Essential Metals - some problematical issues in risk assessment

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WHO, 2002 Monograph (Principles and methods for the assessment of risks from trace elements)

***Essential for Human Health*:**

copper, zinc, iron, chromium, molybdenum, selenium, cobalt and iodine

***Probably Essential for Human Health*:**

silicon, manganese, nickel, boron and vanadium

Carcinogenicity (1)

- Many risk assessment based on non-threshold extrapolations do not allow for normal body defence systems (e.g. Cr VI)
- Inhaled Cr VI can be reduced (detoxified) to Cr III to a measurable degree but not allowed for in linear risk assessment of cancer risks

Carcinogenicity (2)

- Speciation is a problem for target-organ concentrations as well as perhaps carcinogenic action (nickel and vanadium).
- For Cr it seems a clear valency distinction but not for vanadium compounds.
- Read-across for carcinogenicity depends on good knowledge of mechanisms.
- Missing in many cases.
- Metals carcinogens seem site specific

Carcinogenicity (3)

- Route to route extrapolation (inhaled to oral) usually inappropriate for site-specific toxicity
- Dose-rate dependency may be critical (low-steady state from diet but high bolus effect from inhaled occupational exposures)
- Mechanistic gaps preclude robust risk assessments

Neurotoxicity

- Critical health effect of manganese is neurobehavioural impairment (motor).
- About 30 studies on exposed workers but all vary in methodology with the greatest weakness in exposure assessment.
- Most risk assessments assume a threshold and choose one “best” study to drive exposure/effect to arrive at an OEL.
- This may not be the best use of all the data if the one chosen study is not “typical” for all Mn-related work scenarios.

Selective use of the dataset

"Reviews of toxicity ignore the nutritional literature" (Craig Boreiko, EMW, 2008)

- *Upside*: it helps "strengthen" the negative nature of any harmful effects, even for marginal changes.
- *Downside*: it may by default, ignore a very useful set of biological and mechanistic data which would enhance any risk assessment

HERAG

- Health risk assessment guidance for metals
- Fact sheet 7 is excellent overview for dealing with essentiality
- www.metalsriskasessment.org