Meaningful Exposure Assessment

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Bioavailability and speciation are relevant to both numerator (exposure) and denominator (TRV or Hazard)

Consideration of bioavailability and speciation is critical for meaningful risk estimation
Ni (as sulfate or oxide or metal)

TRV (based on Ni sulfate)

• Focus on bioavailability today
Current Issues in Bioavailability of Metals and Metalloids

• Bioaccessibility (gastrointestinal, alveolar, and dermal) is being used routinely as a proxy for bioavailability under REACH in Europe.
• In Canada, regulatory acceptance of bioaccessibility is inconsistent. This must change.
• It is important to have open exchange of ideas between stakeholders to “get the science right”.
• Some areas of bioaccessibility science are still under development and aren’t adequately understood
  – e.g. “solubility limitation” and soil:extractant ratios
• Richardson et al. (2006) introduced this concept
  – Bioaccessibility should not be inversely related to soil [metal] (i.e. should not be “solubility limited”)
  – The mass of extracted metal should have a positive slope
  – Large dilutions (up to 10,000:1) are desirable
Bioaccessibility is inversely related to soil [Ni].
- Does this mean the method isn’t valid?
...actually, bioaccessibility is directly related to the amount of H\(^+\) available per µg of Ni. This is expected, as the extractions use a fixed amount of H\(^+\).
What Conditions Should be Used for Bioaccessibility Extractions?

- Stomach acid contains H⁺ ions at 150 mmol/L
- Basal acid output ≈ 3 mmol/h (20 mL/h)
- Peak acid output ≈ 30 mmol/h (200 mL/h)
- 0.1g soil ingested during BAO ≈ H⁺:soil of 30 mmol/g
- 0.1g soil ingested during PAO ≈ H⁺:soil of 300 mmol/g

- H⁺:soil ratios of 30-300 mmol/g represent a reasonable range of conditions for GI bioaccessibility
- These conditions are expected to exceed the ability of the GI tract to solubilize some metals
- Speciation is important
Bioaccessibility SHOULD be “solubility limited”. On a mass basis, the slopes SHOULD be zero.

- this is what is expected in the GIT!
What about dilution effects?

Trend in Leached Metal in NIST 2710 as a Function of Leachate: Soil ratio (from Table 1 of Hamel et al. (1998))
Trend in Leached Metal in Jersey City Soil as a Function of Leachate: Soil ratio
(from Table 2 of Hamel et al. (1998))
• Importance of extract/soil ratios is overstated (issue is whether $H^+$:soil ratio is appropriate)

• Dilution of soil 10,000:1 with extractant is overstated (the issue is whether the $H^+$:soil ratio is appropriate)

• Other issues (e.g. appropriate particle size to use; standardization of methods, etc.) require further research and discussion
How Can We Use Bioaccessibility Meaningfully?
### Potential Application of Site-Specific Bioaccessibility &/or Bioavailability in Risk Assessments

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<th>Tier</th>
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<tr>
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Ni

- EPA RfD derived from Ambrose et al. 1976 is based on a NOAEL of 100 mg Ni/kg food
- To correct for bioaccessibility from site soil relative to the reference study...

1) Determine bioaccessibility for site soil
2) Determine bioaccessibility for rat chow spiked with Ni at same level as reference study
3) Calculate the Tier 1 Correction (RBAF)
   \[ \text{RBAF} = \frac{\text{Bioac}_{\text{test}}}{\text{Bioac}_{\text{ref}}} \]
To Summarize...

- Further refinements (e.g. linking bioaccessibility and bioavailability) will require validation via animal models (Tier 2)
- Requirement for validation of a Tier 2 approach should not hinder the more conservative Tier 1 application of relative bioaccessibility for ingestion of chemical from incidental soil ingestion.
- Tier 1 approach is parsimonious and precautionary but does not give as large a correction as would be the case with bioavailability.
- Meaningful exposure assessment tools such as bioaccessibility must be incorporated into the Canadian regulatory regimes.