Meaningful Exposure Assessment

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

- 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

$$\frac{Ni\,(as\ sulfate\ or\ oxide\ or\ metal)}{TRV\,(based\ on\ Ni\ sulfate)}$$

- Focus on bioavailability today

Current Issues in Bioavailability of Metals and Metalloids

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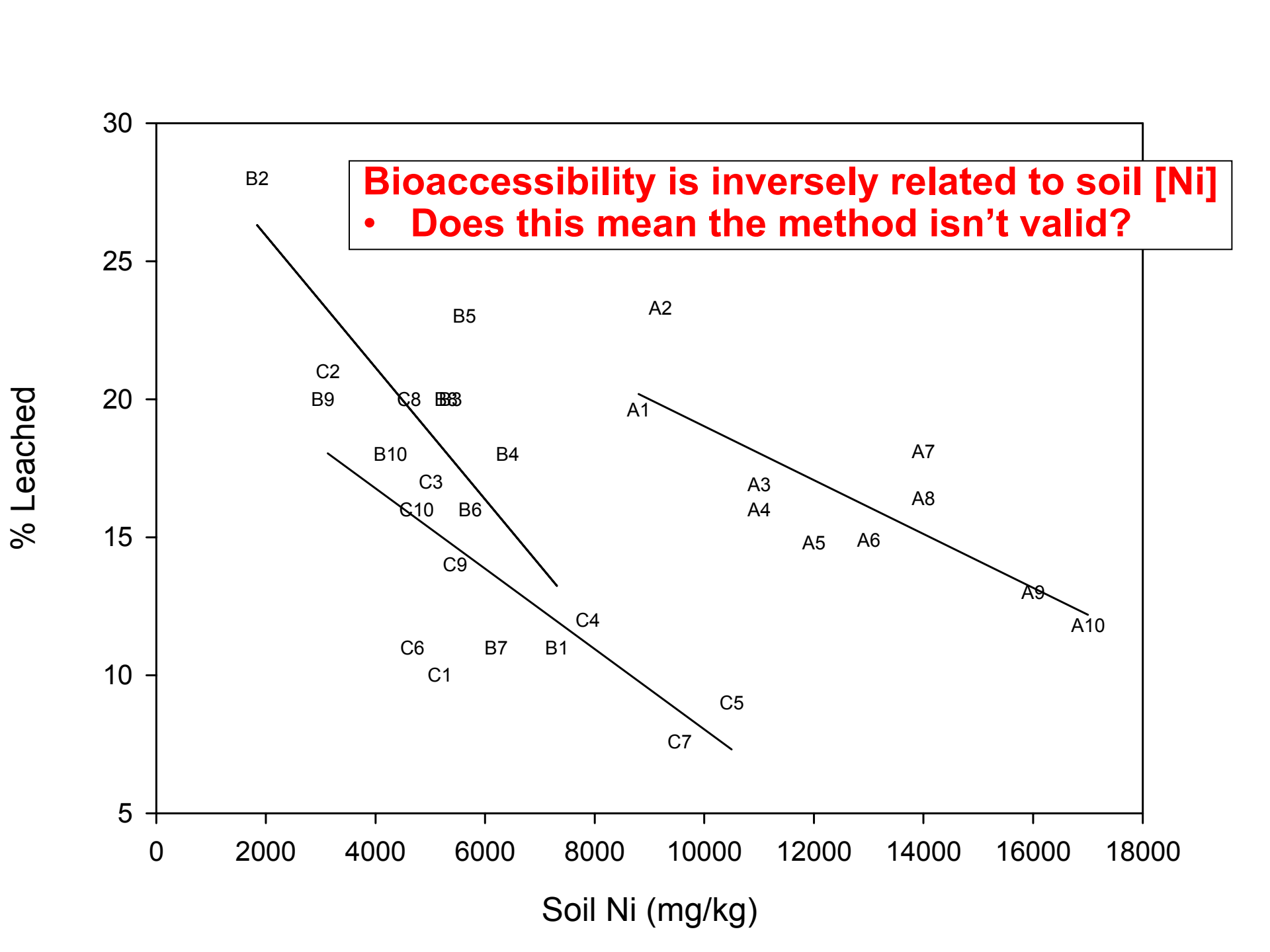
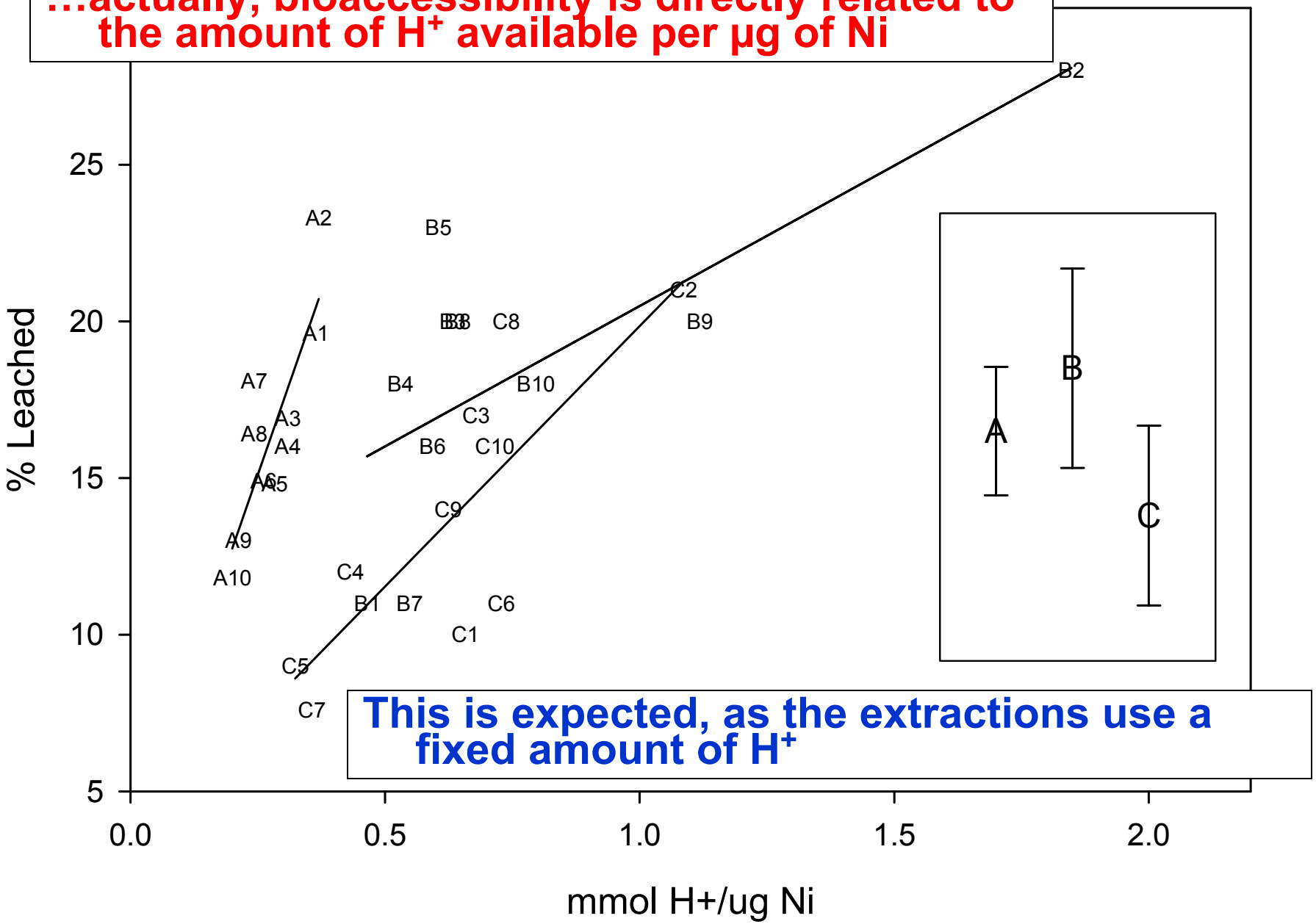
- Bioaccessibility (gastrointestinal, alveolar, and dermal) is being used routinely as a proxy for bioavailability under REACH in Europe
- In Canada, regulatory acceptance of bioaccessibility is inconsistent. This must change.
- It is important to have open exchange of ideas between stakeholders to “get 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?
% Leached
Soil Ni (mg/kg)
30
25
20
15
10
5
0
2000
4000
6000
8000
10000
12000
14000
16000
18000
B2
B5
A2
C2
B9
C8
A1
B10
B4
A7
C3
A3
A8
C10
B6
A4
A5
A6
C9
A9
C4
A10
C6
B7
B1
C1
C5
C7

…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?

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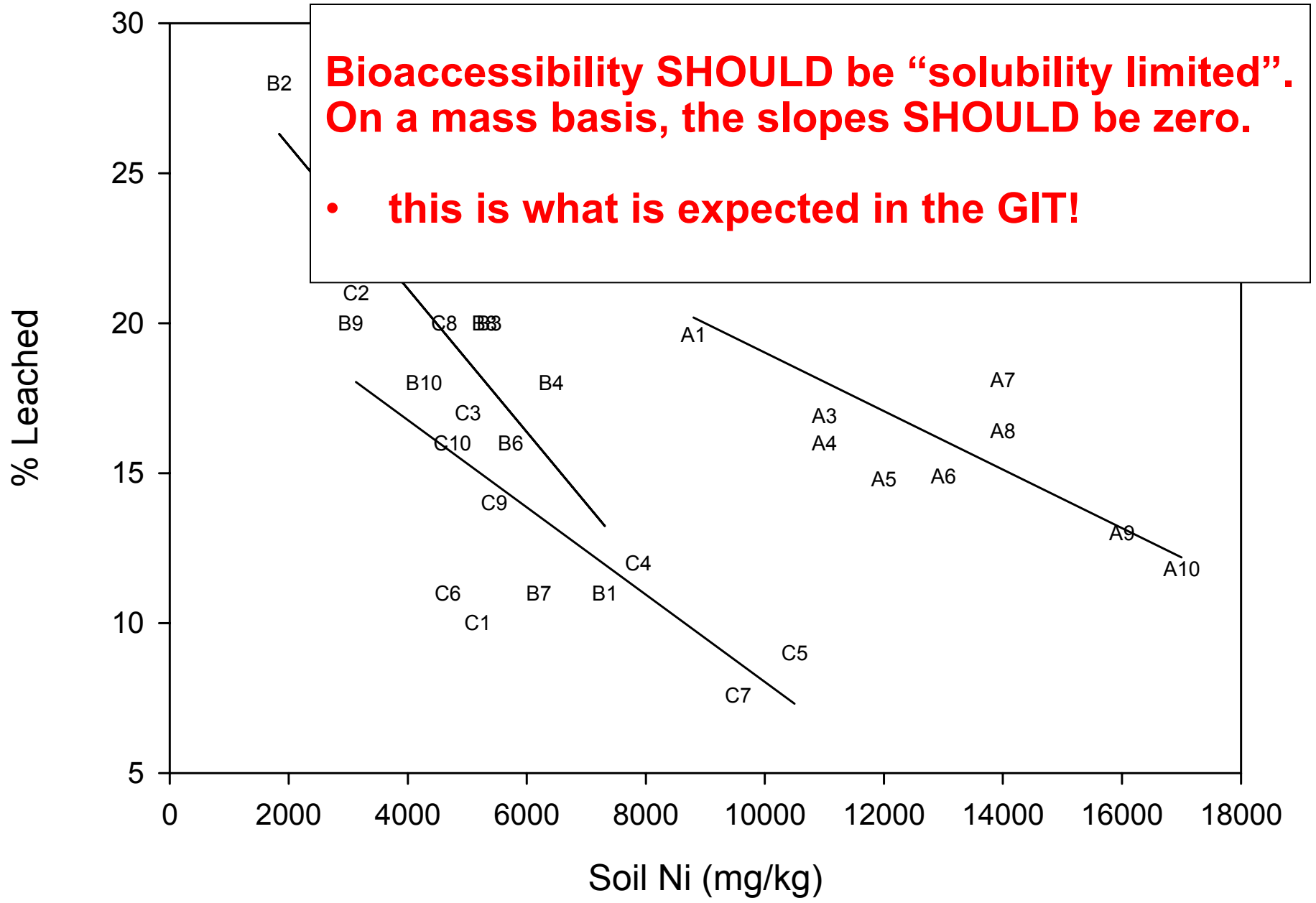
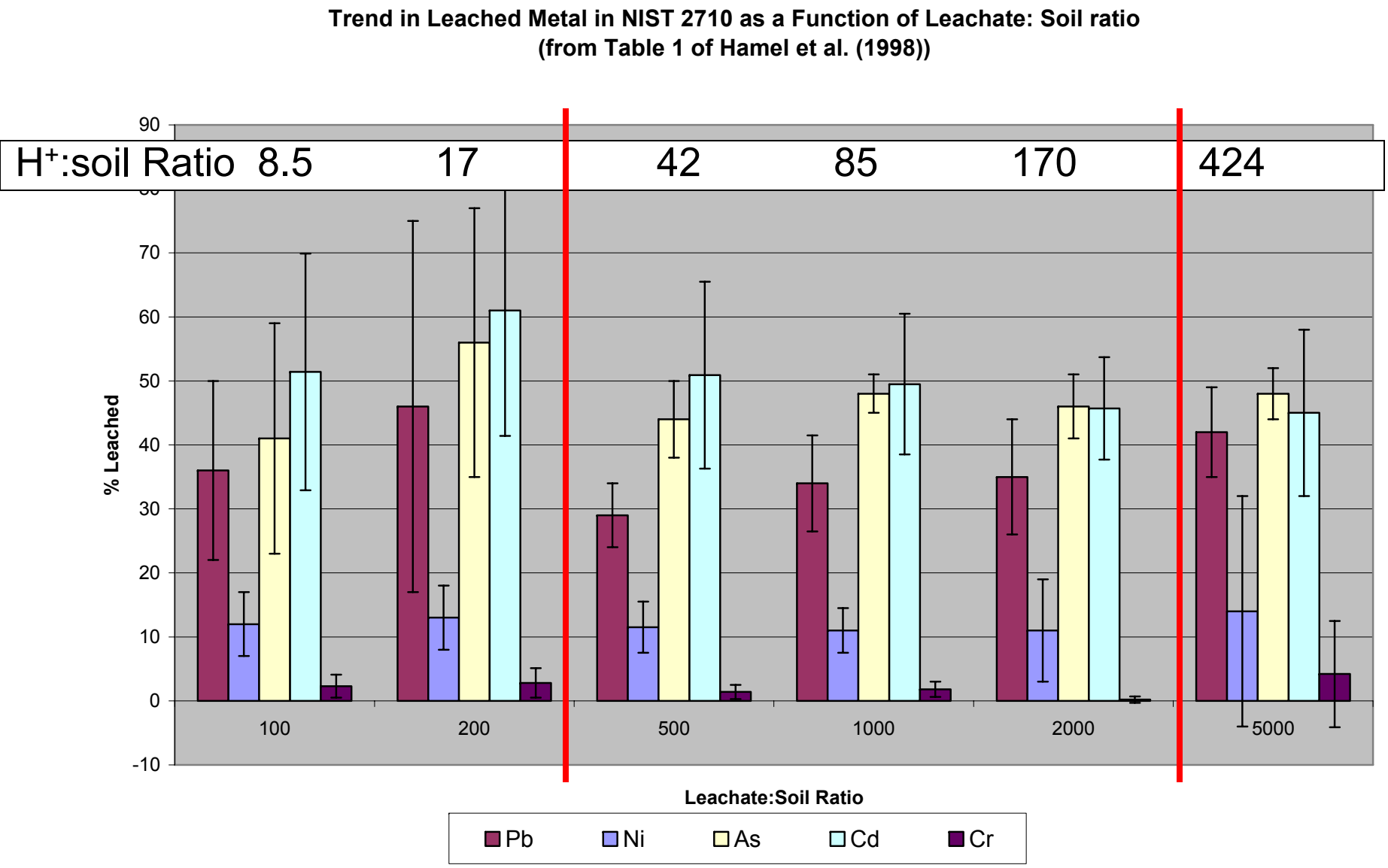
- Stomach acid contains H^+ ions at 150 mmol/L
- Basal acid output ≈ 3 mmol/h (20 mL/h)
- Peak acid output ≈ 30 mmol/h (200mL/h)
- 0.1g soil ingested during BAO ≈ H^+:soil of 30 mmol/g
- 0.1g soil ingested during PAO ≈ H^+:soil of 300 mmol/g

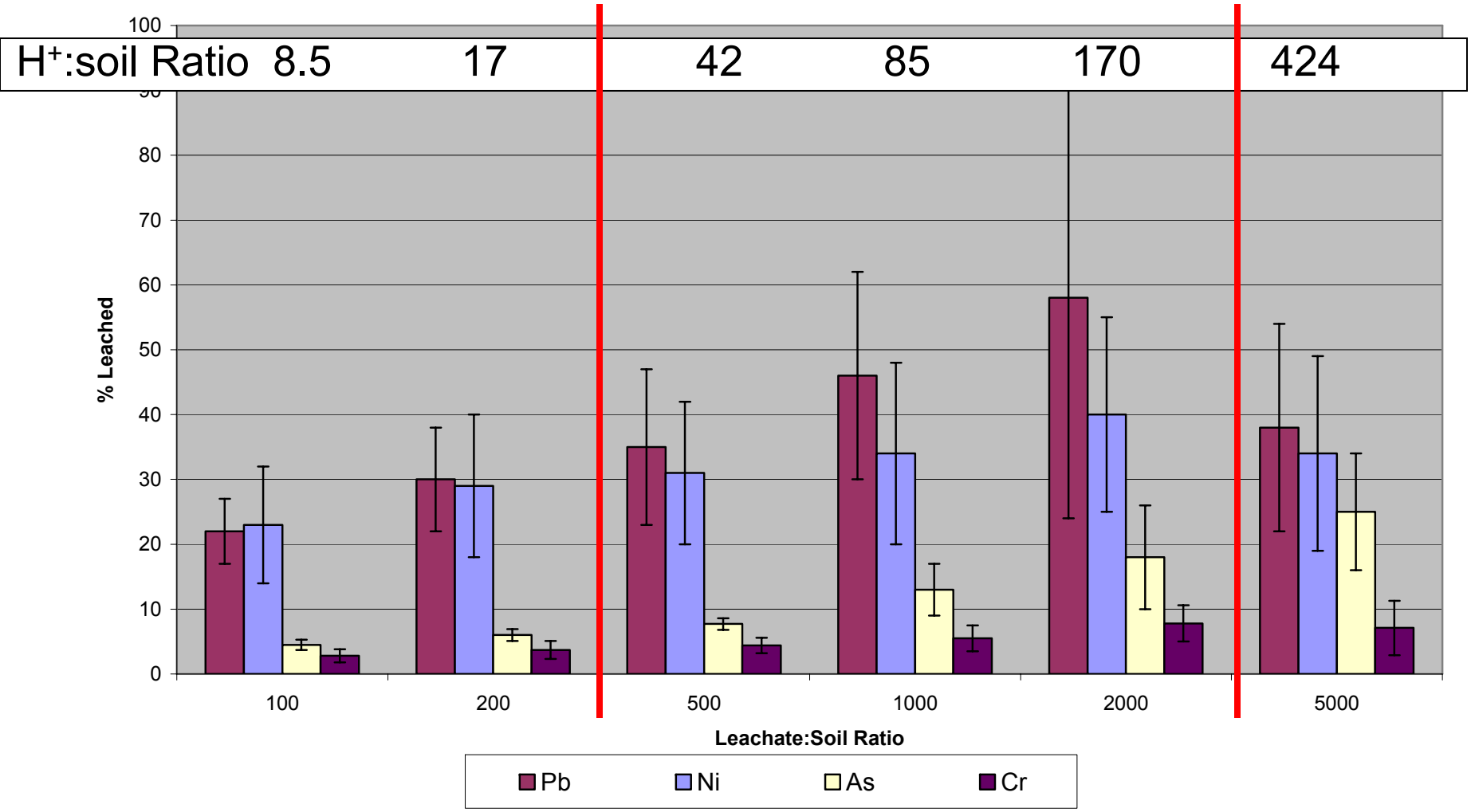
- **H^+:soil ratios of 30-300 mmol/g represent a reasonable range of conditions for GI bioaccessibility**
- **These conditions are expected to exceed the ability of the GI tract to solubilize some metals**
- **Speciation is important**


Bioaccessibility SHOULD be “solubility limited”.
On a mass basis, the slopes SHOULD be zero.
• this is what is expected in the GIT!
% Leached
Soil Ni (mg/kg)
30
25
20
15
10
5
0
2000
4000
6000
8000
10000
12000
14000
16000
18000
B2
C2
B9
C8
B10
B4
C3
C10
B6
C9
C4
C6
B7
B1
C1
C5
C7
A1
A7
A3
A8
A4
A5
A6
A9
A10

What about dilution effects?



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…

Application Factor	Tier	Validation Req'd?
$Bioav_{test}$ / $Bioav_{ref}$	2	Yes
$Bioac_{test}$ / $Bioav_{test}$	2	Yes
$Bioac_{test}$ / $Bioac_{ref}$	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)
   = $Bioac_{test}$ / $Bioac_{ref}$

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.