January 8, 2024

Via Email (https://oehha.ca.gov/comments)

Pesticide and Environmental Toxicology Branch
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
P.O. Box 4010, MS-12B
Sacramento, California 95812-4010
Attention: PHG Program, Ms. Hermelinda Jimenez

Subject: Joint comments on OEHHA's First Public Review Draft Proposed Health-Protective Concentration for the Noncancer Effects of Hexavalent Chromium in Drinking Water

Dear Ms. Jimenez:

The undersigned organizations appreciate this opportunity to comment on the Office of Environmental Health Hazard Assessment's (OEHHA) first Public Review Draft of the Proposed Health-Protective Concentration for the Noncancer Effects of Hexavalent Chromium in Drinking Water (First Public Review Draft). Our organizations collectively represent a broad range of water users and non-transient, non-community (NTNC) water system operators who have a strong interest in the development of drinking water standards in the manner intended, and required, by the California Safe Drinking Water Act (SDWA). Indeed, one of the fundamental requirements of the SDWA is that such standards be adopted only after a clear and transparent process that relies on the best available information, meaningfully engages the public, and results in drinking

water standards that are protective of public health without imposing onerous, unnecessary costs on water system operators or ratepayers.

We remain concerned that the many departures from statutory requirements and past practice in updating the 2011 public health goal (PHG) and developing a new maximum contaminant level (MCL) for hexavalent chromium (Cr(VI)) are driven by a desire to simply reestablish the previous MCL of 10 parts per billion (ppb). Using a previously set number as the regulatory goal does not allow for an objective evaluation of the best available science and is likely to produce an outcome that is not in the public interest—an MCL that substantially increases the cost of drinking water, especially in communities served by smaller water systems, in exchange for minimal, if any, gains in public health protection.

The First Public Review Draft does not reflect the application of the most current principles, practices, and methods in toxicology or risk assessment.

In comparison to OEHHA's 2011 noncancer PHG for Cr(VI), the First Public Review Draft appears at first blush to employ more current data and scientific methods, consistent with the purpose of the PHG update process. However, as demonstrated in the enclosed technical analysis prepared by the scientific research and consulting firm ToxStrategies, a more thorough evaluation of the First Public Review Draft reveals serious deficiencies in OEHHA's analysis, including:

- An insufficient demonstration that liver inflammation in rats is an adverse effect of Cr(VI) exposure, or that it is relevant to humans.
- Inconsistent application of scientific methods (e.g., benchmark dose (BMD) modeling, allometric scaling) to multiple adverse effects to determine which endpoint is the most sensitive and relevant basis to derive the proposed health-protective concentration (HPC) for noncancer effects of Cr(VI) in drinking water.
- Unexplained and seemingly unjustified presumption that intestinal lesions are more relevant to the cancer PHG than the non-cancer PHG.
- Application of uncertainty factors adapted from 2008 air toxics guidance that were not applied in 2011 and have not been established as relevant to drinking water risk assessments, especially given the availability of human modeling data.
- An inexplicable *increase* in the total uncertainty factors applied to the same endpoint *after* using physiologically-based pharmacokinetic (PBPK) models to reduce uncertainty in interspecies extrapolation and intraspecies variability.

These deficiencies seem intended to counteract the effects of using updated risk assessment methods such as BMD modeling, allometric scaling, and use of PBPK models, and render the First Public Review Draft unreliable to support subsequent regulatory decision making. ToxStrategies concludes that proper application of updated risk assessment methods is likely to lead to a higher noncancer HPC, consistent with the findings of other regulatory agencies and public health authorities.

Procedural flaws call into question the validity of the proposed noncancer HPC for Cr(VI) and erode public confidence in the drinking water standard-setting process.

Any adjustment of the final PHGs for both noncancer and cancer effects of Cr(VI) relative to the 2011 values will impact the public health benefits attributable to compliance with the proposed Cr(VI) MCL and, as the SDWA requires, should inform the selection of the final MCL. However, the process employed for the development of the proposed Cr(VI) MCL, including the process for updating the Cr(VI) PHG, departs significantly from the process intended and prescribed by the SDWA and from OEHHA's and the State Water Resources Control Board's (SWRCB) past practices. The actions taken by both agencies over the past 18 months call into question the objectivity and integrity of this MCL development process and appear to support a predetermined outcome—to reestablish the MCL at 10 ppb—rather than to apply the best available information to select an MCL that provides additional public health protection without exacerbating drinking water access and affordability problems for systems serving smaller populations and disadvantaged communities.

As discussed in our August 18, 2023 comments on the SWRCB's notice of proposed rulemaking for the Cr(VI) MCL, OEHHA's July 6, 2022 memorandum to Darrin Polhemus, Deputy Director for the SWRCB's Division of Drinking Water (DDW), presented sweeping conclusions about the state of the health effects science that were not supported by the current published research or consistent with any of the substantive analytical and procedural steps required by the SDWA, which OEHHA had not completed. OEHHA subsequently attempted to correct those errors by initiating a new data call-in on March 27, 2023, and clarifying that it would complete the PHG-update process required by the SDWA. OEHHA's action reaffirmed the inadequacy of the 2011 PHG as the scientific basis for a new MCL. At that time, and consistent with its past practice, the SWRCB should have suspended the MCL rulemaking process pending completion of the PHG update for both noncancer and cancer effects to allow it to fully evaluate the impact of the new PHGs on the health benefits, economic feasibility, and cost-effectiveness of the proposed MCL. Instead, less than three months after OEHHA's announcement, the SWRCB released the proposed Cr(VI) MCL, relying on the outdated 2011 PHG as the basis for its proposal.

Deputy Director Polhemus further asserted during the August 2, 2023 public workshop on the proposed Cr(VI) MCL that DDW expected OEHHA to complete the PHG update before the SWRCB adopts the MCL. OEHHA has since opted to bifurcate the PHG-update process, starting with the release of the First Public Review Draft on November 22, 2023, to be followed at some later, unknown date by a separate public review draft for cancer effects. This action is another conspicuous departure from both the statutory framework and past practice. While OEHHA has developed endpoint-specific HPCs to support drinking water notification and action levels, a review of PHGs adopted by OEHHA over the past decade indicates that whenever the available scientific evidence indicates the potential for both noncancer and cancer health effects,

OEHHA's technical support document incorporates values for both endpoints, beginning with the first public review draft.

More importantly, it seems highly unlikely that OEHHA will complete two separate public processes, including separate external scientific peer reviews and second public review drafts, in time to issue final PHGs for both noncancer and cancer effects before the SWRCB adopts the final Cr(VI) MCL. Even if OEHHA does complete this herculean task, the public would have no opportunity to comment on the impact of OEHHA's final PHGs on the proposed MCL and the SWRCB would have little to no opportunity to meaningfully consider whether the revised PHGs warrant a change in the proposed MCL.

Finally, the SWRCB's release of proposed changes to the MCL for a 15-day public comment period on November 23, 2023, the day after OEHHA released the First Public Review Draft invites renewed speculation that both agencies are driving toward a predetermined outcome and have no intention of considering new scientific information in the Cr(VI) MCL rulemaking process. We hope this is not the case, and as an expression of good faith and commitment to the public process required by the SDWA, we request that OEHHA work with the SWRCB to adjust the timeframe for the MCL rulemaking in a manner that allows OEHHA to complete the PHG update for both noncancer and cancer effects and to allow the SWRCB to revise the proposed Cr(VI) MCL to account for any changes in the PHGs.

Thank you for considering our comments.

Sincerely,

Tim Shestek, Senior Director, State Affairs
American Chemistry Council

Michael Miller, Director of Government Affairs
California Association of Winegrape Growers

Brenda Bass, Policy Advocate
California Chamber of Commerce

Trudi Hughes, President & CEO
California League of Food Producers

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Enclosure

cc: Yana Garcia, Secretary for Environmental Protection, CalEPA
Anna Naimark, Deputy Secretary and Special Counsel for Water Policy, CalEPA
Dr. Lauren Zeise, Director, OEHHA
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ToxStrategies

Innovative solutions
Sound science

Technical Comments on OEHHA's Proposed Non-Cancer Health Protective Concentration for Hexavalent Chromium

January 8, 2024

As indicated in OEHHA's 2023 "Public Review Draft: Proposed Health-Protective Concentration for the Noncancer Effects of Hexavalent Chromium in Drinking Water" (OEHHA 2023), development of a health protective concentration (HPC) is a two-part process. The first part involves a toxicological evaluation of the available data, and the second part involves the derivation of a public health goal (PHG).[1] At first blush, OEHHA appears to employ more current data and scientific methods to each part of the proposed non-cancer HPC derivation for hexavalent chromium (Cr(VI)), consistent with the purpose of the PHG update process. However, as we demonstrate below, there are serious deficiencies in each part of OEHHA's first public review draft technical support document (TSD) for Cr(VI) that render OEHHA's initial conclusions unreliable, either for purposes of risk assessment or for subsequent regulatory decision making.

1. Deficiencies in the toxicological evaluation

In OEHHA's 2011 "Public Health Goals for Hexavalent Chromium (Cr VI) in Drinking Water" (OEHHA, 2011), six studies (or endpoints) were "evaluated for derivation of health protective concentrations" and six acceptable daily dose (ADD) values were derived and compared (see Table 17 therein). OEHHA (2011) subsequently states, "The most sensitive endpoint is then identified and employed to derive a health-protective concentration." Among the six ADD values OEHHA derived, liver effects in female rats in the NTP (2008) study provided the lowest ADD value. It is important to note that the ADD incorporates two components. The first is the point of departure (POD), which represents the dose at which the target effect occurs. These are typically no-observable-adverse-effect-level (NOAEL), lowest-observable-adverse-effect-level (LOAEL), or 95th percentile lower confidence level benchmark dose (BMDL) values. The second component in the ADD is an aggregation of all the uncertainty, variability, or data-driven adjustments to the POD. As such, the ADD is the quotient of the POD divided (i.e., reduced) by the aggregation of various uncertainties, variabilities, and other science policy adjustments. It is important to note that both the POD and the aggregated adjustments can differ across endpoints and for the same endpoint in different species (e.g., rats vs mice).

[1] It is not clear why OEHHA (2023) refers to this as the PHG derivation on page 3 since the document refers to the non-cancer PHC derivation. The PHG is not derived, but rather is the lower of the cancer and non-cancer HPC values.

OEHHA (2023) proposes various changes to the ADD approach in the 2011 PHG. For example, OEHHA changed the POD for liver effects in female rats from a LOAEL in 2011 to a BMDL in 2023. OEHHA also changed the adjustments to the POD. For example, OEHHA relied entirely on uncertainty factors in 2011, but applied pharmacokinetic models and allometric scaling adjustments in 2023. These changes resulted in the ADD increasing from 0.0002 mg/kg-day in 2011 to 0.00034 mg/kg-day in 2023. However, OEHHA does not make similar adjustments in the derivation of the other five studies/endpoints listed in Table 17 of OEHHA (2011). As such, OEHHA has not demonstrated that the newly calculated ADD for liver effects in female rats is, in fact, the lowest ADD. Instead, OEHHA appears to have only updated their analysis for the endpoint that was ultimately selected as the basis for the 2011 non-cancer HPC (i.e., liver effects in female rats).

There are also fundamental problems with how OEHHA identified the critical effects within each of the six studies it considered as the basis for the 2011 HPC. Many studies report multiple health effects, and some include multiple species. When comparing effects in different laboratory species, it is important to recognize that calculation of human equivalent doses differs for rats and mice. For example, OEHHA identified the most sensitive effect in the NTP bioassay by comparing the mg/kg-day doses in rats and mice (NTP 2008). The lowest dose where effects were observed in rats and mice were 0.2 mg/kg-day and 0.38 mg/kg-day, respectively. The nearly 2-fold difference in dose alone does not support the conclusion that rats are more sensitive than mice. Rather, one must first calculate human equivalent doses using allometric scaling techniques. Since OEHHA now includes allometric scaling in its ADD derivations, endpoint selection will be driven largely by the human equivalent dose, i.e., the allometrically adjusted dose from animals to humans. Based on allometric scaling principles, the above-mentioned doses in rats and mice are much more comparable - 0.2 mg/kg-day in rats is equivalent to ~0.05 mg/kg-day in humans and 0.38 mg/kg-day in mice is equivalent to ~0.054 mg/kg-day in humans.[2] Furthermore, OEHHA (2011) reported the lowest dose in rats to one decimal place and the lowest dose in mice to two decimal places. Both USEPA (2010) and OEHHA (2023) list the lowest dose in female rats as 0.24 mg/kg-day[3], equivalent to ~0.060 mg/kg-day in humans, which is *higher* than the 0.054 mg/kg-day human equivalent dose for mice. This indicates that mice are likely more sensitive to Cr(VI) than rats and that OEHHA's 2011 determination of the most sensitive species and non-cancer effect was incorrect. This conclusion is supported by numerous groups that have developed toxicity criteria based on effects in mice (FSCJ 2019; Health Canada 2016; TCEQ 2016; U.S. EPA 2010; 2022).

[2] For transparency, we are using generic allometric adjustment factors of 4 and 7 for rats and mice, respectively (USEPA, 2002).

[3] EPA (2010) lists the doses in female rats as 0.24, 0.94, 2.4 and 7.0 mg/kg-day, whereas OEHHA (2011) lists the doses as 0.2, 0.9, 2.4, and 7 (OEHHA is inconsistent in the use of decimal places or significant digits). Notably, both EPA (2010) and OEHHA (2011) list the lowest dose in mice as 0.38 mg/kg-day, out to two decimal places (i.e., OEHHA (2011) is inconsistent with the reporting of the lowest doses to rats and mice). OEHHA (2023) now lists the lowest dose in female rats as 0.24 mg/kg-day.

The above observations underscore that to meaningfully compare ADD values to identify the lowest or most sensitive effect, one must make 'apples to apples' comparisons; that is, model all effects to the extent feasible (i.e., use BMDL instead of NOAEL or LOAEL) and make appropriate species- and endpoint-specific adjustments (e.g., allometrically scale rodent doses to human equivalent doses). Since OEHHA did not model or allometrically scale all the effects *within* studies or *between* studies, OEHHA has not demonstrated that it has identified the most sensitive effect as the basis for the non-cancer HPC. As such, the analyses in OEHHA (2023) are incomplete and cannot be adopted or used to support regulatory decisions.

In addition to the technical deficiencies related to inappropriate comparison of doses within and across studies, selection of the liver endpoint requires toxicological commentary. The NTP (2008) report does not list liver inflammation in their summary table of lesions. Rather, the NTP (2008) report concludes that "Chronic inflammation is consistent with changes that are considered to be background or spontaneous lesions commonly observed in aged rats and appears to be exacerbated by exposure." This statement indicates that Cr(VI) does not cause liver inflammation, but rather that liver inflammation is commonly observed at the end of two year rat bioassays, regardless of chemical exposure. In fact, as we discuss in the next section, 24 percent of female rats exhibited liver inflammation in the absence of Cr(VI) exposure. Moreover, the incidence of liver inflammation in female rats exposed to Cr(VI) for 13 weeks was not significantly elevated except in rats exposed to approximately 350 ppm Cr(VI), an overtly toxic concentration resulting in a 100 percent incidence of stomach ulceration (this toxic concentration was not used in the 2-year bioassay). These data provide evidence that Cr(VI) exposure does not cause liver inflammation and indicate that this endpoint is not likely to be relevant for human health risk assessment. Given this evidence, other non-cancer effects in test species must be evaluated to support non-cancer endpoint selection. Absent such analyses, OEHHA's draft non-cancer HPC derivation is incomplete and cannot be adopted or used to inform regulatory decisions.

The most widely used endpoint for setting drinking water toxicity criteria for Cr(VI) is diffuse epithelial hyperplasia in the mouse small intestine (FSCJ 2019; Health Canada 2016; TCEQ 2016; U.S. EPA 2010; 2022). USEPA has twice selected this endpoint for their non-cancer oral reference dose (RfD) (U.S. EPA 2010; 2022). OEHHA is the only agency that selected a different non-cancer endpoint, but it does not provide a clear, scientifically defensible rationale for this decision. OEHHA (2023) states, "OEHHA is considering [epithelial hyperplasia in the mouse duodenum] as a preneoplastic endpoint and will be analyzing the data as part of the cancer dose-response analysis. Because the noncancer effects observed in the liver are more sensitive than the noncancer effects in the [gastrointestinal tract], health-protective concentrations derived from liver endpoints will be protective of effects in the [gastrointestinal tract]." As already indicated, OEHHA has not demonstrated that the effects in the liver are, in fact, more sensitive than the mouse intestine. Moreover, it is entirely unclear why OEHHA plans to analyze the intestinal effects considered non-cancerous by EPA and other agencies in their cancer

PHG as opposed to their non-cancer PHG update. Given the lack of toxicological basis for this decision and the apparent greater sensitivity of the mouse intestine compared to the rat liver, OEHHA's draft non-cancer HPC derivation is incomplete and cannot be adopted or used to inform regulatory decisions.

2. Deficiencies in the HPC derivation

2.1 POD determination

The first step in HPC derivation is determination of a POD. Even if one disregards the available evidence and assumes that liver effects in female rats is the critical effect and uses the doses reported in OEHHA (2023), modeling of liver inflammation results in a $BMDL_5$ of 0.065 mg/kg-day (see **Figure 1** below), identical to that reported in OEHHA (2023). However, the model results reveal a flaw in OEHHA's policy to use a default 5% benchmark response (BMR) instead of EPA's default 10% BMR for POD derivation. In this case, the $BMDL_5$ is more than 3-fold lower than the lowest non-zero dose of 0.24 mg/kg-day. This indicates uncertainty in the $BMDL_5$ value because it is below the range of empirical observation. Several other viable models resulted in $BMDL_5$ values ranging from 0.18 to 0.35 mg/kg-day; OEHHA could have selected one of these values. Alternatively, OEHHA could have used the default 10% BMR typically used by the USEPA (U.S. EPA 2012). Figure 1 also shows the high 24% background incidence of liver inflammation in unexposed female rats mentioned previously. Taken together, the available evidence warrants use of a different model or a 10% BMR in deriving the POD.

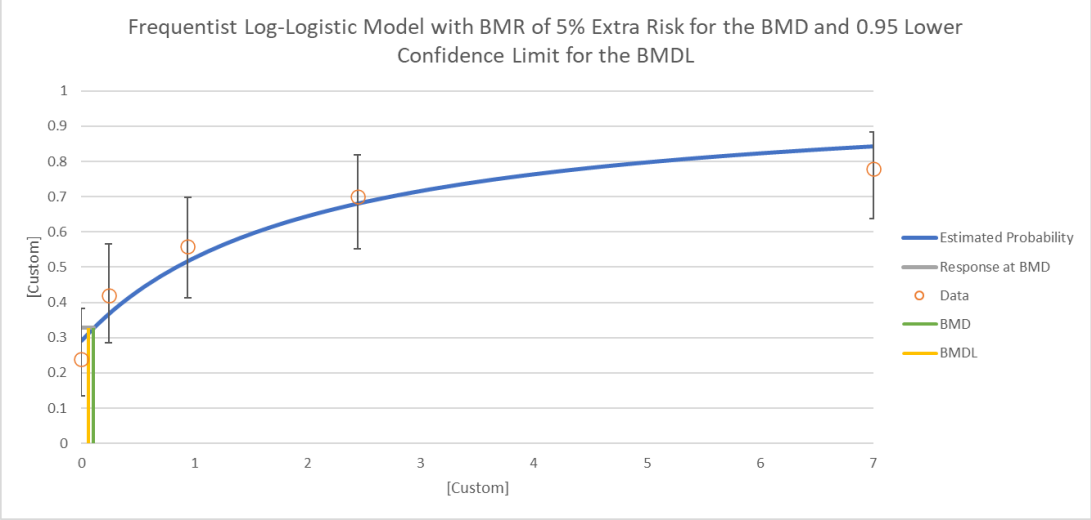

Figure 1. BMD model plot of liver inflammation in female rats after 2 years of exposure to Cr(VI) in drinking water (BMDS v3.3). The BMDS software provides warnings that the $BMDL_5$ is more than 3-fold lower than the lowest dose in the study (indicting uncertainty). Note the high background incidence in the unexposed control group (24%). Data from Table 3 in OEHHA (2023).

2.2 ADD determination

2.2.1 Uncertainty and variability factors

The second step in the HPC derivation is the conversion of the POD to an ADD using a combination of uncertainty factors (UFs), variability factors, and data-driven adjustments. Table 4 in OEHHA (2023) compares the uncertainty factors applied to the POD for liver effects in female rats in 2011 and 2012 (OEHHA 2011; 2023). The above issues notwithstanding, OEHHA should be commended for replacing the default 10-fold LOAEL to NOAEL UF with BMD modeling. OEHHA should also be commended for reducing the interspecies UF_A in OEHHA (2011) from 10-fold to 3-fold reflecting the use of allometric scaling and pharmacokinetic models in OEHHA (2023) that were not available to the agency in 2011 (discussed further below). However, OEHHA's application of intraspecies uncertainty/variability factors (UF_H) in OEHHA (2023) is neither clear nor scientifically valid. OEHHA (2011) applied a 10-fold UF_H equally divided between toxicokinetic ($UF_{H\text{-}TK}$) and toxicodynamic ($UF_{H\text{-}TD}$) differences among humans, whereas OEHHA (2023) applied a 20-fold UF_H.[4] OEHHA references its own 2008 guidance[5] to support this higher UF_H value, but it is unclear why this guidance did not inform the UF_H OEHHA used in 2011. The guidance cited for the larger UF_H is the "Air Toxics Hot Spots Risk Assessment Guideline" (OEHHA 2008); however, the first line of that guidance states that "This document describes the methodology used in developing acute, 8-hour and chronic Reference Exposure Levels (RELs) for use in risk assessments conducted under California's Air Toxics Hot Spots and Toxic Air Contaminants programs." It is unclear whether this guidance is applicable to the development of PHG values for drinking water contaminants since it was not cited in OEHHA (2011).

In the absence of data, USEPA applies a maximum 10-fold UF_H in noncancer risk assessments (U.S. EPA 2002). In the recent USEPA (2022) draft Integrated Risk Information System (IRIS) toxicological review of Cr(VI), USEPA applied a 3-fold UF_H to account for uncertainties in human toxicodynamic variability after addressing human variability in toxicokinetics using physiologically-based pharmacokinetic (PBPK) models (USEPA 2022). Using the same model as EPA, OEHHA applied a rounded 20-fold UF_H comprised of a 3-fold $UF_{H\text{-}TD}$ and 6-fold $UF_{H\text{-}TK}$. OEHHA reduced the 10-fold $UF_{H\text{-}TK}$ to 6-fold due to the use of PBPK models. OEHHA's reference to 2008 air toxics risk assessment guidance does not justify its use of an intraspecies adjustment factor that is more than 6 times higher than USEPA's intraspecies adjustment factor despite having acquired the relevant PBPK model from USEPA.

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[4] This 20-fold value was reduced from a supposed default value of 30-fold ($UF_{H\text{-}TD}$=3; $UF_{H\text{-}TK}$=10) due to use of PBPK models.

[5] A footnote to Table 4 on page 33 of OEHHA (2023) indicates that the UF_H has changed since 2011. However, it is unclear where this is documented as elsewhere OEHHA cites 2008 guidance for the default 30-fold UF_H.

Notwithstanding the policy basis for the inexplicable increase in the default UF_H between the 2011 and 2023 Cr(VI) HPCs and the use of a UF_H that is 6-fold higher than applied by USEPA (2022), the application of a ***higher*** UF_H in 2023 ***after*** using PBPK models to address human variability in Cr(VI) toxicokinetics (see below) is antithetical to the use of PBPK models. The goal of using PBPK models in risk assessment is to ***reduce*** uncertainty by quantifying variability, not to ***increase*** uncertainty and reliance on larger default UFs. If OEHHA believes the PBPK model has increased uncertainty in intraspecies variability in pharmacokinetics by 100 percent, then OEHHA should not use the PBPK model and simply apply the 10-fold UF_H it used in 2011. If, on the other hand, OEHHA believes that the PBPK model has reduced uncertainty in the ADD by at least partially quantifying human variability, then the toxicokinetic portion of the UF_H should be reduced to 1 or, at the very least, OEHHA should retain the 3-fold value it used in the 2011 HPC. The increase in the UF_H from 10-fold in 2011 to 20-fold in 2023 lacks both policy and scientific justification and therefore the OEHHA (2023) HPC cannot be adopted or used to support regulatory decisions.

2.2.2 Toxicokinetic adjustments

OEHHA (2023) used a PBPK model (Sasso and Schlosser 2015) to convert the applied dose of 0.065 mg/kg-day Cr(VI) to an 'internal' dose. This is not really an internal dose because it is not a dose reflective of blood or tissue concentration, but rather is just an adjustment of the Cr(VI) dose leaving the stomach and transiting to the small intestine. In contrast, Thompson et al. (2018) demonstrated the use of a more extensive PBPK model (Kirman et al. 2017) to develop RfD values for effects in both the gastrointestinal tract and systemic effects such as the liver. These authors derived an RfD for liver inflammation of 0.003 mg/kg-day solely for comparison with the OEHHA PHG (Thompson et al. 2018). This value is ~9-fold higher than the ADD of 0.00034 mg/kg-day derived in OEHHA (2023) using the partial model. Aside from the difference resulting from the use of different PBPK models, the difference in RfD and ADD values is driven by the lower BMR used by OEHHA (5% vs 10%) and the larger UF_H applied by OEHHA (20-fold vs 3-fold), which as noted above, is antithetical to the intended use of PBPK models to reduce uncertainties in species extrapolation and human variability in response to chemical exposures.

3. Conclusion

There are multiple, fundamental scientific deficiencies in OEHHA's draft non-cancer HPC for Cr(VI) that preclude its adoption and use to support regulatory decisions. These deficiencies include:

- Insufficient demonstration that liver inflammation in rats is an adverse effect of Cr(VI) exposure, or that it is relevant to humans.

- Inconsistent application of scientific methods (e.g., BMD modeling, allometric scaling) to multiple adverse effects to determine which endpoint is the most sensitive and relevant basis for the HPC derivation.
- Unexplained and seemingly unjustified consideration of non-cancer intestinal effects for OEHHA's cancer PHG as opposed to their non-cancer PHG.
- Application of a higher UF_H value from 2008 air toxics guidance that was not applied in 2011 and has not been established as relevant to a drinking water risk assessment, especially given the availability of modeling data.
- Incoherent *increase* in the total *uncertainty factors* applied to the same endpoint *after* using PBPK models to reduce uncertainty in interspecies extrapolation and intraspecies variability.

While it appears that OEHHA is claiming the default UF_H is 30 in some recent reports, the only purported basis for this value in the draft TSD is OEHHA (2008). Absent further explanation and given OEHHA's use of a 10-fold UF_H in 2011 in the absence of data from PBPK models, the change in UF_H policy seems intended to counteract the effects of using updated risk assessment methods such as BMD modeling, allometric scaling, and use of PBPK models. With proper application of the available PBPK models, the 60-fold (UF_A = 3, UF_H = 20) composite uncertainty factor proposed in the draft TSD should be reduced to 10-fold (UF_A = 3, UF_H = 3). These UF_A and UF_H values are grounded in the best available science and are consistent with those applied in USEPA (2022). As such, the proposed PHG of 5 ppb should be 6-fold higher.

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