Oral Carcinogenicity of Hexavalent Chromium

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Introduction

- Similar to other sciences, toxicology continues to evolve
- New toxicological data affects:
  - risk-based approaches
  - standards/guidelines
- Standards assessors and risk assessors should be aware of the continuing evolution of toxicological data

Inhalation Exposures to Hexavalent Chromium

- Hexavalent chromium has long been treated as an inhalation carcinogen by agencies that include:
  - Health Canada
  - US Environmental Protection Agency (US EPA)
  - World Health Organization (WHO)

Inhalation Exposures to Hexavalent Chromium

- Based on increased lung cancer incidences in workers, unit risk factors developed by these agencies for addressing air quality include:
  - Health Canada: 0.076 $(ug/m^3)^{-1}$
  - US EPA: 0.012 $(ug/m^3)^{-1}$
  - WHO: 0.040 $(ug/m^3)^{-1}$

Oral Exposures to Hexavalent Chromium

- At the current time, no major agency (HC, US EPA or WHO) considers hexavalent chromium to be carcinogenic via the oral route
  - Years ago, California EPA did consider hexavalent chromium to be an oral carcinogen but revoked that classification

Oral Exposures to Hexavalent Chromium

- In 2008, NTP released a hexavalent chromium drinking water study that showed:
  - Dose dependent in increased incidences of rare neoplasms of the oral cavity in male and female rats
  - Dose-dependent increased incidences of small intestine tumours in male and female mice
- Authors and the technical reports review subcommittee considered this to be clear evidence of oral carcinogenic activity in rats and mice of both genders

Oral Exposures to Hexavalent Chromium

- At the current time, no major health agency has formally adopted the NTP (2008) data to develop a toxicity reference value
  - But it is likely just a matter of time (NTP studies are well regarded as the gold standard in toxicity testing)

NTP (2008): Summary of Mice Data - Males

Lesion	Dose Group				
	0 mg/L	14 mg/L	29 mg/L	86 mg/L	260 mg/L
Small Intestine Adenoma	1/50	1/50	1/50	5/50	17/50
Small Intestine Carcinoma	0/50	2/50	1/50	3/50	5/50
Combined	1/50	3/50	2/50	7/50	20/50

NTP (2008): Summary of Mice Data - Females

Lesion	Dose Group				
	0 mg/L	**14 mg/L**	**29 mg/L**	**86 mg/L**	**260 mg/L**
Small Intestine Adenoma	0/50	1/50	2/50	15/50	16/50
Small Intestine Carcinoma	1/50	0/50	2/50	3/50	7/50
Combined	1/50	1/50	4/50	17/50	22/50

Other Trends in Chromium Assessment

- No major health agency considers trivalent chromium to be carcinogenic
- Ratio of trivalent to hexavalent chromium is a sensitive parameter when interpreting results for total chromium
  - Past use of 6:1 ratio should be re-evaluated (may be overly strict)

Conclusions

- A revised approach to addressing hexavalent chromium exposures may be required which may affect:
  - Soil quality standards/guidelines
  - Risk assessment