Uncertainty in soil Bioaccessibility Measurements – where do we stand?

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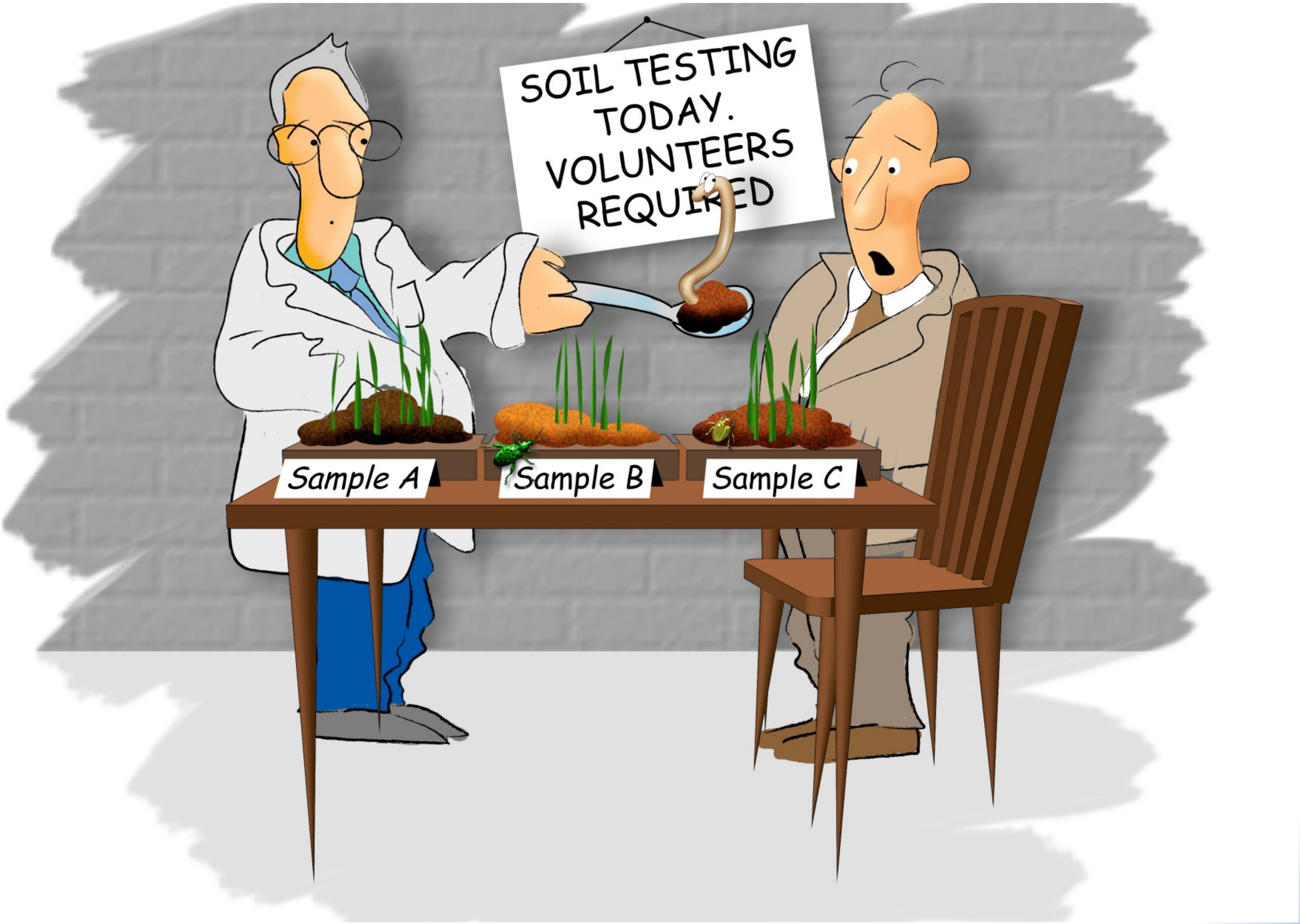
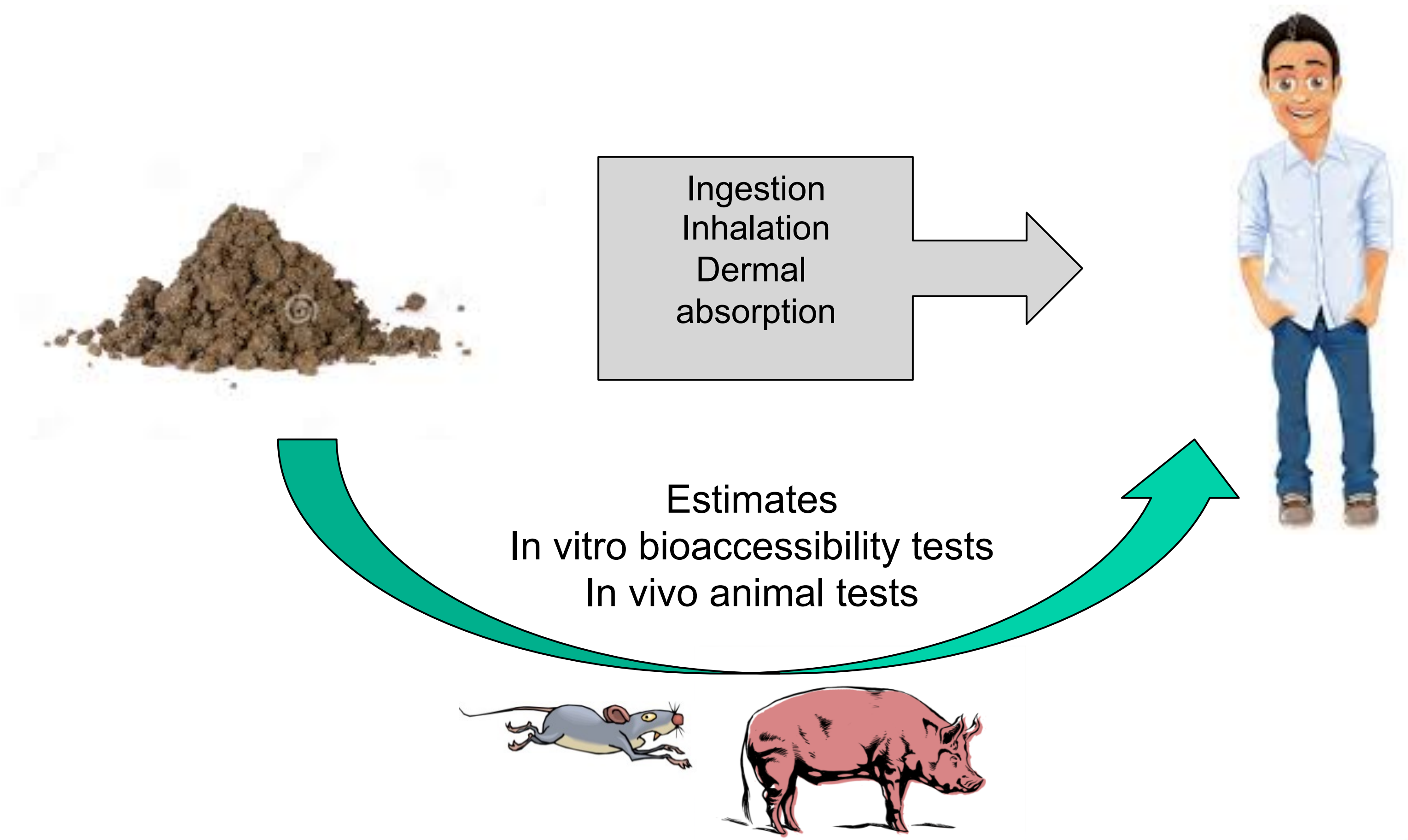
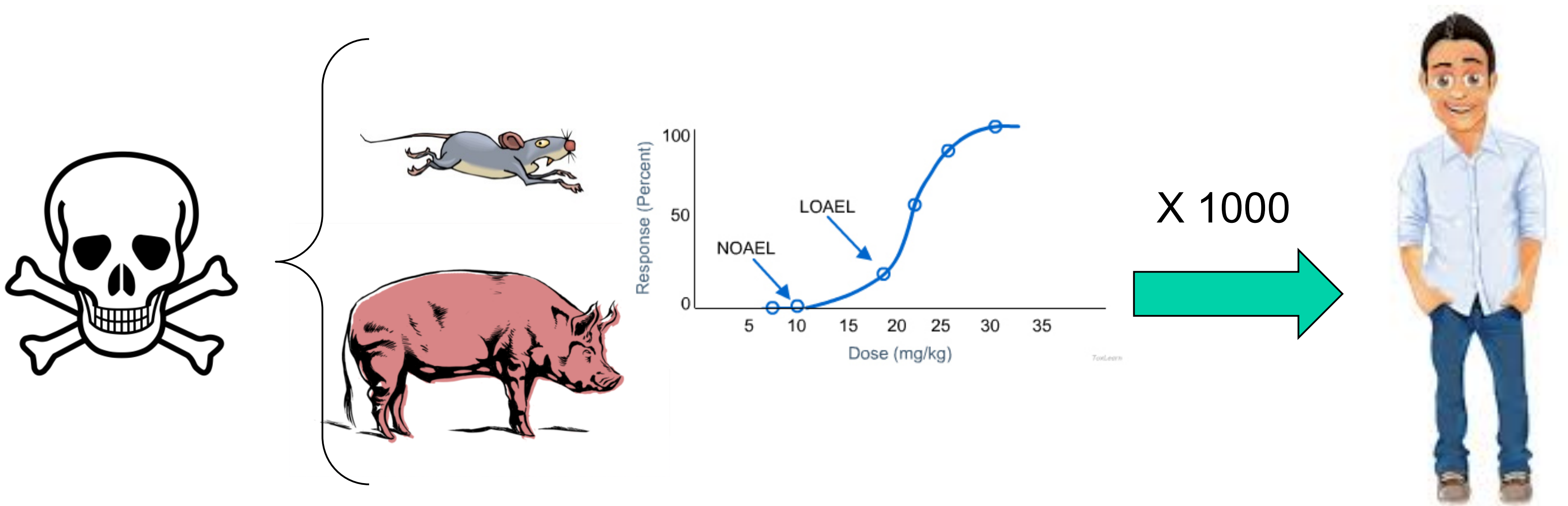

SOIL TESTING TODAY. VOLUNTEERS REQUIRED
Sample A
Sample B
Sample C

Exposure


Ingestion
Inhalation
Dermal
absorption
Estimates
In vitro bioaccessibility tests
In vivo animal tests

Toxicology



Response (Percent)
100
50
0
NOAEL
LOAEL
5
10
15
20
25
30
35
Dose (mg/kg)
X 1000

Misuses of bioaccessibility based estimates (after Nathanail (2009))

Insufficient samples	**A minimum of 10 samples per averaging area is typical to gain a good appreciation of the variation**
Use of peer review data rather than site specific values	**There is not necessarily a relationship between literature values and the site you are investigating**
Application of e.g. UBM to non ingestion pathways	**The UBM seeks only to simulate direct oral ingestion**
Application to other substances	**Inappropriate appreciation of substance specific bioaccessibility**

Misuses of bioaccessibility based estimates (continued)

Lack of evidence	Bioaccessibility results may not be compatible with geological history, geochemistry etc.,
Mixing samples from different soil/ ground types	Bioaccessibility varies with medium
Poorly documented test procedure	Bioaccessibility tests are empirical and interpretation should be based on the specific method applied
Analysis of samples not representative of concentrations of concern	Bioaccessibility varies with total concentration but the relationship is not necessarily either linear or positive

Misuses of bioaccessibility based estimates (continued)

Inappropriate use of statistics	**Statistical summaries of bioaccessibility may result in discordant matching of bioaccessibility estimate and total concentration**
Application of summary (average) or single values to a dataset	**The relationship between total and bioaccessible concentrations is not necessarily linear**
Use of wrong test	**Results are not relevant to the risk estimation**
Lack of details in reports	**Reviewer cannot evaluate the robustness of the risk estimate and the compliance of the risk evaluation with the specific legal context**

What is the biggest misuse of all ??????????

NOT USING BIOACCESSIBILITY AT ALL

Other considerations….

- For use in Risk Assessment
  - Bioaccessibility data may be used to refine the level of estimated risk.
  - But…..misuse could be used to demonstrate negligence.

- Land use practices can change the biochemical conditions in soil
  - This can increase/reduce bioaccessibility.
    - e.g. liming low pH soils, adding phosphate fertiliser or increasing the soil organic matter (common gardening practices) are all likely to have an effect on the mobility of lead and arsenic. Changes can increase or reduce the bioavailability

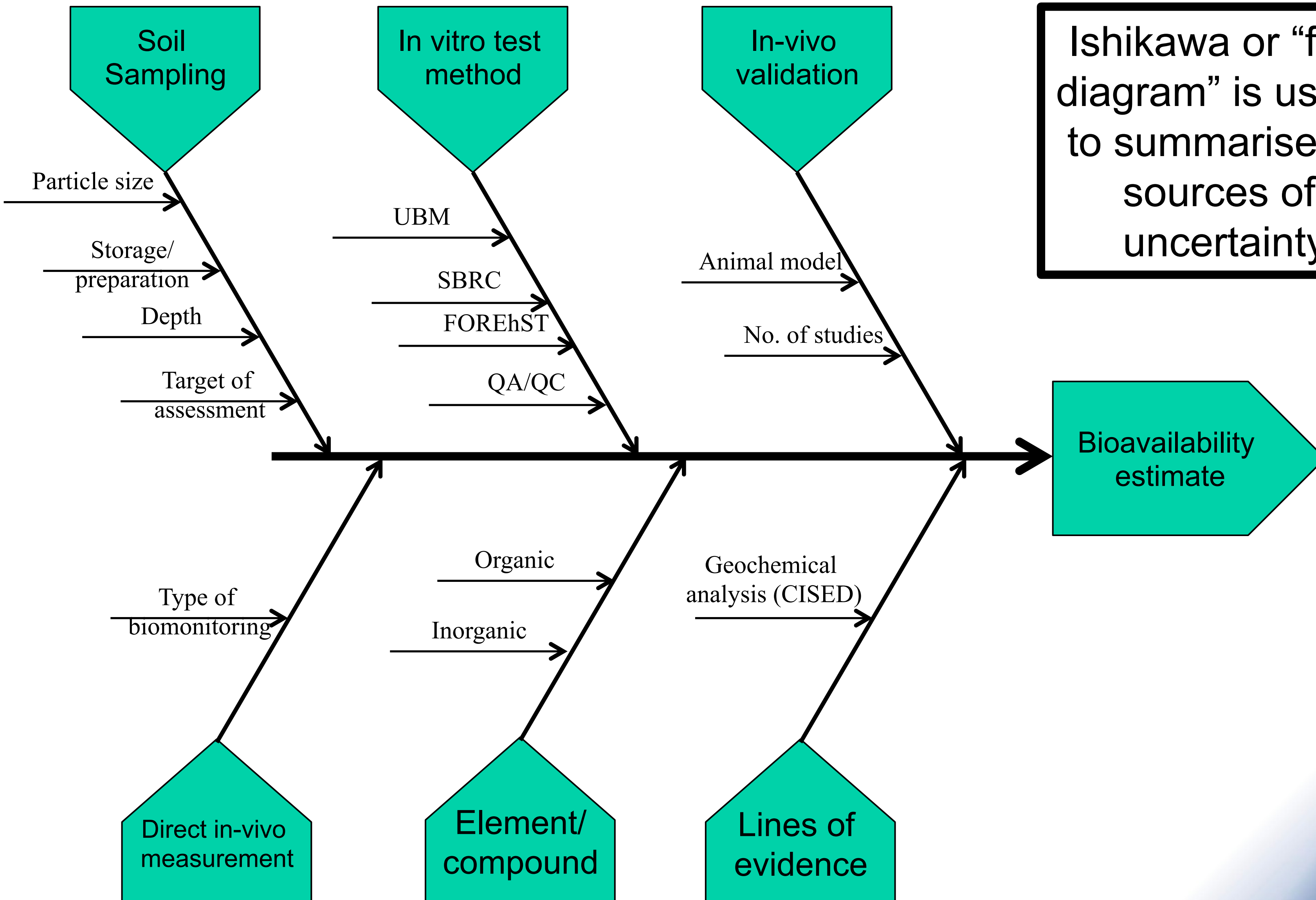
Types of Uncertainty

Aleatory Variability and Epistemic Uncertainty

- **Aleatory** variability is the natural randomness in a process. The randomness is parameterized by the probability density function.
- **Epistemic** uncertainty is the scientific uncertainty in the model of the process. It is due to limited data and knowledge. Uncertainty is modelled by alternative probability density functions. In addition, there is epistemic uncertainty in parameters that are not random by have only a single correct (but unknown) value.

Benchmark Criteria

- It should be physiologically based, mimicking the human GI physico-chemical environment in the stomach and small intestine. This should not only help to obtain good agreement with *in vivo* data but would also enhance public understanding of the test;
- It should represent a conservative case;
- There should be one set of conditions for all potentially harmful elements (PHE) being studied;
- It must be demonstrated that the test is a good analogue of *in vivo* conditions; and
- The test must be able to produce repeatable and reproducible results within and between testing laboratories.



Ishikawa or "fish diagram" is useful to summarise all sources of uncertainty

Environmental Science & Technology

Article

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In Vivo Validation of the Unified BARGE Method to Assess the Bioaccessibility of Arsenic, Antimony, Cadmium, and Lead in Soils

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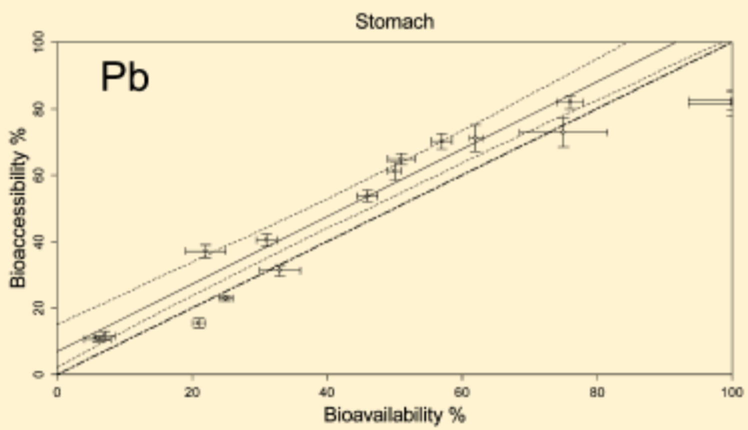
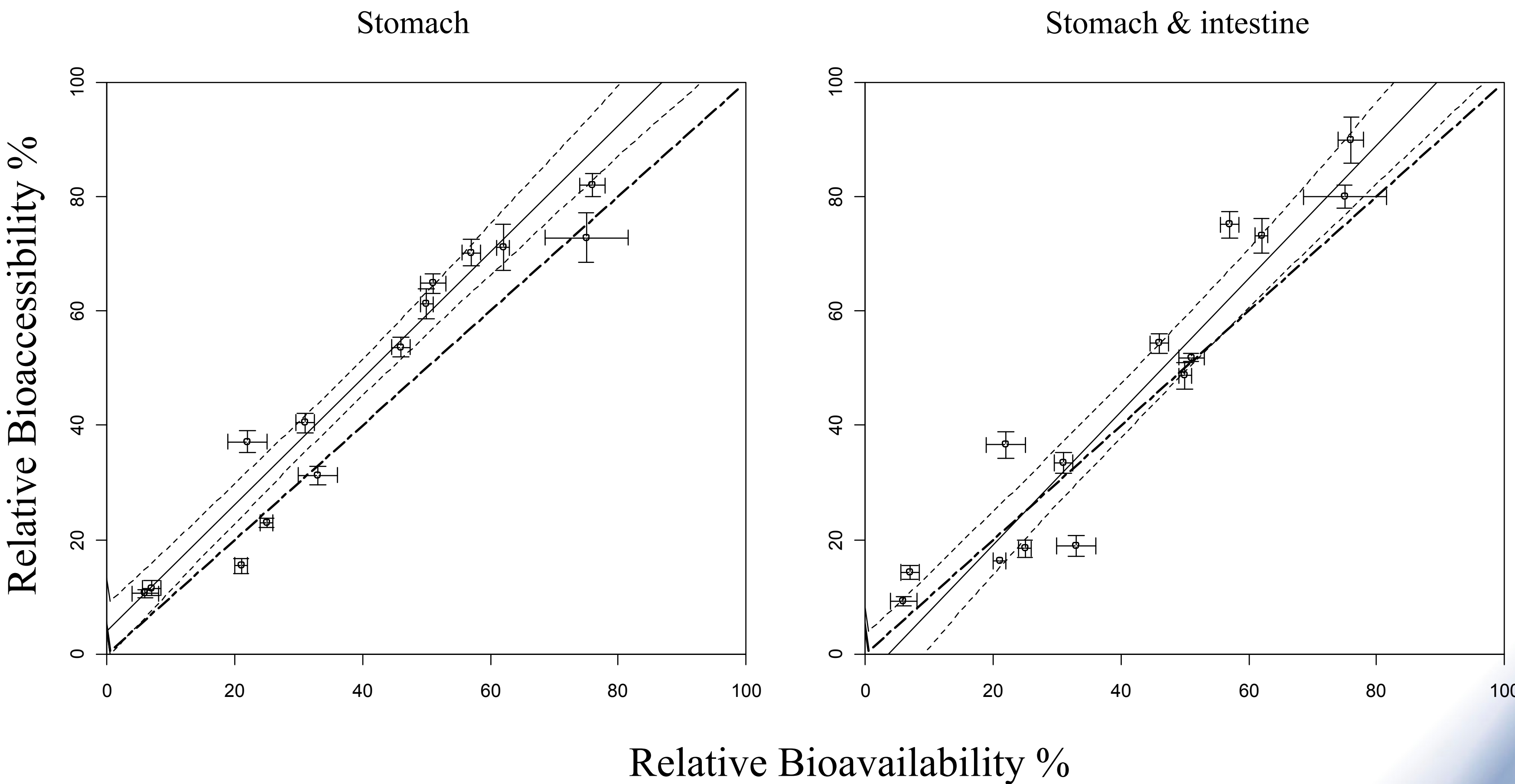
Supporting Information



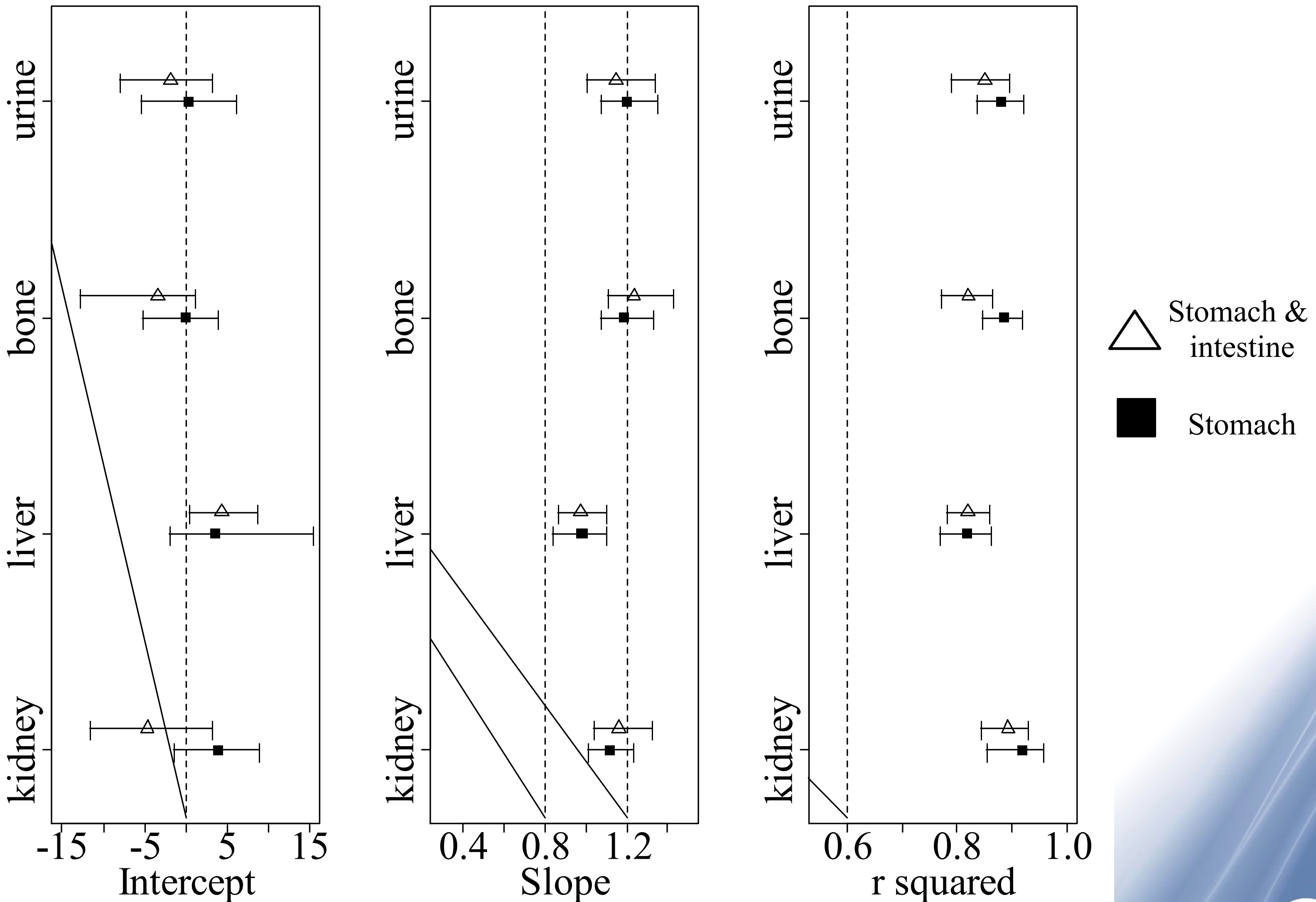
ABSTRACT: The relative bioavailability of arsenic, antimony, cadmium, and lead for the ingestion pathway was measured in 16 soils contaminated by either smelting or mining activities using a juvenile swine model. The soils contained 18 to 25 000 mg kg^{-1} As, 18 to 60 000 mg kg^{-1} Sb, 20 to 184 mg kg^{-1} Cd, and 1460 to 40 214 mg kg^{-1} Pb. The bioavailability in the soils was measured in kidney, liver, bone, and urine relative to soluble salts of the four elements. The variety of soil types, the total concentrations of the elements, and the range of bioavailabilities found were considered to be suitable for calibrating the in vitro Unified BARGE bioaccessibility method. The bioaccessibility test has been developed by the BioAccessibility Research Group of Europe (BARGE) and is known as the Unified BARGE Method (UBM). The study looked at four end points from the in vivo measurements and two compartments in the in vitro study ("stomach" and "stomach and intestine"). Using benchmark criteria for assessing the "fitness for purpose" of the UBM bioaccessibility data to act as an analogue for bioavailability in risk assessment, the study shows that the UBM met criteria on repeatability (median relative standard deviation value <10%) and the regression statistics (slope 0.8 to 1.2 and r-square > 0.6) for As, Cd, and Pb. The data suggest a small bias in the UBM relative bioaccessibility of As and Pb compared to the relative bioavailability measurements of 3% and 5% respectively. Sb did not meet the criteria due to the small range of bioaccessibility values found in the samples.

Pb - kidney



Stomach
Stomach & intestine
Relative Bioaccessibility %
Relative Bioavailability %
0
20
40
60
80
100

Lead – Regression line descriptive statistics



National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Bioavailability of lead from Dutch made grounds
A validation study

RIVM report 607711015/2014
P.C.E. van Kesteren et al.

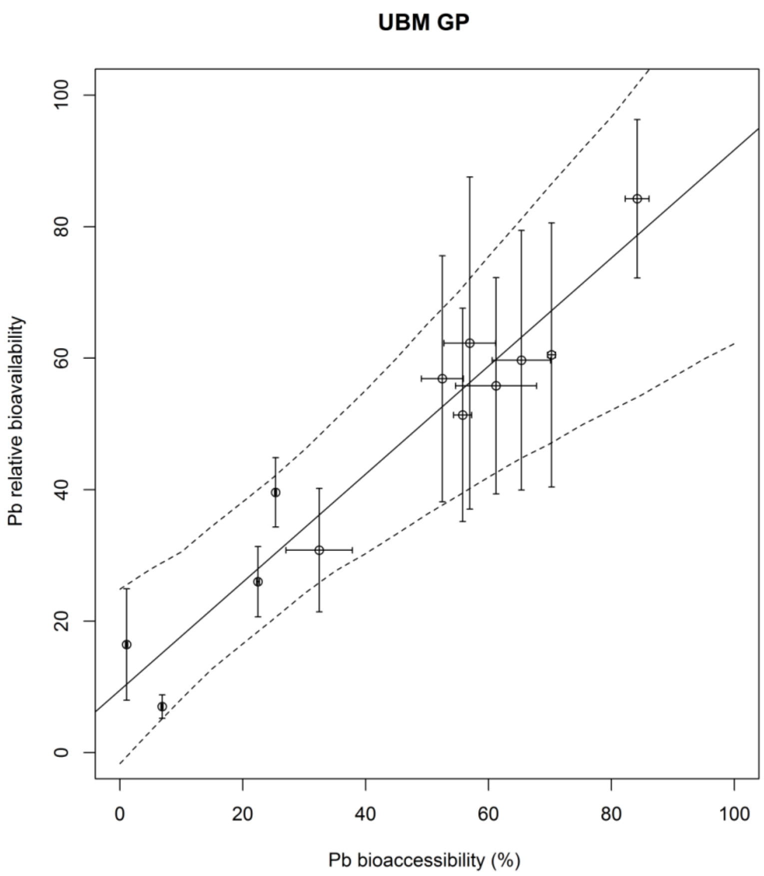
The bioavailability of lead in six soils was estimated using the three models and the results were compared with the results of a bioavailability study conducted on juvenile swine.

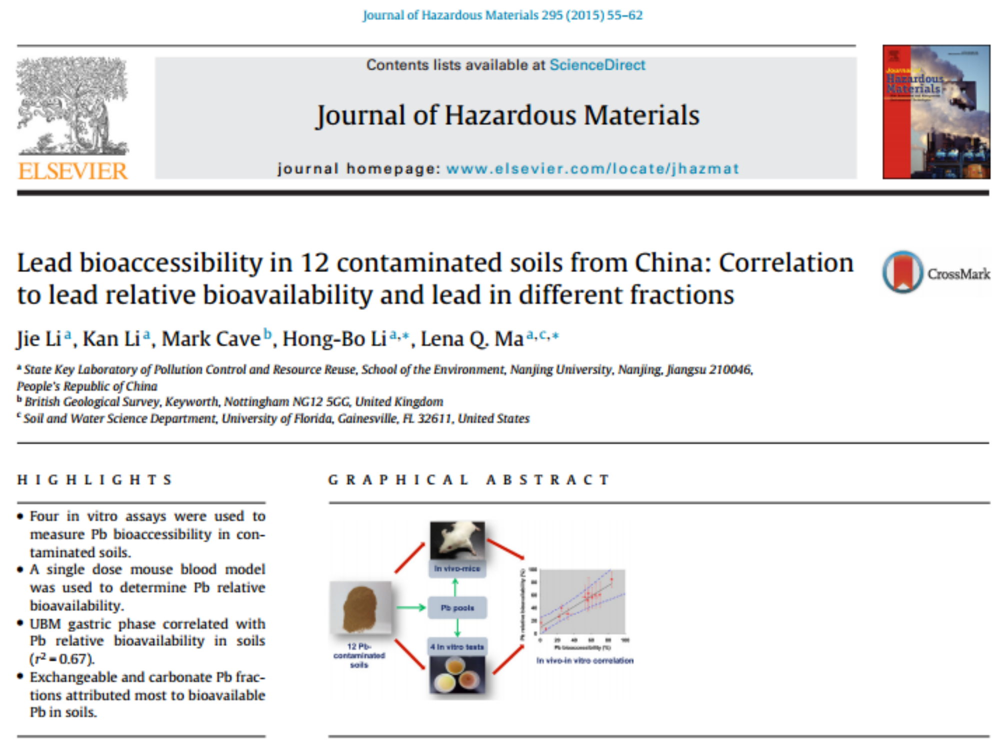
The behavior of lead in the gastrointestinal tract of swine was comparable to that in children.

Both the Unified BARGE model and the Tiny-TIM model show the same pattern as the results of the animal experiments. However, the Tiny-TIM values underestimate the true bioavailability.

The IVD model is only suitable after a correction for calcium content of the soil.

In-vivo mouse study in China





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Lead bioaccessibility in 12 contaminated soils from China: Correlation to lead relative bioavailability and lead in different fractions

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HIGHLIGHTS

- Four in vitro assays were used to measure Pb bioaccessibility in contaminated soils.
- A single dose mouse blood model was used to determine Pb relative bioavailability.
- UBM gastric phase correlated with Pb relative bioavailability in soils ($r^2 = 0.67$).
- Exchangeable and carbonate Pb fractions attributed most to bioavailable Pb in soils.

GRAPHICAL ABSTRACT

BGS Bioaccessibility Guidance Soil

Bulk soil sample collected

Crushed and dried sample is loaded into the mixing drum

Sample is homogenised in the mixing drum for 10 days

Homogenised sample is split into 50 g batches prior to homogeneity testing and certification

Microchemical Journal

Volume 123, November 2015, Pages 131–138

Bioaccessibility performance data for fifty-seven elements in guidance material BGS 102

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doi:10.1016/j.microc.2015.06.001

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Highlights

- Broadened scope of Unified Bioaccessibility Method measurements from As, Cd, and Pb
- Performance data categorised for stomach and intestinal phase
- Scope could be expanded for 28 elements given performance criteria.
- 19 elements with further validation effort and new reference materials
- Increased bioaccessibility applications for environmental assessment or food security

Stomach

Element	Measurements (n)	Mean (mg kg^{-1})	S.D.	%RSD
As	89	3.9	0.36	9
Pb	75	15.3	2.97	19

Stomach + Intestine

Element	Measurements (n)	Mean (mg kg^{-1})	S.D.	%RSD
As	77	3.3	0.41	12
Pb	56	1.9	0.44	23

FOREhST

- Simulated the nutritional status of a 2-3 yr old
- Only intestine phase sampled
- PAH separation and analysis by HPLC-Fluorescence detection
- PAHs investigated
  - Benzo(a)anthracene;
    Benzo(b and k)fluoranthene;
    Benzo(a)pyrene;
    Dibenzo(ah)anthracene;
    Indeno(123cd)pyrene.

Using data from the UBM in a Risk assessment

UBM and total element data

- Calculate mg/kg bioaccessible
- Convert to % bioaccessible

Convert to relative bioaccessibility

- Use recovery of soluble salt in UBM to convert to relative bioaccessibility

Convert to Relative bioavailability

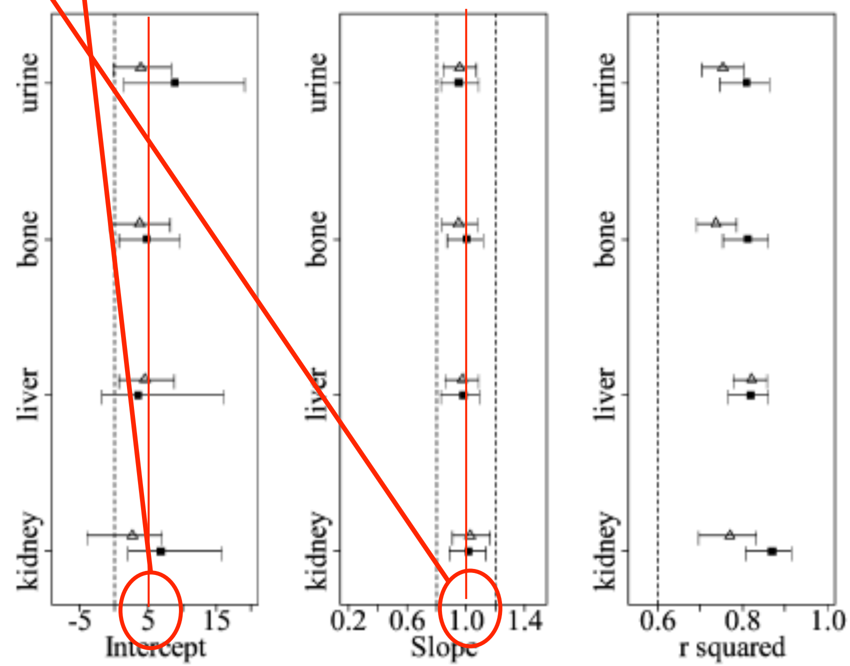
- Correct for the slope and intercept the RBA vs RBAc graph

Example

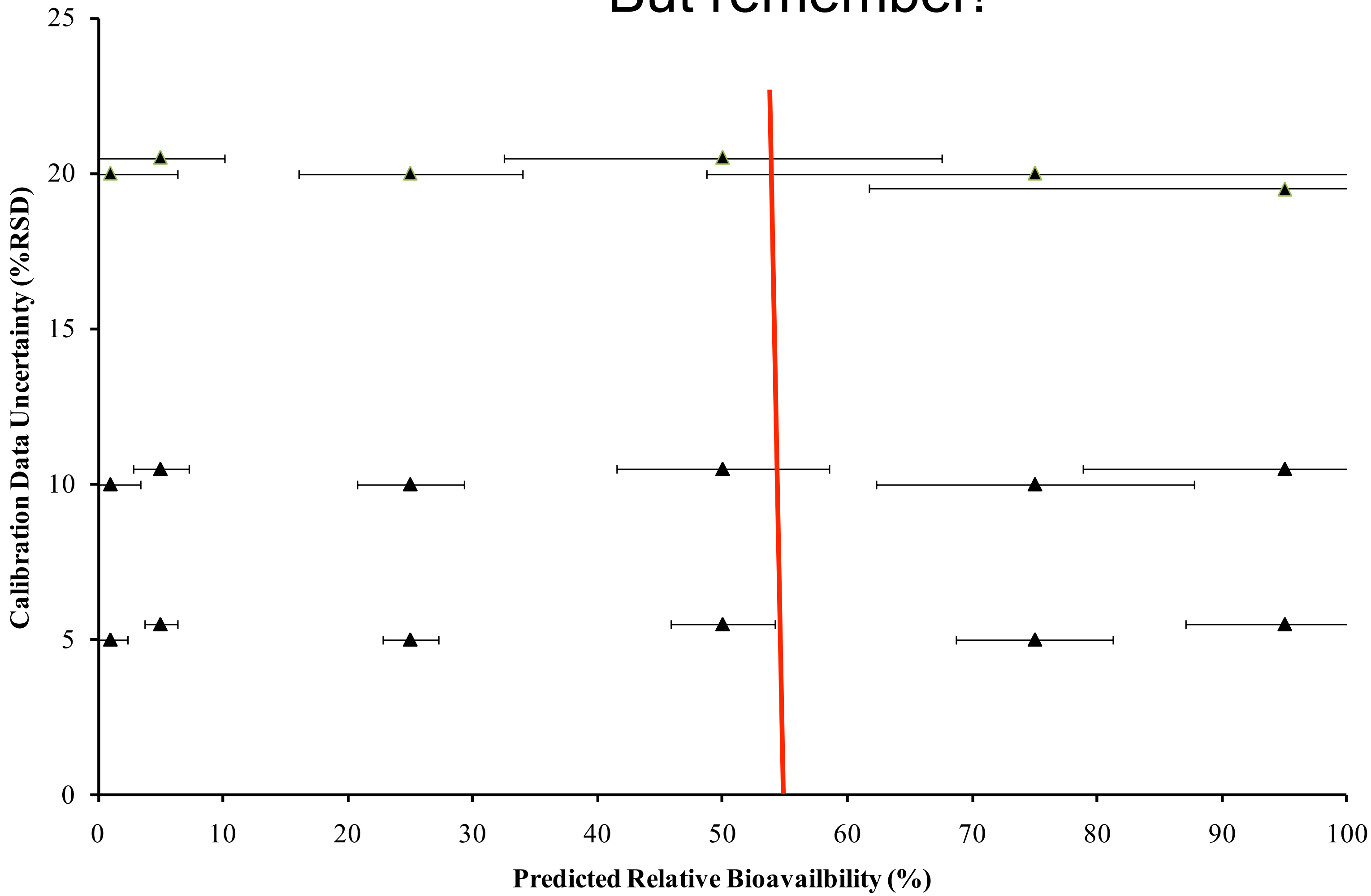
		Total Pb	Bioaccessible Pb (st)	
UBM for Pb in a soil		100	60	
% bioaccessibility		(60/100)x100	60	
%relative bioaccessible Pb		(60/99)x100	61	
%relative bioavailable Pb		(61/1)-5	56	

Relative bioaccessibility correction from Denys et al 2012

Compartment	Element	RBAC	Uncertainty
St	Pb	99	2
St&I	Pb	66	3
St	Cd	98	3
St&I	Cd	68	3
St	As	95	3
St&I	As	92	4



But remember!



Effect of increasing uncertainty in the bioaccessibility and bioavailability calibration data on the predicted bioavailability.

Summary

- There are a number of considerations to take into account when considering uncertainty in bioaccessibility/ bioavailability measurements.
- Produce a summary for your specific study (fish diagram)
- Take all the sources into account and make <u>appropriate</u> use of the data.