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

April 28, 2025

In January 2024, ToxStrategies submitted comments on OEHHA's 2023 "Public Review Draft: Proposed Health-Protective Concentration for the Noncancer Effects of Hexavalent Chromium in Drinking Water" (OEHHA 2023). We were pleased to see that OEHHA addressed some of our concerns in their Second Public Review Draft (OEHHA 2025), such as consideration of the small intestine effects in mice in the development of a non-cancer health protective concentration (HPC). However, two important concerns were not adequately addressed. These include selection of the critical effect as the basis of the HPC and the unjustifiably large 20-fold uncertainty factor for human variability (UF_H). These issues are addressed below along with brief commentary on OEHHA's default UF_H of 30.

1. Lack of Justification for Selection of Liver Effects in Rats as the Basis of the HPC

As indicated in the OEHHA draft HPC document (2025; Table 4 p. 32), OEHHA derived human equivalent dose point of departure (POD_{HED}) values of 0.020 and 0.024 mg/kg-day for liver inflammation in rats and diffuse epithelial hyperplasia in the mouse small intestine, respectively. Because liver inflammation resulted in a slightly lower HPC (5 ppb) compared to small intestine effects (6 ppb), OEHHA selected liver inflammation as the basis of the HPC. Using slightly different methods, EPA calculated that liver inflammation in rats resulted in a reference dose (RfD) of 7E-4 mg/kg-day whereas small intestine effects in mice resulted in an RfD of 9E-4 mg/kg-day (U.S. EPA 2024). Despite liver inflammation providing a slightly lower RfD, EPA (2024) ultimately concluded that there was greater uncertainty associated with liver effects and therefore did not select the liver as the basis of their RfD, stating:

"While the osRfD for liver was slightly lower, due to the minimal severity of the chronic liver inflammation observed in female rats in the two-year bioassay (characterized by NTP (2008) as a "chronic inflammatory process of minimal severity" and "consistent with changes that are considered to be background or spontaneous lesions commonly observed in aged rats"), the uncertainty in the POD is considered to be larger for the hepatic osRfD, as more severe manifestations of toxicity (e.g., necrosis, fibrosis) were not observed in the selected study." (emphasis added)

EPA's rationale is similar to that in our 2024 comments on the OEHHA (2023) draft HPC document. These points are reiterated here:

- The NTP chronic bioassay does not list liver inflammation in their summary table of nonneoplastic effects observed in rats (NTP 2008).
- The NTP chronic bioassay concludes that "[c]hronic 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" (NTP 2008).
- The background incidence of liver inflammation in unexposed female rats was high at 24% (NTP 2008).
- In the NTP 13-week Cr(VI) study, the incidence of liver inflammation in female rats 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 (NTP 2007); this toxic concentration was not used in the NTP (2008) chronic bioassay.

Taken together, these observations indicate that Cr(VI) exposure does not cause liver inflammation in rats except perhaps at extremely high concentrations, but may exacerbate an apparent predisposition for liver inflammation in rats. To date, OEHHA is the only organization that we are aware of that has used liver effects to develop toxicity criteria for Cr(VI). OEHHA should reevaluate this endpoint as the basis of their noncancer HPC, especially considering the concerns raised by EPA.

2. Lack of Scientific Justification for the 20-fold UF_H

In our 2024 comments on the OEHHA (2023) draft noncancer HPC, we noted the inexplicable increase in the UF_H from 10-fold in OEHHA's 2011 PHG Technical Support Document to 20-fold in OEHHA (2023) given that the latter employed physiologically-based pharmacokinetic (PBPK) models that reduce uncertainty in intraspecies variability and should lead to a reduction in the uncertainty factors used to calculate health reference values (U.S. EPA 2006). OEHHA (2023) cited an earlier guidance document developed for the Air Toxic Hot Spots Program (OEHHA 2008) as support for using a default UF_H of 30 for drinking water values. Because the 2008 guidance was not cited in the OEHHA (2011) PHG that used a default UF_H of 10, we previously questioned whether the OEHHA (2008) guidance was misapplied or cited in error in the OEHHA (2023) document. Based on our own non-exhaustive review of UF_H values in OEHHA PHG documents from 2010-2018, it appears that OEHHA began applying the OEHHA (2008) default 30-fold UF_H around 2014 (**Table 1**). It remains unclear as to why OEHHA (2011) did not follow the 2008 guidance. The basis for OEHHA's unique 20-fold UF_H for Cr(VI) and default 30-fold default UF_H are discussed below.

Table 1. Partial list of PHGs and UFH Values (2010-2018)*

Chemical Name	Year	Cites	Species	UFH	Notes
<u>Chromium-hexavalent</u>	2025	Yes	Rat	20	<30 due to PBPK model
<u>Nitrate</u>	2018	Yes	Human	1	Infant methemoglobinemia
<u>Nitrite</u>	2018	Yes	Human	1	Infant methemoglobinemia
Nitrite and Nitrate	2018	Yes	Human	1	Infant methemoglobinemia
Antimony	2016	Yes	Rat	30	
<u>Carbofuran</u>	2016	Yes	Rat	30	
<u>Diquat</u>	2016	Yes	Rat	30	
<u>Endrin</u>	2016	Yes	Dog	100	
<u>Picloram</u>	2016	Yes	Dog	30	
<u>Thiobencarb</u>	2016	Yes	Rat	30	
<u>Perchlorate</u>	2015	No	Human	10	
<u>Chlorobenzene</u>	2014	Yes	Rat	30	
<u>Endothall</u>	2014	Yes	Dog	10	
<u>Hexachlorocyclopentadiene</u>	2014	Yes	Rat	30	
Silvex	2014	Yes	Dog	30	
Trichlorofluoromethane (Freon 11)	2014	Yes	Rat	30	
<u>Chromium-hexavalent</u>	2011	No	Rat	10	
trichlorotrifluoroethane (Freon	2011	No	Human	10	
<u>113)</u>	2010		Human	10	
Styrene	2010	No	Mouse	10	
Selenium	2010	No	Human	3	
Benzo(a)pyrene	2010	No	Rat	10	
Methoxychlor	2010	No	Mice	10	
TCDDs	2010	No	Rat	10	

^{*}This list is not exhaustive, but it is assumed that all PHGs from 2018 to present will consider the default UF_H to be 30. The highlighted rows demonstrate the increase in UF_H used for Cr(VI) between 2011 and 2025.

<u>2a. The 20-fold UF_H for Cr(V) is Inconsistent with OEHHA (2008) Guidance and is Based on</u> Application of Arbitrary Adjustment Factors

Many regulatory authorities, including EPA, apply a 10-fold uncertainty factor for interspecies (animal-to-human) extrapolation (UF_A) and a 10-fold uncertainty (or human variability) factor to account for potential sensitive individuals or lifestages (UF_H) (U.S. EPA 2002b). The standard 10-fold UF_H and UF_A values are comprised equally of 3.16 for toxicokinetic differences and 3.16 for toxicodynamic differences. These values represent the $\sqrt{10}$, such that their multiplication equals 10 (3.16 × 3.16 = 10). Typically, the individual 3.16 factors are rounded to 3, and their multiplication is said to equal 10. As will be discussed in Section 3, OEHHA's default UF_H retains a $\sqrt{10}$ (rounded to 3) value for toxicodynamic differences but uses a full 10-fold value for potential toxicokinetic differences—resulting in a 30-fold UF_H expressed mathematically as $\sqrt{10}$ × 10 = 31.6 (rounded to 30). The toxicodynamic and toxicokinetic portions can also be written as

 UF_{Hd} and UF_{Hk} , respectively. With this primer, we can begin to assess the UF_H value that OEHHA applied for Cr(VI).

OEHHA (2008) lists possible default values for the UF_{Hk} as 1, 3, or 10 (see **Table 2**). Row 2 in **Table 2** justifies a UF_{HK}=1 when PBPK models include measures of 'inter-individual variability' (note there is no reference to lifestages). Importantly, both OEHHA (2025) and EPA (2024) used the same PBPK model to incorporate human susceptibility to Cr(VI) by comparing post-gastric reduction doses in individuals with normal and high gastric fluid pH that would limit Cr(VI) reduction to more inert Cr(III). EPA (2024) characterizes the Cr(VI) gastric fluid PBPK model as adequately addressing inter-individual variability:

"To account for **interindividual variability**, the human equivalent dose was determined by Monte Carlo analysis. The lower 1% value of 20000 Monte Carlo PK simulations needed to achieve the internal dose POD was used. As a result, the intraspecies uncertainty factor **(UFH) was lowered from 10 to 3** (the pharmacokinetic component of the uncertainty factor was removed as it was accounted for with this analysis)." (emphasis added)

OEHHA (2025, p. 15) uses similar language regarding inter-individual variability:

"An estimated daily Cr(VI) dose to achieve the human equivalent internal dose calculated in step 2 was derived using the human model by Sasso and Schlosser (Schlosser and Sasso, 2014; Sasso and Schlosser, 2015). Monte Carlo analysis was used in this step to account for interindividual variability."

The use of the human PBPK model to address *inter-individual variability* in both EPA (2024) and OEHHA (2025) support use of a UF_{Hk}=1 in OEHHA's non-cancer HPC calculation (see **Table 2**, row 2).

Table 2. Possible Default Values for UF_{Hk} (OEHHA, 2008)*

UF _{HK} Value	Justification	Notes
1	"human study including sensitive subpopulations (e.g., infants and children)"	
1	"where a PBPK model including measured inter-individual variability is used"	Based on OEHHA (2008) and the analysis in EPA (2024), this should be the value used in the Cr(VI) noncancer HPC calculation. See above citation.
√10 (3)	"for residual susceptibility differences where there are some toxicokinetic data (e.g., PBPK models for adults only)"	Based on OEHHA (2008), and use of the above-noted PBPK modeling, this would be the maximum UF _{Hk} for Cr(VI).
10	"to allow for diversity, including infants and children, with no human kinetic data"	

 $^{^*}$ Adapted from Table 4.4.1 in OEHHA (2008).

Alternatively, if OEHHA believes there are still uncertainties in the PBPK model related to non-adult lifestages, then row 3 in **Table 2** indicates that the maximum UF_{Hk} for Cr(VI) should be 3. Instead, OEHHA (2025, p. 33) argues for a 6-fold UF_{Hk} as follows:

"To account for toxicokinetic diversity within susceptible populations, including infants and children, an intraspecies toxicokinetic UF of 10 is applied when human toxicokinetic data are not available. OEHHA modeled gastric reduction of Cr(VI) using a toxicokinetic model with Monte Carlo simulation, which simulated stomach pH variability up to approximately 5.25. This pH range encompasses typical adults, plus those with hypochlorhydria (high stomach pH, typically in the range of pH 3-5). However, adults medicated with proton pump inhibitors (stomach pH \approx 6) and infants and children up to about 2.5 years of age (stomach pH \approx 7) fall outside of the pH range included in this model (Laine et al., 2008; Neal-Kluever et al., 2019; Rahman et al., 2016). Thus, **OEHHA** incorporated an additional uncertainty factor of 2 to account for residual uncertainty related to pH that was not adequately captured by the gastric reduction model, resulting in an overall intraspecies toxicokinetic UF of 6 (\vee 10 × 2)." (emphasis added)

Based on the quote above, in addition to the $\sqrt{10}$ (i.e., 3)-fold UF_{Hk} that OEHHA might typically apply to account for "residual susceptibility differences where there are some toxicokinetic data (e.g., PBPK models for adults only)" (**Table 2**, row 3), OEHHA is adding an additional 2-fold factor because the PBPK model may not adequately address higher pH values in infants and children or adults taking proton pump inhibitors (see **Table 3**). Regarding the pH in infants and children, the additional 2-fold factor is clearly double counting, compounding, and/or conflating the uncertainty already addressed by the $\sqrt{10}$ (i.e., 3)-fold UF_{Hk} that OEHHA attributes to the use of 'adult-only' PBPK models (**Table 2**, row 3). OEHHA's proposal to use a 6-fold UF_{Hk} for Cr(VI) is a clear departure from what it has done for every other chemical noted in Table 1 above, and appears to violate OEHHA's 2008 policy for use of uncertainty factors. Specifically, and as discussed further in comment 3 below, there is no scientific or science-policy basis in OEHHA (2008) to use a UF_{Hk} between $\sqrt{10}$ and 10 when the data available for the subject chemical clearly meet the criteria for a UF_{Hk} of 1 or $\sqrt{10}$.

Moreover, regarding adult users of proton pump inhibitors, the difference in pH 5.25 and pH 6 is minimal and certainly not a chronic lifetime condition. Not only is OEHHA speculating about the adequacy of the PBPK model, but as noted above, the 2-fold multiplier is arbitrary. This can be demonstrated by considering two similar values, 1 or 3. The former would have no impact and would simply result in a UF_{Hk} of 3 ($\sqrt{10} \times 1 = 3$), identical to **Table 2**, row 3. If OEHHA instead used a value slightly higher than 2 (e.g., 3), then the UF_{Hk} would be equal to their default value of 10 ($\sqrt{10} \times 3 = 10$) despite having used PBPK models. If OEHHA selected a value >3, then the UF_{HK} would be >10 (e.g., $\sqrt{10} \times 4 = 12$) and would imply that the use of PBPK models actually *increased* uncertainty above the default. This demonstrates that the additional 2-fold factor is not only inconsistent with OEHHA (2008) guidance, but also arbitrary and not scientifically justified.

Table 3. UF_H Value for Cr(VI) in OEHHA (2025)

UF _H Component	Value
UF _{Hd}	$\sqrt{10} = 3$
UF _{Hk}	$\sqrt{10} \times 2 = 6$
UF _H	$3 \times 6 = 18$ (rounded to 20)

<u>2b. The OEHHA (2025) 20-fold UF_H is Inconsistent with Proper Application of U.S. EPA</u> Guidance

To assess the validity of the 20-fold UF $_{\rm H}$ OEHHA applied in their HPC calculation, it is informative to compare it to the 3-fold UF $_{\rm H}$ that EPA applied in their toxicological evaluation of Cr(VI) (U.S. EPA 2024). As mentioned, both EPA and OEHHA used the same PBPK model to incorporate human susceptibility to Cr(VI). EPA's justification for the 3-fold UF $_{\rm H}$ is as follows:

"An intraspecies uncertainty factor, UF_H, of 3 (10^{1/2} = 3.16, rounded to 3) was applied to account for variability and uncertainty in pharmacodynamic susceptibility in extrapolating to subgroups of the human population most sensitive to the health hazards of Cr(VI) (U.S. EPA, 2002). In the case of Cr(VI), the PODs were derived from studies in inbred animal strains and are not considered sufficiently representative of the exposure and doseresponse of the most susceptible human subpopulations (see Section 3.3.1). In certain cases, the pharmacokinetic component of this factor may be replaced when a PK model is available that incorporates the best available information on variability in pharmacokinetic disposition in the human population (including sensitive populations). In the case of Cr(VI), a Monte Carlo analysis using PBPK modeling (see Appendix Section C.1.5) was applied to account for pharmacokinetic variability. The POD was based on the lower 1% value, and therefore a value of 1 was applied for pharmacokinetic variability. A value of 3 was retained for pharmacodynamic variability." (emphasis added)

The disparity in UF_H between EPA and OEHHA is striking. It is notable that Cr(VI) is not metabolized but rather undergoes non-enzymatic reduction to Cr(III); as such, potential pharmacokinetic differences between adults and children are limited. The potential for prenatal pharmacokinetic susceptibility should be minimal as dose is highly dependent on the mother's gastric reduction thereby leaving pharmacodynamic susceptibility as the primary concern for the fetus, which is accounted for by EPA's 3-fold UFH (identical to OEHHA's 3-fold UF_{Hd}). Postnatal pharmacodynamic concern is likewise accounted for by the 3-fold UF_H applied by EPA and OEHHA, whereas pharmacokinetic concern is largely addressed among those individuals with high gastric pH (comparable to neonates) and the overall short developmental window where postnatal gastric pH is higher than adults. OEHHA (2025) asserts that the PBPK model does not apply to infants and children, because "infants and children up to about 2.5 years of age" have a "stomach pH ≈7" which "fall(s) outside of the pH range included in this model." OEHHA cites a review by Neal-Kluever et al. (2019) to support this statement. However, OEHHA mischaracterized the duration of elevated infant gastric pH, as Neal-Kleuver et al. explain that postnatal gastric pH remains elevated for only hours before steadily decreasing, reaching a pH of 3-3.5 within one week, regardless of gestational age at birth (Neal-Kluever et al. 2019).

Thus, within one week of birth, infant gastric pH is well within the applicability domain of this PBPK model.

Importantly, the NTP scored the histopathological effects selected by EPA and OEHHA as the basis of their respective toxicity criteria on a 4-tier scale of minimal, mild, moderate, and marked. Both effects were diagnosed as having average severity scores in the highest group equivalent to mild. In the lower dose groups closer to the points of departure (e.g., benchmark dose lower limit [BMDL₅]) the average severity was lower (i.e., minimal). As such, the endpoints themselves are not overtly toxicity. Moreover, the points of departure represent low incidence rates (e.g., 5% extra risk) in animals prior to interspecies extrapolation to humans. Restated, a low incidence of a mild effect in animals was extrapolated to humans, with appropriate dose and uncertainty adjustments, and a PBPK model was used to estimate a dose at which 1% of the population might have a low probability (i.e., incidence) of developing a mild effect. Neither liver inflammation nor intestinal hyperplasia are irreversible. If a child were more susceptible to Cr(VI) for a small window of development, which, as noted above, is only the first week after birth, the effects are anticipated to be very rare, minimal, and transient, as evidence by EPA's selection of a 3-fold UF_H based solely on toxicodynamic uncertainties (see quote above). There is simply no biological justification for OEHHA to use a UF $_{\rm H}$ greater than 3.

3. OEHHA's Default 30-fold UF_H is Unjustifiably Larger than U.S. EPA's Default UF_H As explained above, OEHHA's 30-fold UF_H is expressed mathematically as $\sqrt{10} \times 10 = 31.6$ (rounded to 30). OEHHA (2008) states:

"Whenever possible, OEHHA will assess differences between children and adults using PBPK modeling when developing oral RELs. As is the case of the inhalation RELS, an intraspecies UF of 30 (v10 x 10) instead of 10 may be considered in some cases to protect children's health when insufficient data exists for PBPK modeling" (p. xvii; emphasis added).

"When an uncertainty factor approach is used due to the lack of data for compound-specific models of toxicokinetics and toxicodynamics, an overall intraspecies uncertainty factor (UFH) of 30 rather than 10 (toxicokinetic component, UFHk 1 = 10; toxicodynamic component, UFHd = $\sqrt{10}$) will be used as a default procedure to protect infants' and children's health, for example in cases where **differences in metabolism and excretion are key to the toxicological activity**" (p. 6) (emphasis added).

From the above citations, it is clear that protection of infants and children is the motivating factor for the higher UF_H. OEHHA attempts to justify this concern by citing the Federal Food Quality Protection Act (FQPA) that mandated EPA to consider an additional 10-fold safety factor for protection of children:

"The difference in toxicokinetics is even more pressing when considering infants and children as part of the affected population. As discussed in Section 3.1, it has been

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¹ UF_{Hk} and UF_{Hd} refer to the kinetic and dynamic portions of the UF_H, respectively.

suggested that children may be both more sensitive, and more diverse, than adults, as a result of both pharmacodynamic and pharmacokinetic factors affecting toxicity. Several revisions in this version of OEHHA's risk assessment methodology are designed to address this concern. An additional 10-fold UF (presumably to account for both toxicokinetic and toxicodynamic factors) has been mandated by Congress to specifically protect children in assessments conducted for pesticides in accordance with the Federal Food Quality Protection Act (FQPA), assuming infants and children are more sensitive than adults, unless data to the contrary exist. U.S. EPA (2002b) has developed guidelines for evaluating data to determine an appropriate value (generally between 1 and 10) for the FQPA-specified uncertainty factor. In the following discussion, the approach will be to determine an appropriate value to substitute for the default value for the two separate components of UFH, rather than to specify additional overall UFS." (p. 64)

The 2002 document referenced above describes a process by which the FQPA could be included in EPA's risk assessments (U.S. EPA 2002a)². Specifically, EPA (2002a) developed a process by which the standard toxicity value process conducted for decades was not significantly impacted. The solution was to derive toxicity criteria (e.g., RfD values) as usual and then apply an additional³ 10-fold "FQPA safety factor" to the RfD to derive a population adjusted dose (PAD). However, USEPA (2002a) also states:

"it is important to recognize that the FQPA safety factor, as defined in FQPA, does not stand wholly apart from traditional agency practice but rather incorporates that practice as a part of the safety factor. Thus, there is a large degree of overlap between the FQPA safety factor and traditional agency practice as to the use of uncertainty factors to account for incomplete characterization of a chemical's toxicity." (emphasis added)

A second 2002 EPA document titled A Review of the Reference Dose and Reference Concentration Processes (U.S. EPA 2002b) states:

"In considering the robustness of the RfC/RfD methodology and its adequacy for assessing hazards to infants and children, the Technical Panel also recognized the overlap of areas covered by the FQPA factor and those addressed by the traditional UFs. For example, the database UF may be invoked where data are unavailable or are insufficient to explicitly consider the potential sensitivity of the developing organism. The Technical Panel agrees with the 10X Task Force draft Toxicology Working Group report (U.S. EPA, 1999b) that the current interspecies, intraspecies, LOAEL-to-NOAEL, subchronic-to-chronic, and database-deficiency UFs, if appropriately applied using the approaches recommended in this review, will be adequate in most cases to cover concerns and uncertainties regarding the potential for pre- and postnatal toxicity and the completeness of the toxicology database. In other words, an additional UF is not needed in the RfC/RfD methodology because the currently available factors are considered sufficient to account for uncertainties in the database from which the reference values

² For clarity, EPA (2002a) in this memo is the EPA (2002b) in the quoted text.

³ USEPA (2002a): "Any reference in this document to an "additional" FQPA safety factor is simply meant to convey that the FQPA factor is in addition the intra- and interspecies uncertainty factors. Generally, this document does not repeat the term "additional" throughout on the assumption that the reader will understand that FQPA safety factors are additional to the standard, baseline uncertainty factors for intra- and interspecies."

are derived (and it does not exclude the possibility that these UFs may be decreased or increased from the default value of 10)." (emphasis added)

It is evident from the above citations that EPA believes that uncertainty related to infants and children can be addressed by endpoint selection and the appropriate application of uncertainty factors related to interspecies, intraspecies, LOAEL-to-NOAEL, subchronic-to-chronic, and database-deficiency without additional (or unusually large) uncertainty factors *per se*.

In addition to citing EPA guidance, OEHHA also argues that available data support the application of a higher UF_H. This includes reference to differences in xenobiotic metabolism due to genetic polymorphisms and/or lifestage differences in enzyme expression. OEHHA (2008) also argues that an analysis of 25 chemicals with PBPK models (by OEHHA or in literature) found that "of the 25 chemicals and metabolites...13 have UF_{Hk} greater than V10. This results primarily in differences in toxicokinetics between infants and adults, resulting in higher internal doses of the compounds and longer clearance half-lives" (OEHHA, 2008, p. 65). However, OEHHA seems to disregard the fact that lifestage differences occur over a relatively short period of time and not over the course of a lifetime, which is the relevant timeframe for chronic toxicity values. With respect to Cr(VI), which undergoes non-enzymatic reduction, potential lifestage differences in enzyme expression are not relevant considerations. Moreover, there are reproductive and developmental toxicity studies for Cr(VI) that can be used to address concerns for infants and children without application of a 20-fold UF_H. The arguments OEHHA presents as justification for its proposed UF_H for Cr(VI) are not supported by its own (2008) guidance, the EPA guidance it cites, or any other available data cited in the revised non-cancer HPC document.

4. Conclusion

While we appreciate OEHHA's effort to address some of the concerns we identified with its first public review draft non-cancer HPC for Cr(VI), the revised draft retains critical deficiencies that directly impact the calculation of the HPC. These deficiencies include:

- An insufficient demonstration that liver inflammation in rats is an adverse effect of Cr(VI) exposure, or that it is relevant to humans.
- Application of a 6-fold UF_{Hk} that is not consistent with OEHHA (2008) guidance,
 US EPA guidance, the use of available PBPK models, or available biological evidence.
- Application of an arbitrary 2-fold factor, in addition to a $UF_{Hk} = \sqrt{10}$ (3) that already more than adequately accounts for residual uncertainty, results in double counting uncertainties.

- Mischaracterization of the human PBPK modeling and failure to consider strong biological evidence indicating minimal pharmacokinetic differences between adults and infants/children, both of which support a UF_{Hk} of 1, consistent with EPA (2024)).
- The purported justification for OEHHA's default 30-fold UF_H is inconsistent with uncertainty factor policies employed by many other regulators, including EPA, and protection of infants and children can be adequately addressed in most cases, including for Cr(VI), by proper endpoint selection and application of traditional UF values.

The application of a composite 60-fold UF consisting of a 3-fold UF_A and 20-fold UF_H results in a HPC of 5 ppb Cr(VI). Correction of the UF_H to 3 would result in a composite UF of 10, equating to a 6-fold reduction in the composite UF and therefore a 6-fold increase in the HPC to 30 ppb. This value would be derived in a manner consistent with OEHHA guidance and would be protective of all lifestages.

Until these issues are resolved, the current draft document should not be adopted or cited in support of regulatory decisions.

5. References

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