

Meaningful Exposure Assessment

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$$\frac{\textit{Exposure}}{\textit{TRV}}$$

- 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)

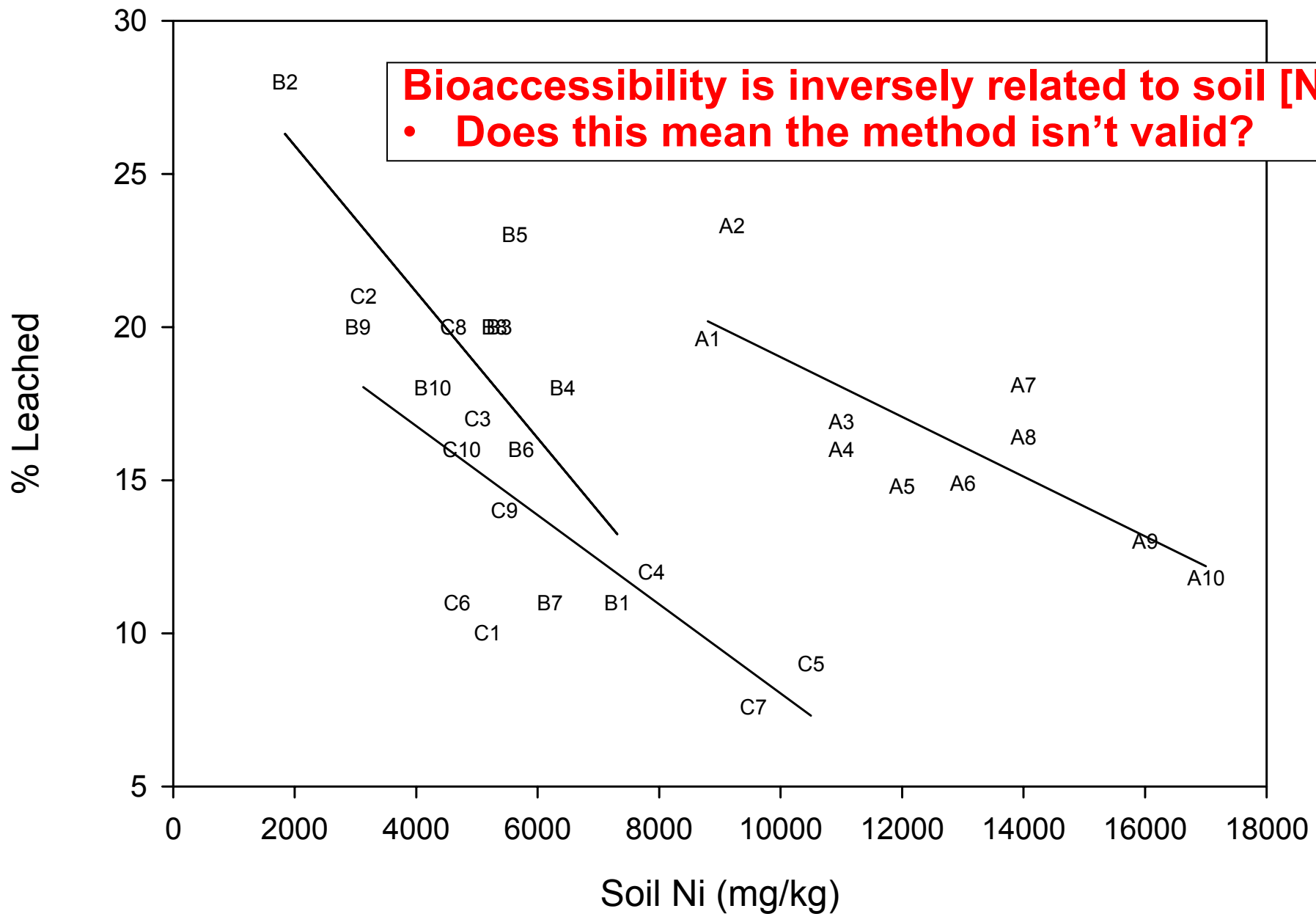
- Focus on bioavailability today

Current Issues in Bioavailability of Metals and Metalloids

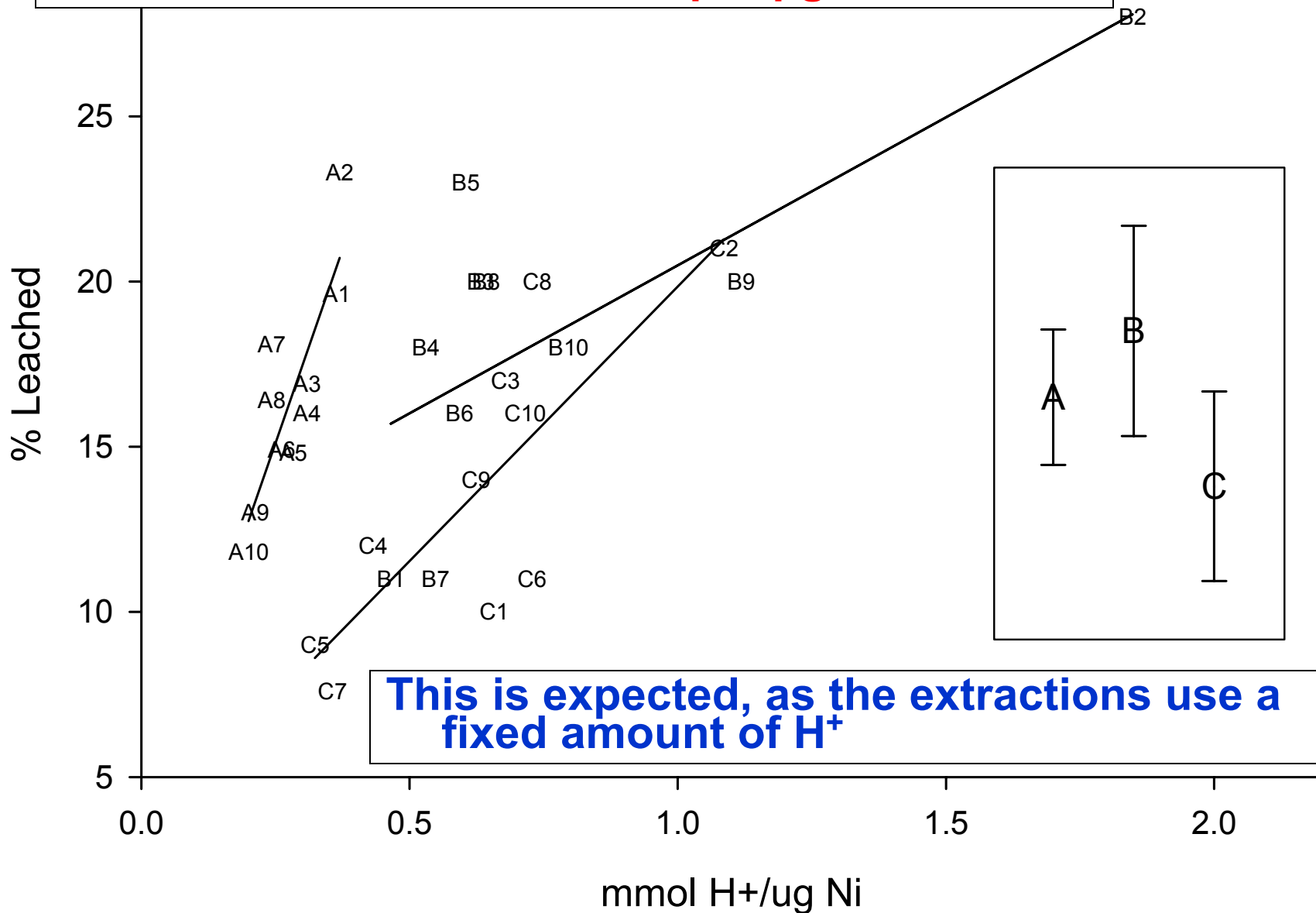


- Bioaccessibility (gastrointestinal, alveolar, and dermal) is being used routinely as a proxy for bioavailability under REACH in Europe
- In Canada, regulatory acceptance of bioaccessibility is inconsistent. This must change.
- It is important to have open exchange of ideas between stakeholders to “get 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



...actually, bioaccessibility is directly related to the amount of H⁺ available per μg of Ni

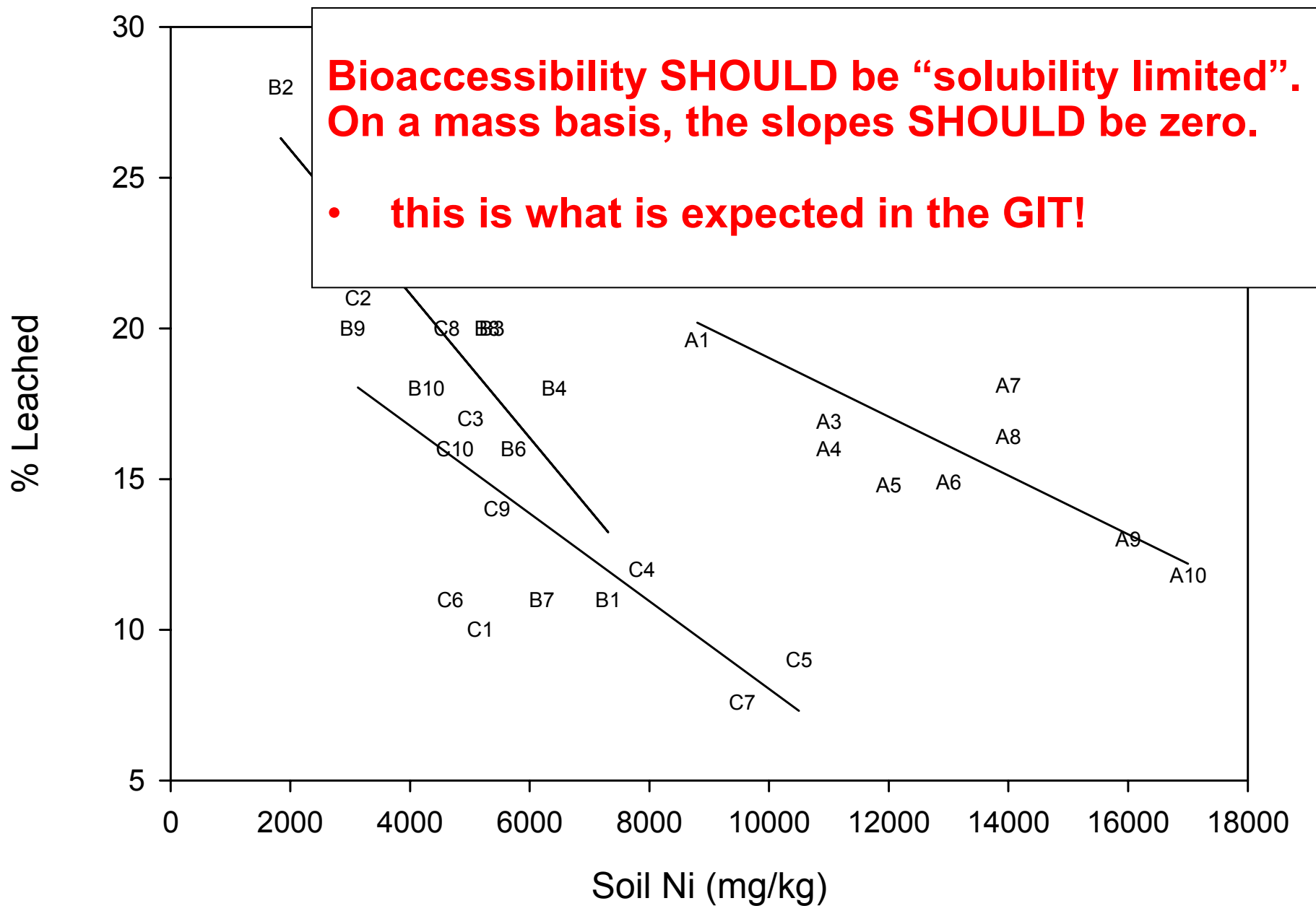


This is expected, as the extractions use a fixed amount of H⁺

What Conditions Should be Used for Bioaccessibility Extractions?

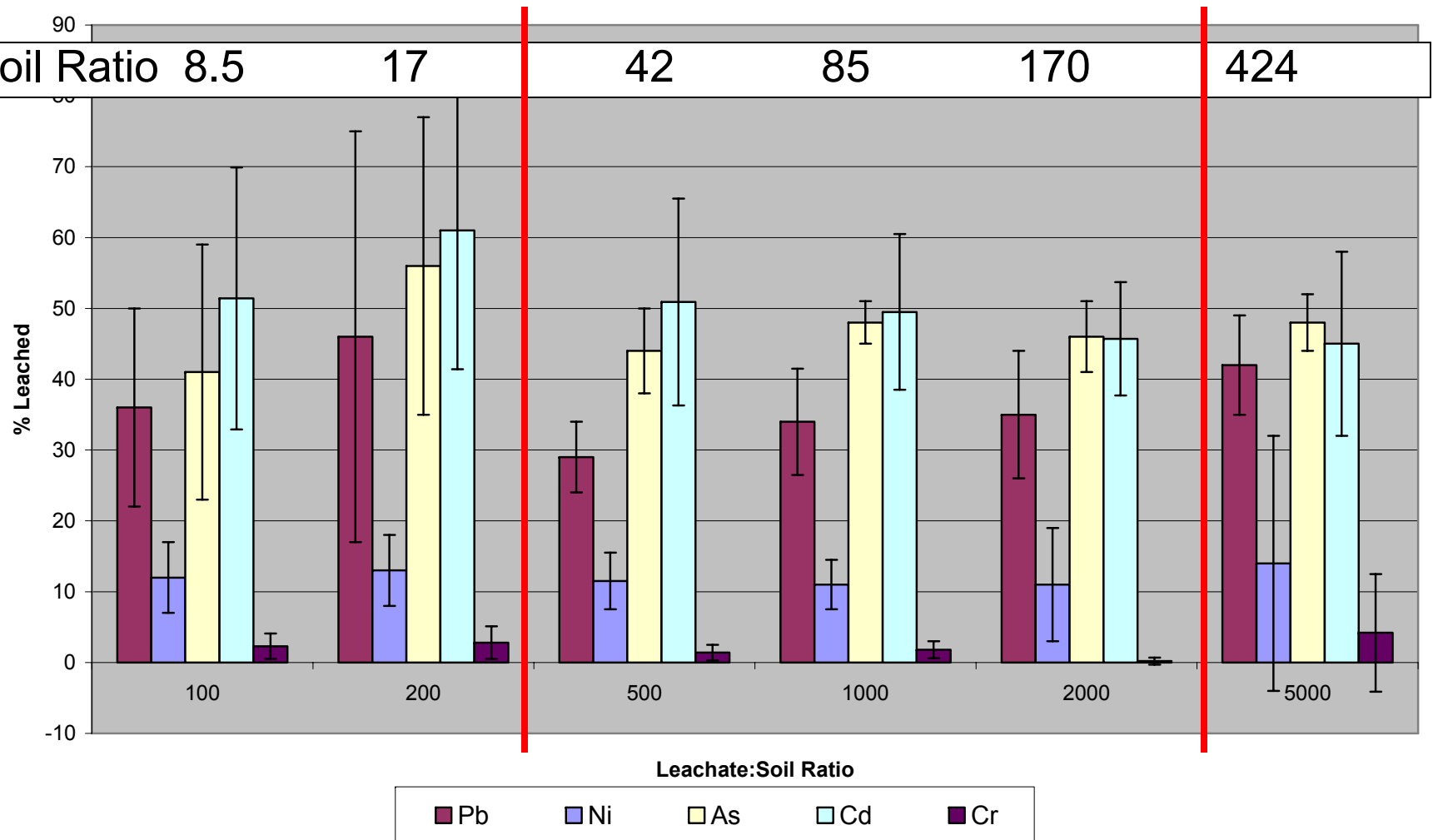


- Stomach acid contains H^+ ions at 150 mmol/L
- Basal acid output \approx 3 mmol/h (20 mL/h)
- Peak acid output \approx 30 mmol/h (200mL/h)
- 0.1g soil ingested during BAO \approx H^+ :soil of 30 mmol/g
- 0.1g soil ingested during PAO \approx H^+ :soil of 300 mmol/g
- **H^+ :soil ratios of 30-300 mmol/g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

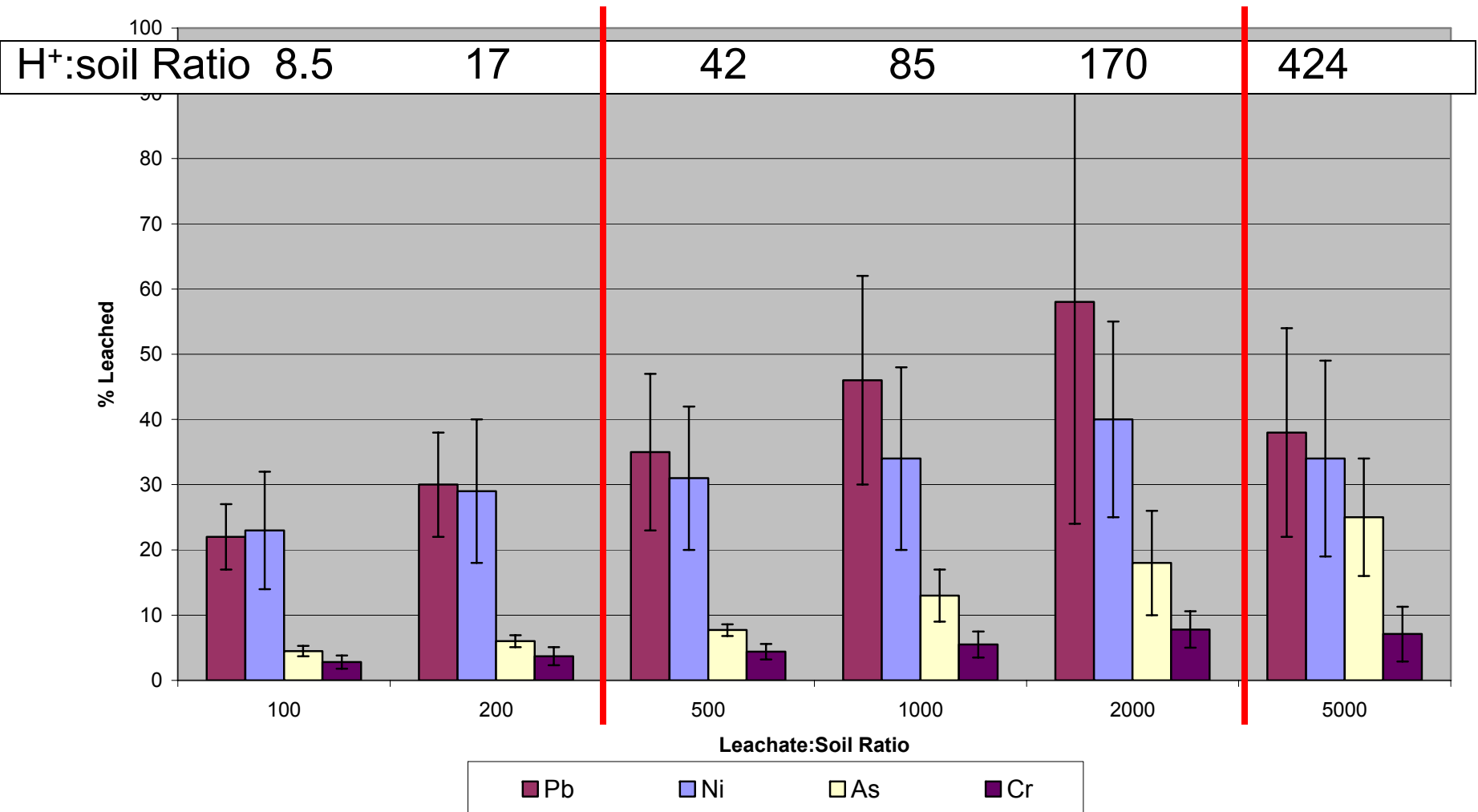


What about dilution effects?

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?

Bioaccessibility

– solubilization

Bioavailability

– solubilization
& absorption

Potential Application of Site-Specific Bioaccessibility &/or Bioavailability in Risk Assessments...

<u>Application Factor</u>	<u>Tier</u>	<u>Validation Req'd?</u>
$\text{Bioav}_{\text{test}} / \text{Bioav}_{\text{ref}}$	2	Yes
$\text{Bioac}_{\text{test}} / \text{Bioav}_{\text{test}}$	2	Yes
$\text{Bioac}_{\text{test}} / \text{Bioac}_{\text{ref}}$	1	No/limited

Application of Tier 1 Approach



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)
$$= \text{Bioac}_{\text{test}} / \text{Bioac}_{\text{ref}}$$

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.