Summary of the Hexavalent Chromium IRIS Update

NC Secretaries' Science Advisory Board

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Hexavalent Chromium Refresher and IRIS Update

Hexavalent Chromium (CrIV)

Hexavalent Chromiun is chromium in the hexavalent (+6) oxidation state, denoted as Cr(VI).

Cr(VI) compounds have many industrial applications, including pigment manufacturing, corrosion inhibition and metal finishing.

Because many Cr(VI) compounds are water soluble, they are highly mobile in soil and may contaminate drinking water.

Cr(VI) may be emitted into air by industries using Cr(VI) compounds, and by various other sources such as the burning of fossil fuels.

Hexavalent Chromium (CrIV) Health Impacts

- Evidence indicates that Cr(VI) is likely to cause GI tract, liver, developmental, and lower respiratory toxicity in humans.
- Evidence suggests that Cr(VI) may cause male reproductive effects, immune effects, and hematological toxicity in humans.
- Evidence is inadequate to assess whether Cr(VI) causes female reproductive toxicity in humans.
- Organ/system-specific reference values were derived for GI tract, liver, developmental, hematological, and nasal effects.
- As of August 2024: The overall chronic RfD = 9×10^{-4} mg/kg-day, and RfC = 3×10^{-5} mg/m^3.
- These are updated values from the 1998 IRIS values of RfD= $3x10^{-3}$ and RfC= 0.1 µg/m^3.

Hexavalent Chromium (CrIV) Cancer Impacts

- For cancer via the oral route of exposure, Cr(VI) is likely to be carcinogenic to the human GI tract.
- Because a mutagenic mode-of-action (MOA) for Cr(VI) carcinogenicity is “sufficiently supported in (laboratory) animals” and “relevant to humans,” EPA used a linear low dose extrapolation from the POD in accordance with Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005a).
- The total lifetime exposure OSF for Cr(VI) is **0.26 (per mg/kg-day).** *(1998 value = NA)*

- For cancer via the inhalation route of exposure, quantitative exposure-response data were evaluated, and an inhalation unit risk (IUR) was developed for human lung cancer.
- Linear low dose extrapolation and application of ADAFs were performed for the inhalation route of exposure.
- The total lifetime exposure IUR for Cr(VI) is **0.018 × µg/m^3.** *(1998 value = 0.012 µg/m^3)*

NC SSAB History with Hexavalent Chromium

NC SSAB Previous Recommendation

SSAB Recommends that the State apply a linear no-threshold dose response extrapolation approach when estimating human cancer risks from groundwater and surface water exposure to Cr(IV).

Status as of 2021 Recommendation

- The SSAB has examined the method by which a Cr(IV) standard should be derived but has not provided a value that would be appropriate for regulatory use.
- The only human epidemiolocal data that exists for Cr(IV) is inhalation data and the relationship to a cancer outcome is clear. This route of exposure was not included in the SSAB charge and not assessed.
- EPA is currently conducting an updated assessment of Cr(IV).

NC SSAB Previous Action

The Secretary's Science Advisory Board (SSAB) was charged with reviewing the current hexavalent chromium [Cr(IV)] toxicological science relating to a linear or a non-linear response and provide a recommendation regarding the appropriate science to be used for the development of regulatory standards for groundwater and surface water that are protective of public health and the environment. The details provided herein describe the major conclusion reached and the potential next steps in determining a regulatory standard.

April 2018, DHHS asked the SSAB to review the DHHS Hexavalent Chromium health goal and provide guidance about the cancer slope factor.

- Public Comment draft of final report released in Feb 2020; report finalized in Feb 2021.

NC SSAB Previous Deliberation

- The deliberation by the SSAB detailed the two approaches in extrapolating Cr(IV) exposure from lab animals to humans for regulatory use– the linear no-threshold approach (cancerous outcomes), and the non-linear approach (non-cancerous outcomes).

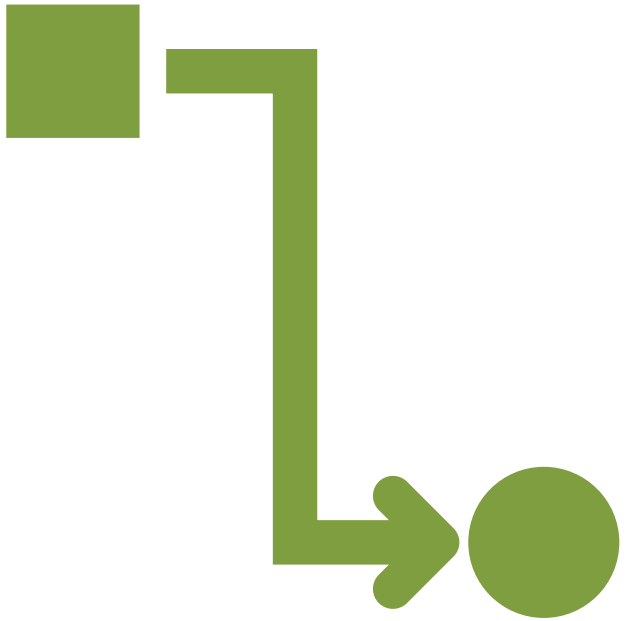
  - Cancerous outcomes = linear no-threshold approach to dose response assessment.
    - This which requires the calculation of an Oral Slope Factor (OSF). The OSF can be combined with environmental data to provide an estimate of the increased cancer risk from a lifetime of oral exposure to a substance.
    - This approach is protective if the biochemical mechanism is unknown.

  - Non-cancerous outcomes= non-linear approach and reference dose (RfD).
    - The RfD is estimated based on the point of departure (chemical concentration eliciting effects) and uncertainty factors.
    - This approach is more accurate since it is based on a known biochemical mechanism and specific chemical concentrations where effects are consistently observed.

NC SSAB Previous Deliberation

- Cr(VI) is known to cause cancer (via inhalation) and targets the respiratory system, kidneys, liver, skin, and eyes (OSHA).
  - There is limited evidence regarding a specific biochemical mechanism that leads to cancerous effects (via inhalation or otherwise). The studies examined by the SSAB report mixed findings for oral exposures.
    - The mixed findings via non-inhalation exposures combined with the clear evidence in humans that Cr(IV) inhalation exposures are carcinogenic, *provide enough evidence to suggest that a cancer-causing mechanism is potentially operative in Cr(IV) exposures via drinking water*.

SSAB Recommends that the State apply a linear no-threshold dose response extrapolation approach when estimating human cancer risks from groundwater and surface water exposure to Cr(IV).



DEQ Next Steps

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- The technical staff from the Divisions of Air Quality, Waste Management, and Water Resources are reviewing the updated IRIS Toxicity Assessment and the associated materials.
  - Divisions are discussing the potential effects of the updated IRIS assessment to program requirements.

- After the technical staff review the materials, the tentative path forward can be shared at a 2025 SAB meeting.