Petition for Review of the Toxic Air Contaminant Human Health Assessment for Hexavalent Chromium Pursuant to Health and Safety Code Section 39662(e)

I. INTRODUCTION

The inhalation unit risk factor (IUR) for hexavalent chromium (Cr(IV)), which applies to regulation of Cr(VI) under both the Toxic Air Contaminant Identification and Control Act[1] (TAC Act) and the Air Toxics Hot Spots Information and Assessment Act[2] (Hot Spots Act), must be updated because it is no longer supported by the best available science. California developed its human health assessment for inhaled Cr(VI) in 1985, nearly 40 years ago, and has not updated it since. In the decades that followed, significant new peer-reviewed epidemiological and toxicological information has become available, along with advancements in health risk assessment methodology and practice. These data and scientific advancements allow for a more accurate health risk assessment than was possible in the mid-1980s, and demonstrate that the current IUR substantially overstates the human health risk from inhaled Cr(VI).

While this new scientific evidence does not change the determination that inhalation of Cr(VI) is carcinogenic (and therefore should continue to be listed as a toxic air contaminant (TAC) and regulated under the Hot Spots Program), it does warrant a quantitative change to the cancer potency and IUR estimated in the 1986 TAC determination.

II. BACKGROUND

a. CALIFORNIA'S AIR TOXICS PROGRAM

Reducing the public's health risk from exposure to airborne toxic chemicals is one of California's most fundamental air quality goals. Several laws, including the TAC Act and the Hot Spots Act, form the basis for the California Air Resources Board (CARB) to identify and control TACs from a multitude of sources, to inform the public of significant risks from exposures to TACs, and provide ways to reduce those risks.[3] CARB, the Office of Environmental Health

[1] Health & Saf. Code, § 39650, *et seq.*
[2] Health & Saf. Code, § 44300, *et seq.*
[3] In addition to programs under the TAC Act and the Hot Spots Act, California's air toxics program includes the Children's Environmental Health Protection Program, the Community Air Protection Program, and local air district regulations. (CARB website, *Air Toxics Program*, available at https://ww2.arb.ca.gov/our-work/programs/air-toxics-program/about.)

Hazard Assessment (OEHHA), and the state's 35 local air districts each play a role in advancing this goal.

Under the TAC Act, CARB identifies TACs and manages potential health risks.[4] CARB relies on health assessments prepared by OEHHA to determine whether regulatory action is necessary to reduce risks posed by TACs, to develop airborne toxic control measures (ATCM), to prioritize TACs for evaluation and potential regulation, and to ensure that ATCMs are cost-effective and appropriately balance public health protection and economic growth.[5]

The Hot Spots Act compliments the TAC Act. It is designed to provide information to state and local agencies and to the general public on the extent of airborne emissions from stationary sources and the potential public health impacts of those emissions. Its purpose is to collect emissions data, to identify facilities having localized impacts, to ascertain health risks, to notify nearby residents of significant risks, and to mitigate those risks.[6] It creates a process to identify sources of TACs and to provide exposure information necessary for CARB to prioritize and develop regulations for TACs.[7]

Local air pollution control districts implement aspects of the Hot Spots Act and enforce air pollution regulations designed to reduce emissions from businesses and industries in the state. The districts use OEHHA's health assessments to regulate stationary sources of TAC emissions. Regulated facilities are required to report the types and quantities of certain TACs their facilities routinely release into the air.[8] CARB compiles this data into publicly available emissions inventories, which are updated every four years.[9]

Local air districts use the CARB inventories to prioritize facilities for risk assessment and to require high risk facilities to prepare health risk assessments utilizing health reference values, including but not limited to IURs for cancer causing substances, prepared by OEHHA.[10] Based on the results of these risk assessments,

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[4] Health & Saf. Code, § 39650.
[5] Health & Saf. Code, §§ 39665-39669; CARB, AB 1807-Toxics Air Contaminant Identification and Control, *available at* https://ww2.arb.ca.gov/resources/documents/ab-1807-toxics-air-contaminant-identification-and-control; CARB, Health Risk Assessment, *available at* https://ww2.arb.ca.gov/resources/documents/health-risk-assessment.
[6] Health & Saf. Code, § 44301.
[7] Health & Saf. Code, §§ 44301, 44364.
[8] Health & Saf. Code, § 44322.
[9] Health & Saf. Code, §§ 44340-44346.
[10] Health & Saf. Code, §§ 44344, 44344.6, 44360-44366; OEHHA, *Air Toxics Hot Spots Program Guidance Manual for the Preparation of Health Risk Assessments (2015)*, Appendix L

facilities may be required to notify surrounding populations of potential health risks associated with exposure to TACs emitted by the facility or invest in airborne toxic risk reduction measures (ATRRMs) to reduce TAC emissions, or both.[11] CARB is required to consider facility emissions reports and risk assessments to identify, establish priorities for, and control TACs.[12]

i. Health Risk Assessments Must be Based on the Best Available Scientific Evidence.

Regulation of TACs based on the best scientific data that is currently available is a fundamental principle of California's comprehensive air toxics programs and consistent with California public policy favoring evidence-based decision-making and scientific integrity.[13] In the TAC Act, the Legislature explicitly found and declared that "the identification and regulation of toxic air contaminants should utilize the best available scientific evidence gathered from the public, private industry, the scientific community, and federal, state, and local agencies."[14] The Act requires OEHHA to base its health assessments on "all available scientific data," including relevant data provided by state, federal, and international health agencies, private industry, academic researchers, and public health and environmental organizations.[15] OEHHA must also use "current principles, practices, and methods used by public health professionals who are experienced practitioners in the fields of epidemiology, human health effects

(OEHHA/ARB Approved Health Values for Use in Hot Spot Facility Risk Assessments), *available at* https://oehha.ca.gov/air/crnr/notice-adoption-air-toxics-hot-spots-program-guidance-manual-preparation-health-risk-0).

[11] Health & Saf. Code, §§ 44390-44394.

[12] Health & Saf. Code, § 44364.

[13] CARB website, *About*, available at https://ww2.arb.ca.gov/about ("Reducing air pollution and protecting public health guide CARB's actions. Our role is to: … Research the causes and effects of air pollution problems – and potential solutions – using the best available science and technology."); *see also* CalEPA website, *About Us*, available at https://calepa.ca.gov/about/ ("Our departments are at the forefront of environmental science, using the most recent research to shape the state's environmental laws."); see also The White House, *Memorandum on Restoring Trust in Government Through Scientific Integrity and Evidence-Based Policymaking*, January 27, 2021, available at https://www.whitehouse.gov/briefing-room/presidential-actions/2021/01/27/memorandum-on-restoring-trust-in-government-through-scientific-integrity-and-evidence-based-policymaking/ ("It is the policy of my Administration to make evidence-based decisions guided by the best available science and data. Scientific and technological information, data, and evidence are central to the development and iterative improvement of sound policies, and to the delivery of equitable programs, across every area of government.").

[14] Health & Saf. Code, § 39650(d).

[15] Health & Saf. Code, § 39660, subd. (b).

assessment, risk assessment, and toxicity," when evaluating the health effects of a substance.[16]

The relevant data that OEHHA must consider in connection with a health assessment under the TAC Act includes the current emissions reports and risk assessments required by the Hot Spots Act. Facilities must update their emission inventories every four years taking into consideration "improvements in measurement techniques and advancing knowledge concerning the types and toxicity of hazardous materials released or potentially released."[17] The Legislature explicitly required CARB to consider this regularly-updated scientific data when regulating TACs.[18]

To ensure OEHHA's TAC health assessments are "based on sound scientific knowledge, methods, and practices," the TAC Act requires independent public and scientific review of OEHHA's TAC health assessments and the related reports that CARB and OEHHA jointly prepare.[19] The Scientific Review Panel on Toxic Air Contaminants (SRP) has the responsibility to perform this independent review and to advise CARB in its evaluation of the health effects of substances.[20]

ii. Health Assessments Must be Reevaluated and Updated When Warranted by New Scientific Evidence

To ensure health assessments continue to be based on the best available scientific evidence, periodic review of the scientific data and methods underlying existing health assessments and related regulations is required by both the TAC Act and the Hot Spots Act.[21] The Hot Spots Act requires consideration of new scientific data by imposing a requirement to collect and update emissions data every four years and to use that current data to prioritize and prepare updated risk assessments for regulated sources, and by requiring CARB to consider these data and risk assessments when regulating TACs.[22] In addition, the TAC Act provides a mechanism for CARB to reevaluate the scientific basis for a TAC in response to a petition alerting CARB to the existence of new scientific evidence.[23]

[16] Health & Saf. Code, § 39660, subd. (b).
[17] Health & Saf. Code, § 44344.
[18] Health & Saf. Code, § 44364.
[19] Health & Saf. Code, §§ 39650(d), 39660(c), 39661.
[20] Health & Saf. Code, §§ 39660(c), 39661, 39670.
[21] See Health & Saf. Code, §§ 39650(d), 39660(b), 39662(d), (e), 44344, 44344.6, 44360.
[22] Health & Saf. Code, §§ 44344, 44344.6, 44360,44364.
[23] Health & Saf. Code, §§ 39650(d), 39660(b), 39662(d), (e).

Any person can alert CARB to the existence of new scientific evidence through a petition process. In response, CARB, in coordination with OEHHA and the SRP, should review its prior TAC health assessment to consider "additional scientific evidence regarding the health effects of a substance which was not available at the time the original determination was made and any other evidence which would justify a revised determination."[24] The petition process is outlined below.

iii. SRP Guidance Set Out Procedures for Petition Review

In anticipation of requests to consider new scientific information that may be relevant to a TAC health assessment and to prevent misuse of valuable agency and SRP resources, CARB and the SRP developed procedures and criteria to guide evaluation of and decisions on petitions to review a TAC health assessment (SRP Guidance). The SRP Guidance provides that CARB and OEHHA will first screen the petition "to determine whether the material contains the necessary elements to warrant the SRP's attention." The petition must "describe specifically what in the original risk assessment will be qualitatively and/or quantitatively changed," including whether and how the new evidence, if accepted, would "change the determination of the health effects of the compound, "change the threshold determination adopted by the Board and contained in the regulation," or "change the potency which was the basis of the original risk assessment." The petition must also "describe the importance of the new evidence as it relates to the science (e.g. evidence, data, calculations, assumptions, and procedures) used to establish the original risk assessment," and "demonstrate that the new evidence is peer reviewed, either in the form of acceptance for publication by an academically or scientifically reputable journal, or documented acceptance by a recognized group of scientific experts (such as the International Agency for Research on Cancer, National Cancer Institute, National Toxicology Program, Environmental Protection Agency, or National Academy of Sciences)."[25]

If OEHHA finds that there is a need for further review of the original health assessment, it transmits the finding to the CARB Chair. If not, the CARB Chair will ask the SRP to review the petition and OEHHA's evaluation, and to advise CARB on whether new information warrants a review of the original TAC health assessment. The SRP's evaluation process includes consultation with OEHHA and other appropriate agencies and individuals, and discussion at a public SRP

[24] Health & Saf. Code, § 39662, subd. (e).

[25] CARB, SRP, *Process for Evaluation and Response to Submittals for New Scientific Information as Evidence for Review of Toxic Air Contaminant Risk Assessments* (Dec. 12, 1989), available at https://ww2.arb.ca.gov/sites/default/files/classic/srp/document/statementofneed_1989_.pdf.

meeting. The SRP will advise the CARB Chair of its conclusion and recommendation, after which CARB may accept the petition and reevaluate the health effects of a substance in coordination with OEHHA and the SRP.[26]

b. CALIFORNIA'S Cr(VI) HEALTH ASSESSMENT AND TAC DETERMINATION

Cr(VI) is the highest oxidation (or valence) state of the element chromium, which is emitted to ambient air from vehicle and engine exhaust as well as from a variety of industries, including pigment manufacturing, chrome plating, welding and production of stainless steel products. The general population may be exposed to Cr(VI) compounds when they inhale ambient air, or ingest water or food containing Cr(VI).

In 1986, CARB identified Cr(VI) as a TAC that has the potential to cause cancer based on an evaluation of health effects developed in 1985 by the Department of Health Services (DHS), OEHHA's predecessor agency.[27] DHS established the current inhalation unit risk factor (IUR) for Cr(VI) at 1.5E-1 as the lifetime increased risk per microgram of Cr(VI) per cubic meter of exposure $(\mu g/m^3)^{-1}$, which is the 95 percent upper confidence limit on the estimated increased cancer risk from a lifetime of exposure at 1 $\mu g/m^3$. DHS used that value to calculate an inhalation cancer slope factor of 5.1E+02 milligrams per kilogram per day $(mg/kg\text{-}day)^{-1}$.[28] Based on the limited scientific evidence available at that time, CARB was unable to identify an exposure level below which carcinogenic effects would not occur.[29]

DHS's 1985 Health Assessment was based primarily on a single epidemiological study evaluating exposures to workers at a Painesville, Ohio chromate

[26] CARB, SRP, *Process for Evaluation and Response to Submittals for New Scientific Information as Evidence for Review of Toxic Air Contaminant Risk Assessments* (Dec. 12, 1989), p. 2, available at https://ww2.arb.ca.gov/sites/default/files/classic/srp/document/statementofneed_1989_.pdf; see Health & Saf. Code, §§ 39660-39662.
[27] CARB, Staff Report: Initial Statement of Reasons for Proposed Rulemaking, pp. 5-11, *available at* https://ww2.arb.ca.gov/sites/default/files/classic/toxics/id/summary/hex.pdf; DHS, Health Assessment for Chromium (Sept. 1985), *available at* https://ww2.arb.ca.gov/sites/default/files/classic/toxics/id/summary/hexchromepartb.pdf.
[27] OEHHA, Technical Support Document for Cancer Potency Values, Appendix B (May 2009).
[28] OEHHA, Technical Support Document for Cancer Potency Values, Appendix B (May 2009), pp. B-201 to B-207.
[29] Cal. Code Regs., tit. 17, § 93000; see also CARB, Staff Report: Initial Statement of Reasons for Proposed Rulemaking, *available at* https://ww2.arb.ca.gov/sites/default/files/classic/toxics/id/summary/hex.pdf.)

production plant (Mancuso, 1975). DHS recommended that CARB apply a linear non-threshold risk model[30] to the data from the Mancuso study.

At the time, DHS judged this study to be "most methodologically sound and to contain the best exposure data to derive dose-response curves for hexavalent chromium."[31] However, DHS had to rely heavily on assumptions and uncertainty factors in the health assessment to overcome limitations in the data.[32] The Mancuso data set reaches back to the 1930s, a time period where exposures were not measured, exposure controls were essentially non-existent, and exposures to other sources of Cr(VI) in and out of the workplace, such as cigarette smoke, abounded. DHS noted uncertainty in the results due to "extrapolating from high occupational exposure levels to low ambient levels, the reliance on imprecise historical exposure levels as the basis for estimating potency, the lack of data differentiating between chromium oxidation states and compound specificity, and the lack of control for potential confounding factors (e.g., cigarette smoking)."[33] DHS acknowledged that it made several assumptions in its 1985 Health Assessment, including deriving results from application of the linear non-threshold model to the Mancuso data, but recognized the "limitations in the epidemiological data which create uncertainty in the risk assessment."[34]

c. CURRENT STATE OF THE SCIENCE RELEVANT TO THE Cr(VI) IUR

i. OEHHA Identified Substantial New Quantitative Risk Assessment Data for Inhaled Cr(VI) in 2011 That Were Not Available to DHS in 1985

Since 1985, significant additional scientific evidence has been developed regarding the health effects of inhaled Cr(VI). In 2011, OEHHA described the new scientific information that was available at that time in its Public Health

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30 A linear non-threshold model assumes that there is a uniform cancer risk per unit dose from higher doses to lower doses. Because the model assumes there is no threshold dose, the model will indicate a nonzero excess cancer risk at very low doses.

31 DHS, Health Assessment for Chromium (Sept. 1985), p. 2, *available at* https://ww2.arb.ca.gov/sites/default/files/classic/toxics/id/summary/hexchromepartb.pdf.

32 DHS, Health Assessment for Chromium (Sept. 1985), pp. 3, 95-97, *available at* https://ww2.arb.ca.gov/sites/default/files/classic/toxics/id/summary/hexchromepartb.pdf.

33 DHS, Health Assessment for Chromium (Sept. 1985), p. 3, *available at* https://ww2.arb.ca.gov/sites/default/files/classic/toxics/id/summary/hexchromepartb.pdf.

34 DHS, Health Assessment for Chromium (Sept. 1985), p. 3, *available at* https://ww2.arb.ca.gov/sites/default/files/classic/toxics/id/summary/hexchromepartb.pdf.

Goal (PHG) for Cr(VI) in drinking water.[35] It found that two studies were particularly relevant. The first study is Mancuso (1997), which included follow-up data on the same cohort as the Mancuso (1975) study, and also reported airborne Cr(VI) exposure measurements. The second study is Gibb *et al.* (2000), which examined mortality rates from lung cancer, prostate cancer, and all cancers combined among 2,357 male chromate production workers at a Baltimore, Maryland chromate production facility who were first employed between 1950 and 1974.[36]

OEHHA found that the Gibb study had several major strengths that "make it a better candidate for potency estimation than the 1975 Mancuso study that has been the basis of previous risk quantifications (U.S. EPA, 1998; California Air Resources Board, 1985)." These include "relatively precise exposure information, a relatively large number of cancer deaths, and control of smoking in some analyses."[37] Gibb included all lengths of employment (instead of a 90-day minimum, and excluded workers first employed before 1950 because of less complete exposure information prior to that date. The analyses controlled for the potentially confounding effects of age, calendar year, gender, and race. It compared the cohort's mortality information for the period from 1950 through 1992 to the United States and the State of Maryland's general population cancer rates. The investigators found a statistically significant increased rate of mortality from lung cancer compared to standardized rates for the State of Maryland.[38]

OEHHA also found that the Gibb study is superior to Mancuso (1997) in several ways: "Some of the most important are the concurrent measurements of exposure, 7-fold larger cohort, 5-fold large[r] number of person years, and 2-fold larger number of cancer deaths. Most importantly, Gibb *et al*. (2000) provided data on expected cancer cases by calendar year, whereas Mancuso (1975, 1997) did not give information allowing assured reconstruction of expected cancer deaths in that regard." OEHHA noted a potential bias in the Mancuso

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[35] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), pp. 61-62, 84, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.
[36] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), p. 94, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.
[37] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), p. 61, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.
[38] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), p. 61, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.

(1997), stating that the annually increasing background rate of lung cancer over the course of the study "is likely to bias risk slopes upwards with the referent population in the modeling." Consequently, OEHHA declined to use the Mancuso (1997) data, concluding that Mancuso (1997), like Mancuso (1975) is too uncertain and, "especially because it does not have a referent population, Mancuso (1997) is subject to too much bias to be useful by the present approaches."[39]

OEHHA did note that the Gibb study has some limitations. It does not account for time since first exposure, which could prevent possible bias due to lag in the effect of exposure. It also lacks individual work histories, which limits the different modeling approaches that can be used for risk analysis.[40]

ii. U.S. Environmental Protection Agency's 2024 Integrated Risk Information System (IRIS) Assessment for Cr(VI)

On August 1, 2024, the U.S. Environmental Protection Agency (EPA) updated its 1998 IRIS assessment for Cr(VI) based on "[s]ignificant new epidemiologic and experimental animal toxicity information for Cr(VI) [that] has become available, including updates of occupational cohort studies."[41] The total lifetime exposure IUR for Cr(VI) for human lung cancer risk estimated in the updated "IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]" (2024 IRIS Assessment) is 1.8×10^{-2} (per µg Cr(VI)/m^3), which is the upper 95 percent confidence limit (95% CI) including age-dependent adjustment factors (ADAFs). The 95% CI value, not including ADAFs,[42] is 1.1×10^{-2} (per µg Cr(VI)/m^3).[43]

Because evidence of carcinogenicity of inhaled Cr(VI) is well established, EPA focused on identifying additional appropriate studies to update the quantitative exposure-response analysis and the derivation of the IUR. EPA notes that "[m]ore recent epidemiologic studies have been identified in the peer-reviewed literature which include higher quality exposure data, longer follow-up times,

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[39] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), p. 94, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.
[40] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), pp. 62, 94, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.
[41] EPA, *Systematic Review Protocol for the Hexavalent Chromium IRIS Assessment (Preliminary Assessment Materials), Supplemental Information – Appendix A*, p. 1-1 (2024), *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549549.
[42] The current California IUR is also based on the 95% CI not including ADAFs. (add citation)
[43] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), p. 4-69 to 4-72, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546.

larger sample sizes, and more sophisticated analyses than were available in 1998."[44] To identify the best available science, EPA conducted a comprehensive systematic review of hundreds of studies on cancer and multiple noncancer health effects of inhalation and oral exposure to Cr(VI) to identify studies that might improve the quantitative dose-response analysis for human lung cancer.[45]

EPA initially identified 64 human lung cancer studies based on title and abstract screening. It conducted a full-text screening of these 64 studies for exposure-response data that may be informative for derivation of a revised IUR. It excluded studies that were not epidemiological analyses examining quantitative measures of chromium exposure in relation to lung cancer incidence or mortality risk. It also excluded studies if Cr(VI) measurements in air, or convertible equivalents such as CrO_3, were not presented, or if group-level exposure assignments were based on job title and not chromium measurements. EPA then restricted the remaining list to studies with the most recent cohort follow up data, and excluded studies that did not conduct exposure-response analyses using estimated airborne concentrations of speciated Cr(VI) compounds from which a slope and its standard error could be obtained. EPA evaluated the remaining studies for risk of bias and sensitivity, including consideration of exposure assessment, outcome ascertainment, population selection, confounding, selective reporting, sensitivity, and data analysis. Applying these criteria, EPA identified four occupational cohort studies classified as "high" or "medium" confidence to be considered for the derivation of the IUR for Cr(IV). Three of these studies involved the chromate production facility in Baltimore, Maryland (Gibb et al., 2020; Gibb et al., 2015; Gibb et al., 2000b), which EPA classified as high confidence. The fourth study involved the chromate production facility in Painesville, Ohio (Proctor et al., 2016), which EPA classified as medium confidence.[46]

Ultimately, EPA based its updated IUR on the Baltimore cohort studies by Gibb et al., (2020; 2015; 2000). EPA selected the Baltimore cohort (Gibb et al., 2020; 2015; 2000) over the Painesville cohort (Proctor et al., 2016) as the basis for deriving the

[44] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), p. 4-56, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546; see EPA, *Systematic Review Protocol for the Hexavalent Chromium IRIS Assessment (Preliminary Assessment Materials), Supplemental Information – Appendix A* (2024), *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549549.

[45] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)] – Supplemental Information* (Aug. 2024), *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549547.

[46] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), p. 4-56 to 4-59, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546.

IUR because the Baltimore cohort was (1) larger than the Painesville cohort, (2) had longer follow-up time, (3) had more deaths from lung cancer, (4) had no deaths from mesothelioma, despite having 66,651 additional years of person-time at risk than in the Painesville cohort, suggesting lower potential for confounding by asbestos exposure, (5) had more than an order of magnitude lower average exposures which can be more relevant to estimating effects at lower exposures and requires less extrapolation, (6) had more air samples to estimate exposures, and (7) had more complete data on smoking.[47] EPA applied the Cox proportional hazards model[48] to the Baltimore data set and controlled for smoking to develop the updated IUR.[49]

The 2024 EPA IRIS Assessment underwent independent external scientific peer review managed by EPA's Science Advisory Board (SAB).[50] The SAB agreed that EPA appropriately synthesized the available data for the IUR to describe its strengths and limitations, noting that "[t]he search parameters are defined, and the process used to narrow the choice to one cohort was logical, rational, and carefully explained in detail," and "the strengths and limitations of the top two choices (i.e., Baltimore, Maryland and Painesville, Ohio) for deriving the IUR are carefully and robustly delineated." It also agreed that the available data supports EPA's conclusions in the draft IRIS Assessment, noting that "the dose-related decisions are transparent and scientifically justified, including study selection for dose-response analyses, point of departure (POD) estimates, modeling choices and assumptions, dosimetric adjustments, derivation of candidate values, and confidence in the calculated values." The SAB stated

[47] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), p. 4-61 to 4-63, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546.
[48] "The Cox proportional hazards model (Cox, 1972) is one of the most commonly used statistical models for the epidemiologic analysis of survival and mortality in cohort studies with extensive follow-up, including studies of the Baltimore, MD cohort (Gibb et al., 2020; Gibb et al., 2015; Gibb et al., 2000b). The Cox proportional hazards model assumes that a function of covariates (e.g., exposures) result in hazard functions that are a constant proportion of the baseline hazard function in unexposed individuals over some timescale, typically calendar time or age (e.g., the background age-specific rates of lung cancer in the population). One of the strengths of this model is that knowledge of the baseline hazard function is not necessary, and no particular shape is assumed for the baseline hazard; rather, it is estimated nonparametrically." (EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), p. 4-64, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546.)
[49] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), p. 4-69 to 4-72, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546.
[50] SAB Review of EPA's draft IRIS Toxicological Review of Hexavalent Chromium (2023), p. 36, https://sab.epa.gov/ords/sab/f?p=114:0:5666222636833:APPLICATION_PROCESS=REPORT_DOC:::REPORT_ID:1121.

that the IUR and ADAF would need to be amended if, upon additional evaluation, the evidence is sufficient to support a nonlinear approach.[51]

The SAB observed that, in the Gibb et al. studies, a large proportion of the cohort members were smokers, and that smokers accounted for 98% of lung cancer deaths that occurred in the study. Because this percentage is high, the SAB expressed concern that it could lead to speculation about the role of Cr(VI) and whether there could be an interaction between Cr(VI) and smoking. At SAB's suggestion, EPA included a discussion of a recent study by Behrens et al. (2023) to further strengthen EPA's adjustment for smoking to note the possibility of an interaction.[52]

iii. New Peer-Review Studies Provide Additional Significant Scientific Evidence on Health Risks From Inhalation of Cr(VI)

Since EPA issued its review draft of the IRIS Assessment in October 2022, several new peer-reviewed studies have been published that add to the currently available scientific evidence on health risks posed by inhalation of Cr(VI). These include the Behrens et al. (2023) study referenced above, and two peer-reviewed papers that were published in the Journal of ____ in ____, 2024 (Lipworth et al. (2024); Allen et al. (2024)).

a. Behrens et al. (2023)

Behrens et al. (2023) provides a pooled analysis of 14 case-controlled studies from Europe and Canada evaluating exposure-response relationships for Cr(VI) and nickel in relation to lung cancer risk (the SYNERGY study). This study includes 16,901 cases of lung cancer and 20,965 controls. A measurement-based job-exposure matrix (JEM) estimated job-year-region specific exposure levels to Cr(VI) and nickel, which were linked to the subjects' occupational histories. The average exposure in this study among controls is 40 $\mu g/m^3$-years among men and 26 $\mu g/m^3$-years among women, which is much lower than the exposures in the Painesville and Baltimore cohorts. The study controlled for smoking in pack-years and found exposure-response associations for never, former, and current

[51] SAB Review of EPA's draft IRIS Toxicological Review of Hexavalent Chromium (2023), pp. 36-37, https://sab.epa.gov/ords/sab/f?p=114:0:5666222636833:APPLICATION_PROCESS=REPORT_DOC:::REPORT_ID:1121.

[52] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), p. 4-76, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546; SAB Review of EPA's draft IRIS Toxicological Review of Hexavalent Chromium (2023), pp. 36-37, https://sab.epa.gov/ords/sab/f?p=114:0:5666222636833:APPLICATION_PROCESS=REPORT_DOC:::REPORT_ID:1121.

smokers. The analysis of the data was stratified for men and women, although the analysis of women was limited by the small sample size among those exposed.

Among men, dose-response results appear to be consistent with results from the Baltimore and Painesville chromate production cohort studies. Among women, the findings were somewhat less consistent and not significant. The authors reported linear associations for Cr(VI) cumulative exposures and lung cancer risk among men. The exposure reconstruction is limited as 35% of reported measures of Cr(VI) were below the limit of detection, introducing uncertainty into this analysis relative to analyses of the Baltimore and Painesville chromate production worker cohorts, and the Burbank, California aircraft worker cohort evaluated by Lipworth at al. (2024) and Allen et al. (2024) discussed in the following sections. The authors concluded that increased duration and cumulative exposure to Cr(VI) was associated with increased odds of lung cancer.[53]

However, the authors of the SYNERGY study acknowledged that the study has limitations, particularly regarding the exposure assessment, that potentially result in differential bias that could have unpredictable effects on reported associations.[54]

b. Lipworth et al. (2024)

Lipworth et al. (2024) presents new research involving Cr(VI)-exposed painters, platers, and aircraft assembly workers, with one to 37 years of exposure, from a Lockheed Martin Aircraft Manufacturing plant in Burbank, California. It reconstructs individual-level exposures using a job-exposure matrix (JEM) and examines mortality among 3,723 CrVI-exposed aircraft manufacturing workers, including 440 women, with long-term low-level CrVI exposures, and long-term follow-up. The study evaluated cumulative exposures, by worker, from 1960 to 1998. A retrospective cohort mortality study was also conducted to calculate standardized mortality ratios (SMRs) by population demographics and exposure, and to conduct internally-referenced dose-response analysis. Smoking

[53] SAB Review of EPA's draft IRIS Toxicological Review of Hexavalent Chromium (2023), pp. 36-37, https://sab.epa.gov/ords/sab/f?p=114:0:5666222636833:APPLICATION_PROCESS=REPORT_DOC:::REPORT_ID:1121.
[54] SAB Review of EPA's draft IRIS Toxicological Review of Hexavalent Chromium (2023), p. 37, https://sab.epa.gov/ords/sab/f?p=114:0:5666222636833:APPLICATION_PROCESS=REPORT_DOC:::REPORT_ID:1121.

prevalence within the cohort, especially for women, was higher than the general population.

The workers in this cohort had mean and median cumulative exposures of 16 μg/m^3-yrs and 2.9 μg/m^3-yrs, respectively. Lipworth et al. 2024 found that, at the comparatively lower exposures observed in the Burbank cohort, there is no discernable relationship between increasing exposure to Cr(VI) and increasing lung cancer risk. Based on 1,758 observed deaths, mortality from cancer overall, smoking-related cancers, and lung cancer were significantly elevated, and lung cancer mortality was more highly elevated among women. The study analyses did not reveal a dose-response relationship between cumulative Cr(VI) exposure and lung cancer mortality, suggesting that elevated cancer risks in this cohort are primarily smoking-related. The authors noted that, possibly as a consequence of the elevated smoking-related risks, any increased risk associated with Cr(VI) exposure was not observable. Nevertheless, the study provides significant new data in the low exposure range and among women, which will be useful for quantitative risk assessment.[55]

c. Allen et al. (2024)

The exposure and lung cancer incidence data from the Burbank cohort were also combined with that of the Painesville and Baltimore cohorts in a quantitative cancer risk assessment that uses all of the available individual-level cohort study data.[56] In this study (Allen et al. 2024), worker-specific exposure and lung cancer occurrence data was pooled across the full range of exposure from the three cohorts[57] for dose-response analysis to generate a more statistically robust lung cancer assessment than can be developed using any single study. The authors noted that use of the pooled cohort broadens the range for dose-response analysis due to the comparatively low level exposures to Cr(VI) in the Burbank cohort. The primary analysis focused only on male workers from all three cohorts with more than one year of exposure. Sensitivity analyses were then conducted to assess the impact of including the female workers from the Burbank cohort and workers with less than one year of exposure.

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[55] Lipworth et al. (2024). Lung cancer mortality among aircraft manufacturing workers with long-term low-level exposure to hexavalent chromium. Journal of Occupational and Environmental Hygiene (*JOEH)* X:XX

[56] Allen et al. (2024), Lung cancer risk assessment associated with exposure to hexavalent chromium: Results of pooled analysis of three cohorts, *JOEH* X:XX (2024).

[57] The studies by Gibb et al. (2020; 2015; 2000) of the Baltimore cohort yield consistent findings. As the Gibb et al. (2000) individual data are publicly available, and the data from the 2015 and 2020 publications are not, the 2000 data are used in the Allen et al. (2024) pooled cohort study.

Allen et al. 2024 found that the IUR was higher when Burbank women and short-term workers were included with the primary cohort. The Burbank women represent a relatively small fraction of the total cohort (440 vs. 3732 total primary pooled cohort) and contributed only 24 lung cancer deaths. The available smoking data, in terms of prevalence and pack-years, indicate that the Burbank women had relatively high smoking prevalence and pack years. As smoking is a strong risk factor for lung cancer, the finding that women are at higher risk than men warrants further investigation.

III. NEW SCIENTIFIC EVIDENCE REQUIRES A CHANGE IN THE 1985 DHS Cr(VI) CANCER POTENCY AND UNIT RISK FACTORS

The 1985 DHS health assessment for Cr(VI), on which CARB's 1986 TAC determination for Cr(VI) is based, must be quantitatively changed based on the new peer-reviewed scientific evidence discussed above. While this new data does not change DHS' 1985 determination that Cr(VI) poses an inhalation cancer risk, or CARB's finding in the 1986 TAC determination that there is no measurable threshold for increased cancer risk related to inhalation of Cr(VI), it does change the potency that was the basis of the 1985 health assessment.[58] When DHS conducted the original Cr(VI) health assessment 40 years ago, the Mancuso (1975) study provided the best available scientific data on Cr(VI) inhalation exposure and respiratory cancer risk. But DHS had to make numerous assumptions to develop a risk assessment based on the data from the Mancuso (1975) study, and it acknowledged these assumptions would impact the accuracy of the risk assessment because of the study's data limitations and related uncertainties. The later peer-reviewed studies discussed above substantially reduce the uncertainties inherent in the Mancuso data, enabling OEHHA to rely on more refined and statistically robust scientific data, instead of assumptions, to derive a more accurate cancer potency value.

DPR's 40-year-old IUR has never been updated to account for advances in scientific evidence and methods of quantitative risk assessment which OEHHA currently uses for newly assessed carcinogens. Although current scientific evidence demonstrates that the 1985 IUR is considerably higher than necessary to protect human health, until it is revised through the statutorily prescribed

[58] The SRP requires submittals of new scientific evidence to address whether and how the new evidence changes (1) the determination of the health effects of a compound, (2) the threshold determination adopted by CARB and contained in the regulation, and (3) the potency that was the basis of the original risk assessment. (CARB, SRP, *Process for Evaluation and Response to Submittals for New Scientific Information as Evidence for Review of Toxic Air Contaminant Risk Assessments* (Dec. 12, 1989).) Because the new evidence does not change either of the first two elements, this petition focuses on the third.

process, OEHHA, CARB, and local air districts must continue using it in their regulatory decision-making and resource allocation decisions.[59] An updated IUR is needed for state and local regulators to update air toxics risk assessments and corresponding risk management actions to reflect the higher quality scientific evidence now available. These actions will ensure more effective investments of limited public and private sector resources to maximize public health protection.

a. NEW SCIENTIFIC EVIDENCE IS MORE ROBUST, AND LESS UNCERTAIN, THAN THE LIMITED EVIDENCE AVAILABLE TO DHS IN 1985

The Mancuso (1975) study is no longer the best scientific evidence available regarding health effects of inhaled Cr(VI). The Mancuso cohort exposures exceed environmental exposures by approximately one million times current background levels in ambient air and the action level established by the South Coast Air Quality Management District (SCAQMD) for ambient Cr(VI), which makes the linear extrapolation highly uncertain.[60] Mancuso (1975) is also based on a single exposure monitoring event conducted in 1949, up to 18 years after exposures began for the study population (1931-37); it lacks direct measurements for Cr(VI), which requires estimates of the Cr(VI) fraction of total chromium; it does not include exposure estimates after 1949 even though the plant continued to operate until 1972, resulting in highly uncertain exposure estimates for long-term workers; and it does not control for confounding factors such as smoking status and exposure to other carcinogenic substances.[61] These limitations compromise the reproducibility and reliability of the results.

Since 1985, there have been considerable advances in the quantity and quality of data available from animal carcinogenesis bioassays, epidemiological studies, and newer mechanistic studies of carcinogenesis and related

[59] See OEHHA, Technical Support Document for Cancer Potency Values, Appendix A (May 2009), *available at* https://oehha.ca.gov/media/downloads/crnr/appendixa.pdf (listing the 1985 Cr(VI) IUR in an appendix to its air toxics risk assessment guidance, which is updated periodically to incorporate new cancer potency factors and inhalation unit risk values for other substances).

[60] See, e.g., SCAQMD, Updated Air Monitoring Plan for Paramount [referencing an ambient concentration of 1 ng/m^3 as the basis for reducing the size of the Paramount monitoring network "to focus on other areas that have higher potential for air toxics exposure"], *available at* http://www.aqmd.gov/docs/default-source/compliance/Paramount/updated-monitoring-plan.pdf?sfvrsn=8.

[61] See DHS, Health Assessment for Chromium (Sept. 1985), pp. 3, 95-97, *available at* https://ww2.arb.ca.gov/sites/default/files/classic/toxics/id/summary/hexchromepartb.pdf; OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), p. 94, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.

phenomena.[62] Mancuso (1975) has been updated twice using a different worker cohort that was larger and better characterized with more representative exposure estimates (Luippold et al., 2003; Proctor et al., 2016). Both of these studies are peer-reviewed. This work has been used to quantitatively estimate lung cancer risk from Cr(VI) exposure in several studies (Crump et al. 2003; U.S. Occupational Safety and Health Administration (OSHA) 2006; Haney et al. 2014; Proctor et al. 2016). The Baltimore cohort has also been studied in several peer-reviewed publications (Gibb et al., 2020, 2015; 2020). In these studies, exposure to Cr(VI) and cancer risk among 2,357 workers has been quantified (Gibb et al., 2020). This improved epidemiological data allows for more refined modeling approaches, including application of both linear and non-linear models, which better predict dose-response in the low exposure range.

There has been an ongoing effort by regulatory agencies in the U.S. and abroad to update older risk assessment documents that relied on Mancuso (1975), including most recently EPA in August 2024.[63] These regulatory agencies are using the more recent and representative data from the Baltimore cohort studies (Gibb et al., 2020, 2015; 2020) to establish inhalation cancer potency estimates for Cr(VI). EPA, OSHA, the National Institute for Occupational Safety and Health (NIOSH), and the Texas Commission on Environmental Quality (TCEQ, 2014) have each developed quantitative measures of inhalation risk from the updated Baltimore cohort data.[64,65] Additionally, the European Commission Scientific Committee on Occupational Exposure Limits (SCOEL) has used Gibb et al. (2000) to recommend a Cr(VI) occupational exposure limit for European

[62] OEHHA, Technical Support Document for Cancer Potency Values (May 2009), p. 93-95, *available at* https://oehha.ca.gov/media/downloads/crnr/tsdcancerpotency.pdf.
[63] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546; EPA, *Systematic Review Protocol for the Hexavalent Chromium IRIS Assessment (Preliminary Assessment Materials), Supplemental Information – Appendix A*, p. 1-1 (2024), *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549549.
[64] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546; OSHA, Occupational Exposure to Hexavalent Chromium; Final Rule (29 CFR Parts 1910, 1915 (Feb. 28, 2006), available at https://www.govinfo.gov/content/pkg/FR-2006-02-28/pdf/06-1589.pdf; NIOSH, *Criteria for a Recommended Standard. Occupational Exposure to Hexavalent Chromium,* DHHS (NIOSH) Publication No. 2013-128, available at https://www.cdc.gov/niosh/docs/2013-128/pdfs/2013_128.pdf; TCEQ, Hexavalent Chromium (Particulate Compounds), Development Support Document (Aug. 4, 2014), available at https://www.tceq.texas.gov/downloads/toxicology/dsd/final/hexavalent_chromium.pdf.
[65] NIOSH, OSHA and TCEQ had access to the individual-level Gibb et al. (2020) worker exposure data, which eliminated the modeling issues encountered by OEHHA in the 2011 PHG evaluation.

Union member states.[66] The values derived by EPA, NIOSH, TCEQ, and SCOEL are markedly different than the value derived from DHS's 40-year old health assessment, which is still being used by CARB and OEHHA.

While OEHHA has taken note of some scientific advances since 1985, the Cr(VI) IUR continues to rely on the outdated Mancuso (1975) study. In 1995, OEHHA acknowledged a study then underway at Johns Hopkins University "evaluating a much larger worker population with better exposure data" that "may help to resolve some of the differences and uncertainties in the [Cr(VI) inhalation] unit risk values."[67] That study was published more than 20 years ago (Gibb *et al.*, 2000). By 2011, when developing the PHG for Cr(VI) in drinking water, OEHHA had already determined that the Mancuso (1975) study is no longer the best available science for quantifying cancer risk from inhalation of Cr(VI). While a later evaluation of the data from the 1975 Mancuso study "apparently reduce[d] some of the uncertainty about the Mancuso (1975) exposure to Cr VI" (Mancuso, 1997), OEHHA determined that the data was still too uncertain to use for quantitative risk assessment purposes. Because the 1975 and 1997 Mancuso studies do not have a referent population and rely on sampling after the major exposures occurred, OEHHA determined the analysis "is subject to too much bias to be useful by the present approaches."

For these reasons, OEHHA found that Gibb *et al.* (2000) provided a better basis for assessing cancer inhalation risk than the 1975 Mancuso study. OEHHA noted that Gibb *et al.* (2000) data "provided superior exposure measurements, which were generally much lower."[68] OEHHA also determined that Gibb et al. (2000) provided more reliable data, "was well conducted, and it contains a comparison documenting superiority to Mancuso (1997)[69] in several ways" including "the concurrent measurements of exposure, 7-fold larger cohort, 5-fold larger number of person years, and 2-fold larger number of cancer deaths," and "data on expected cancer cases by calendar year." In contrast, "Mancuso (1975, 1997) did not give information allowing assured reconstruction of expected cancer deaths in that regard." The Gibb study also "included

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[66] SCOEL REC 386 (2017) available at SCOEL/REC/386 Chromium VI compounds - Publications Office of the EU (europa.eu).

[67] OEHHA. 1995. Appendix B. Comparison of Cal/EPA and US EPA Toxicity Values. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment, *available at* https://oehha.ca.gov/media/downloads/risk-assessment/report/appbraac.pdf

[68] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), pp. 94-95, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.

[69] Mancuso (1997) updates the mortality of Mancuso (1975) study; however the issues with data quality that existed in 1975 could not be improved upon in 1997.

relatively precise exposure information, a relatively large number of lung cancer deaths, and control of smoking in some analyses," which according to OEHHA make the Gibb study "a better candidate for potency estimation than the 1975 Mancuso study that has been the basis of previous risk quantifications (U.S. EPA, 1998; California Air Resources Board, 1985)."[70]

The 2011 OEHHA assessment notes that the Gibb study also has limitations, including "the lack of accounting for time since first exposure, which if accounted for might prevent possible bias due to lag in the effect of exposure," and the lack of individual work histories that caused the analysis to be "limited in exploring different modeling approaches, such as the use of time-dependent multistage models." OEHHA ultimately concluded, because of uncertainties regarding exposure groupings for the dose-response model of the Gibb et al. (2000) study, that the 1985 IUR would not be changed in the Cr(VI) PHG document.[71]

However, these uncertainties were addressed in the later versions of the Baltimore cohort study which, as noted above, EPA relied on to develop its 2024 updated IUR (Gibb et al. 2015; 2020). These updated data include individual work history exposure data, which enabled EPA to assess 5-year and 15-year lag periods. This resolved both of the uncertainties OEHHA encountered when it attempted to model the Gibb et al. (2000) study data based on the publications alone (without the underlying data).[72]

Behrens et al. (2023) has helped to further fill gaps in the scientific data regarding cancer risk associated with occupational exposure to Cr(IV). Behrens et al. (2023) has positive attributes similar to the Gibb et al. (2020) study. The study population is very large and includes detailed smoking data. The cohort also includes women, whereas the Baltimore cohort is male-only. This feature allows for consideration of sex-based differences in health outcomes. The Behrens study also included data allowing evaluation of potential statistical interaction between smoking and Cr(VI) exposure, which could not be evaluated using the Baltimore cohort data. The authors note that their findings add to observations from studies of the Baltimore and Painesville cohorts

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[70] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), p. 61, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.

[71] OEHHA, Public Health Goals for Chemicals in Drinking Water, Hexavalent Chromium (CR VI) (July 2011), pp. 94-95, *available at* https://oehha.ca.gov/media/downloads/water/chemicals/phg/cr6phg072911.pdf.

[72] See EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), pp. 4-59 to 4-63, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546.

indicating a measurable increase in lung-cancer risk with respect to occupational Cr(VI) exposure. While Behrens et al. (2023) did not calculate an IUR based on their exposure-response modeling, Table 1 below shows that an IUR based on the Behrens et al. (2023) data would likely be close to the IUR that EPA derived in 2024 based on the Baltimore cohort data.[73]

The latest studies (Lipworth et al. 2024; Allen et al. 2024), published in the peer reviewed literature after EPA released its updated IRIS Assessment, add substantially to the weight of evidence supporting an update of the 1985 DHS health assessment used to establish the existing California IUR. The Burbank cohort evaluated in Lipworth et al. (2024) is much larger than those of Baltimore or Painesville, and it includes women. Importantly, this research also evaluates airborne exposures that were far lower than in the Painesville and Baltimore cohorts. These levels are more representative of current occupational and environmental exposures than those that are the basis of the existing California IUR, and this study showed that there is no discernable relationship between increasing exposure to Cr(VI) and increasing lung cancer risk at these low exposure levels.[74]

The pooled analysis performed by Allen et al. 2024, expands exposure conditions to those more typical of modern industries, rather than being exclusively reliant on data from the historical chromate production industry. The authors noted that use of the pooled cohort broadens the range for dose-response analysis due to the comparatively low-level exposures to Cr(VI) in the Burbank cohort. The pooled IUR estimate also allows for inclusion of a broader dose-response range and reduced uncertainty by way of a larger population, additional years of follow-up, and incorporation of broader geographical and cohort characteristics that are more relevant to the general population.

Table 1 compares the 1985 DHS California IUR estimate to other values developed from more recent risk assessments using more robust and relevant data sets. This information indicates that the existing California value overpredicts cancer risk from inhalation of Cr(VI) by more than an order of

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[73] See EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), p. 4-76, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546 (concluding that the findings in Behrens et al. (2023) do not change the IUR derived by EPA because, despite uncertainty regarding a possibly synergy between Cr(VI) and smoking, "[t]he unit risk of the lung cancer risk herein would be health protective for any population that had a lower prevalence of smoking than that of the Baltimore cohort").

[74] Lipworth et al. (2024). Lung cancer mortality among aircraft manufacturing workers with long-term low-level exposure to hexavalent chromium. Journal of Occupational and Environmental Hygiene (*JOEH)* X:XX

magnitude. Specifically, the current OEHHA IUR of 0.15 per µg/m^3 is 9 to 37 times higher than all other comparable Cr(VI) IURs developed from the newer datasets.

Table 1. Comparison of IUR values from the 1985 CDHS evaluation with published values developed in other studies of newer, more refined and statistically robust data

Risk Assessment Publication	No. of Workers	Cr(VI) Exp Data	Concurrent Exp Data	Account for Smoking	IUR at Maximum Likelihood Estimate (MLE)	IUR 95% Upper Confidence Limit[1]
CDHS, 1985	332	No	No	No	0.009	**0.15**
Haney 2014 (Based on Gibb 2000 and Crump 2003) Basis of TECQ IUR	1518	Yes	Yes	Yes	0.0023 (weighted combined best estimate)	95% CIs by study were 0.004 (Gibb) and 0.0036 (Crump)
Proctor 2016 (Painesville)	714	Yes	Yes	Yes	0.0083	0.017
EPA 2024 based on Gibb, 2020 (Baltimore)	2357	Yes	Yes	Yes	0.0080	0.011
Allen, 2024 (Primary cohort of workers from Baltimore, Painesville, and Burbank)	3283	Yes	Yes	Yes	0.0096	0.013
Primary + short term workers (Allen et al. 2024)	5,032	Yes	Yes	Yes	0.011	0.014
Primary +Burbank females (Allen et al. 2024)	3723	Yes	Yes	Yes	0.026	0.034

As Table 1 shows, the IUR values at the maximum likelihood estimate (MLE) are remarkably consistent, including the value derived by DHS in 1985. However, at the 95% upper confidence limit, the DHS IUR stands out as a substantial departure from all of the other estimates due to the high uncertainty and very limited statistical power of the Mancuso (1975) study. Use of this study as the basis of the DHS (1985) health assessment resulted in very wide confidence intervals relative to risk assessments based on the more refined data sets.

EPA's new IUR uses much more current, comprehensive, and reliable data to derive the upper 95% confidence interval (CI).[75] The availability of the more robust Baltimore cohort study, and EPA's selection of that study over the Painesville cohort for purposes of quantitative risk assessment by itself warrants a change in the existing California IUR. The rigor and sophistication of these newer data enabled EPA to apply the Cox proportional hazards model to the Baltimore data set, and control for smoking in quantifying cancer risk. This new scientific data resulted in EPA deriving an IUR of 1.1×10^{-2} (per µg Cr(VI)/m^3), which is more than an order of magnitude lower than OEHHA's current value of 1.5×10^{-1} (per µg Cr(VI)/m^3).[76]

The EPA 2024 IRIS Assessment, coupled with the additional evidence from Behrens et al. (2023), Lipworth et al. (2024), and Allen et al. (2024), demonstrate that the 1985 DHS assessment substantially overpredicts cancer risk from inhalation of Cr(VI). The accumulated evidence requires a change to the cancer potency that was developed in the 1985 DHS health assessment to inform more accurate risk assessments and more targeted and effective risk management actions.

b. ADVANCEMENTS IN RISK ASESSMENT METHODOLOGY AND PRACTICE SINCE 1985 HAVE IMPROVED THE RELIABILITY OF RISK ASSESSMENTS

Advancements in health risk assessment methodology and practice since 1985 have improved the accuracy of human health risk assessments, and the science of risk assessment continues to develop rapidly. OEHHA acknowledges that there have been a number of advances in the methodology of cancer risk assessment since the 1980s. These include OEHHA's 2009 Technical Support

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[75] EPA's 1998 IRIS IUR, which is 1.2×10^{-2} (per µg Cr(VI)/m^3), is the maximum likelihood estimate (MLE), and was developed from the Mancuso (1975) study, rather than the upper 95% CI. In 1998, EPA did not report an upper 95% CI, which OEHHA typically uses as the basis of its IURs to ensure they do not underestimate risk. Importantly, the new EPA value is the upper 95% CI IUR, consistent with the approach taken by OEHHA. (See EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), pp. 4-64 to 4-74, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546.)

[76] EPA, *IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]* (Aug. 2024), pp. 4-69 to 4-70, *available at* https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=549546

Document for Cancer Potency Factors,[77] EPA's 2005 Guidelines for Carcinogen Risk Assessment,[78] EPA's 2012 Benchmark Dose Technical Guidance,[79] EPA's Review of the Reference Dose and Reference Concentration Processes,[80] and EPA's Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens.[81]

EPA's August 2024 update to the Cr(IV) IUR provides a helpful reference. For example, EPA used benchmark dose modeling methodology, which is generally considered a preferred method for deriving a point of departure for risk assessment.[82] When DHS conducted its health assessment in 1985, benchmark dose modeling was not commonly used for this derivation. Recent advancements in risk assessment methodology also include conducting a systematic review and risk of bias assessment of all available studies that could be used for derivation of unit risk values and overall confidence classification. EPA conducted such a systematic review, which led to its selection of four studies that it determined provided date suitable for quantitative risk assessment, including the most recent studies of the Baltimore and Painesville cohorts. Notably, EPA did not select any of the Mancuso studies, which it screened out during the literature review process for exposure-response data of Cr(VI) and lung cancer.[83]

c. AN UPDATED IUR IS NEEDED TO ACCURATELY ASSESS HUMAN HEALTH RISK AND DIRECT RESOURCES TO BEST PROTECT PUBLIC HEALTH

[77] OEHHA, *Technical Support Document for Cancer Potency Factors: Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures* (May 2009), available at https://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009.

[78] EPA, *Guidelines for Carcinogen Risk Assessment* (Mar. 2005), https://www.epa.gov/sites/default/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf.

[79] EPA, Benchmark Dose Technical Guidance (Jun. 2012), *available at* https://www.epa.gov/sites/default/files/2015-01/documents/benchmark_dose_guidance.pdf.

[80] EPA, Review of the Reference Dose and Reference Concentration Processes (Dec. 2002), *available at* https://hero.epa.gov/hero/index.cfm?action=search.view&reference_id=88824.

[81] EPA, Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens (Mar. 2005), *available at* https://hero.epa.gov/hero/index.cfm?action=search.view&reference_id=88823.

[82] EPA, IRIS Toxicological Review of Hexavalent Chromium (Final Report, 2024), pp. 4-63 to 4-72, *available at* https://iris.epa.gov/document/&deid=361833.

[83] EPA, IRIS Toxicological Review of Hexavalent Chromium (Final Report, 2024), pp. 1-1, 1-13 to 2-3, *available at* https://iris.epa.gov/document/&deid=361833; see also EPA, *Final Systematic Review Protocol for the Hexavalent Chromium IRIS Assessment* (Aug. 2024), *available at* https://iris.epa.gov/document/&deid=343950.

The 1985 IUR is still used by CARB and local air districts to evaluate the potential for increased cancer risk from inhalation of Cr(VI) in the vicinity of stationary sources and in ambient air. It may be tempting to conclude that no public harm could result from using a factor that is lower than necessary to protect human health, but that is a false premise with negative societal consequences.

Based on the outdated 1985 IUR, Cr(VI) continues to be a significant risk driver throughout the state. The range of annual mean concentrations and estimated risks from Cr(VI) exposure reported by CARB between 2015 and 2022 at certain California sites are presented below in Table 2.[84] Calculated risks range from 10 to 35 per million, which exceed de minimis risk levels established by several air districts.

Table 2. Range of mean concentrations and estimated risks of Cr(VI) at California locations between 2015 and 2022 (source: CARB [a])

	CrVI [b]	
Location (years)	**Mean Concentration Range (ng/m³)**	**Estimated Risk Range (per million)**
Riverside, CA (2015-2022)	0.032 – 0.083	13 – 34
Simi Valley, CA (2015-2022)	0.025 – 0.063	10 – 26
Roseville, CA (2015-2022)	0.025 – 0.035	11 – 14
San Francisco, CA (2015-2022)	0.043 – 0.083	18 – 35

[a.] California Air Resources Board (CARB). Monitoring Sites with Ambient Toxics Summaries, Hexavalent Chromium https://www.arb.ca.gov/adam/toxics/sitelists/cr6sites.html

[b.] Means and risks only shown for years with data in all 12 months. The annual mean is calculated by averaging the monthly means of all measurements taken at the site. Estimated risks represent the risk that one person in a population of one million may have of developing cancer from exposure to the annual mean concentration over 70 years, based on a IUR of 0.15 $\mu g/m^3$ for hexavalent chromium.

The South Coast Air Quality Management District (SCAQMD) provides a relevant example. SCAQMD issued a 2021 update to their Multiple Air Toxics Exposure

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[84] The available data for the selected locations generally do not include annual mean concentrations of Cr(VI) from 2018, 2020, and 2021.

Study (MATES V),[85] which reported ambient concentrations of a wide range of air toxics at several locations in Southern California based on data collected in 2018 and 2019 (SCAQMD 2021). The average Cr(VI) concentrations at the 10 Southern California monitoring locations presented in MATES V are extremely low, ranging from 0.0264 nanograms per cubic meter of air (ng/m^3) to 0.0607 ng/m^3, and have decreased significantly since 1998 (MATES II). However, based on the 1985 IUR, cancer risks are still reported to exceed 20 per million in MATES V.

The concentrations of Cr(VI) in the South Coast Air Basin and the corresponding cancer risks are shown in Figure 1, below.

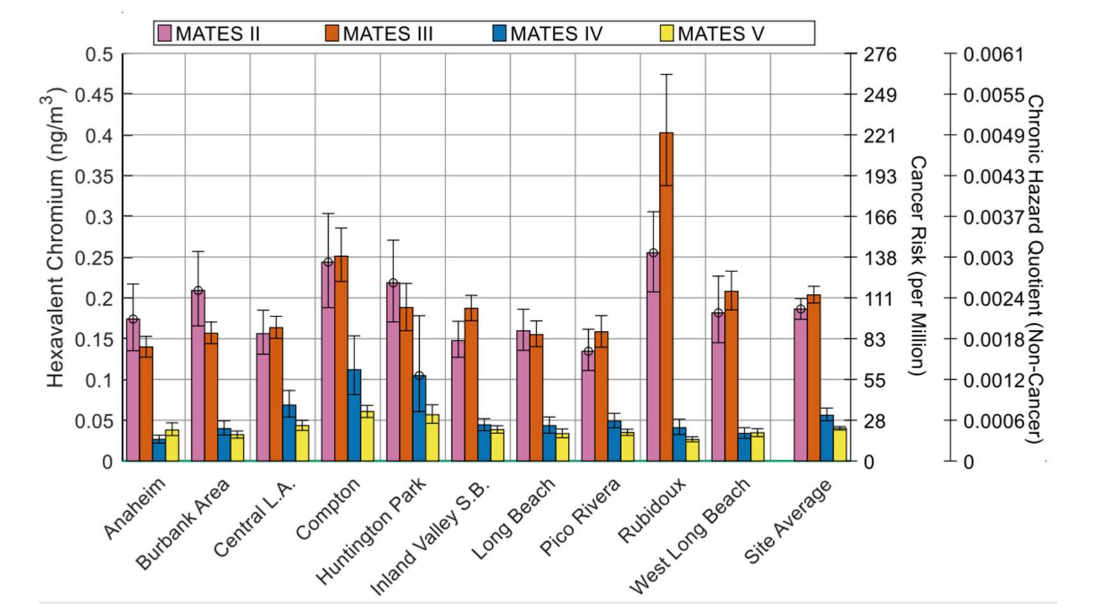

Figure 1. Average Concentrations of Hexavalent Chromium as TSP Reported in MATES V. Error bars denote the 95% confidence interval. [MATES II (1998-1999), MATES III (2004-2006), MATES IV (2012-2013), MATES V (2018-2019)]

At these levels, virtually any emissions of Cr(VI) from stationary sources are likely to trigger the requirements of SCAQMD's Rule 1402 [86], including but not limited to public notification and facility-specific risk reduction audits and plans. The latter often require substantial capital investments in emissions control equipment and ongoing operations and maintenance costs. Where this process is driven by health reference values based on outdated science, as is the case

[85] South Coast Air Quality Management District (SCAQMD). 2021. Multiple Air Toxics Exposure Study in the South Coast AQMD, MATES V. Appendix IV. August.

[86] SCAQMD, Rule 1402, available at https://www.aqmd.gov/docs/default-source/rule-book/reg-xiv/rule-1402.pdf?sfvrsn=4.

for Cr(VI), there is a higher probability that both regulatory and facility resources will be misdirected toward actions that do not yield meaningful public health benefits. These resources will not be available to mitigate exposures to other higher risk substances (there are hundreds of substances subject to regulation pursuant to federal, state, and local air toxics regulatory programs[87]) or to address cumulative risks in overburdened communities. These outcomes also present risk communication challenges for the regulatory agency, the regulated facility, and the surrounding community because perceptions of involuntary risk from exposure to facility emissions often causes unnecessary alarm and tension between facility operators, local regulatory and elected officials, and the surrounding community. Furthermore, escalating operating costs, regulatory, and political pressures on affected businesses can lead to lost economic productivity in the form of facility curtailments and closures, and lost jobs and tax revenues in the communities in which they operate. CARB and OEHHA should not turn a blind eye to these broader public health and public policy impacts when considering this petition.

Accordingly, the decision to update health reference values used in air toxics regulatory programs should not be limited only to those instances where new scientific information indicates that the substance may pose a higher risk than previously determined.

IV. CONCLUSION

Petitioner(s) request(s) that that CARB, OEHHA, and the SRP reevaluate the TAC health assessment based on the significant scientific evidence developed since 1985, including the 2024 EPA IRIS Assessment, the case-control study of welders by Behrens et al. (2023), the newly published study of the Burbank cohort by Lipworth et al. (2024), and the newly published pooled risk assessment by Allen et al. (2024). Petitioner(s) does(do) not dispute that Cr(VI) is an inhalation carcinogen or that it should be designated as a TAC. Petitioner(s) does(do) dispute the cancer potency and inhalation unit risk established for Cr(VI) by DHS in 1985. Petitioner's(s') concern is that the 1985 DHS health assessment and 1986 TAC determination are not based on the best available science. As a result, continued reliance on the 1985 DHS health assessment and inhalation unit risk factor biases regulatory decision-making by CARB and local air districts in favor

[87] For example, CARB has identified over 200 substances and groups of substances as TACs. (CARB website, CARB Identified Toxic Air Contaminants, *available at* https://ww2.arb.ca.gov/resources/documents/carb-identified-toxic-air-contaminants.)

of actions that come at a substantial cost to regulated entities and the public at large, but do not meaningfully improve public health protection.