DRAFT observations for consideration in working toward consensus recommendations and identifying where we lack consensus

The SSAB recommends that State risk assessment staff participate in or closely monitor the IRIS update of hexavalent chromium toxicity. The EPA's data synthesis and review is going on now; a contemporary review of that magnitude is extremely valuable for further refinement of mode of action recommendations. According to the most recent IRIS timeline, the target date for the hexavalent chromium Public Comment Draft is late 2020.

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The SSAB recommends that State base any health protective drinking water goal on the full body of hexavalent chromium toxicity data, examining the modes of action in various in vivo and in vitro studies and applying the low dose-response modeling most appropriate for individual studies and endpoints, then apply a weight of evidence approach to the compiled toxicity data.

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DRAFT observations for consideration in working toward consensus recommendations and identifying where we lack consensus

The SSAB has considered the strengths, limitations and extent of the available studies. Multiple MOAs may be occurring simultaneously including various types of genetic/mutation (and potentially epigenetic) effects as well as cell proliferation. The sequence of events leading to cancer formation is uncertain, i.e., whether mutation proceeds or follows cell proliferation.

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DRAFT observations for consideration in working toward consensus recommendations and identifying where we lack consensus

Data from drinking water studies with rats and mice have been the subject of robust mechanistic toxicity assessments between 2011 and 2019. Mutagenicity data are negative; there were no dose-related increases in K-Ras mutant frequency, micronuclei formation, or change in mitotic or apoptotic indices. Toxicant localization and histological examinations have helped elucidate the mode of action in the rodent drinking water papers. If considering the mouse and rat drinking water exposure papers only, there is strong support for a non-mutagenic mode of action involving chronic wounding of intestinal villi and crypt cell hyperplasia.

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The mixed positive and negative results from laboratory studies via non-inhalation exposures, coupled with clear evidence in humans that Cr+6 via inhalation is mutagenic and carcinogenic, provide sufficient evidence to conclude a mutagenic mode of action is potentially operative for Cr+6 exposures via drinking water.

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Though data gaps and uncertainties remain, it is prudent to conclude that Cr+6 via drinking water exposure may cause mutational changes that proceed cell proliferation, supporting a linear no-threshold dose-response relationship.

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There is little evidence that would support the default assumption of a genotoxic mode of carcinogenic action for Cr(VI) exposures via drinking water.

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