volume and increased breathing frequency), highly elevated lung weights, and associated inflammatory lung tissue resulting from the study exposures clearly indicate that the physiological status of the lungs of the rats in the study was severely compromised. The exposure conditions (18h/day at average concentrations of 10 mg/m³) extended clearance half times to approximately 1 year, documenting a critical impairment of lung function. Tumour formation occurred only under lung burdens corresponding to an alveolar macrophage loading of >60% representing an extreme lung overload condition.

In addition, the General Court of the European Union specifically ruled the Heinrich study was not reliable or acceptable as the principal basis for the classification of titanium dioxide in Europe. In a November 23, 2022 decision the court ruled that titanium dioxide is not a category 2 carcinogen by inhalation under Regulation (EC) No 1272/2008 on classification and labelling.⁵ The principal reasons for the annulment of the classification were failure "to base the classification of a carcinogenic substance on reliable and acceptable studies was not satisfied" and the incorrect application of the criteria for carcinogenicity under the classification and labelling rules, which require the substance to exhibit an intrinsic hazard.

Finally, we support comments submitted by the Personal Care Products Council concerning the need for particle size definitions that are consistent with the human health risk assessment in NIOSH's 2011 risk assessment. Clear and consistent particle size definitions

⁴ IARC (2010). Carbon Black, Titanium Dioxide, and Talc. *IARC Monogr Eval Carcinog Risks Hum*, 93:193–276.

⁵ <https://curia.europa.eu/juris/document/document.jsf?text=&docid=268096&pageIndex=0&doclang=EN&mode=req&dir=&occ=first&part=1&cid=1840069> CWS Powder Coatings and Others v Commission Cases T-279/20 and T-28320 at <https://curia.europa.eu/juris/documents.jsf?num=T-279/20>. See also, Court of Justice of the European Union Press Release No 190/22 at <https://curia.europa.eu/jcms/upload/docs/application/pdf/2022-11/cp220190en.pdf>.

would reduce uncertainty and facilitate proactive measures by companies that wish to evaluate their compliance with the proposed NSRL.

Thank you for the opportunity to comment on the draft NSRL for titanium dioxide (airborne, unbound particles of respirable size). As stated previously, we appreciate that OEHHA is proposing an NSRL that can help evaluate the significance of an exposure and potentially reduce the need for litigation. Please contact me if you have any questions about these comments.

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