What can *in vitro* digestion models add to human risk assessment of contaminated soil ?

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National Institute for Public Health and the Environment

History *in vitro* digestion models in soil

- Closer look at *human* risk assessment methodology

- Contaminant levels above the intervention values
- Especially the case for lead in the Netherlands
- For PAH's in countries like Denmark and Sweden
- Due to incorrect or too stringent assumptions in risk assessment ?

Risk assessment methodologies

CSOIL applied for intervention values and *human* risk assessment

comparable to other european models

SUS site specific remediation urgency system (ecotox, human tox, risk of migration)

applied for site specific risk assessment

Both used for Dutch Soil Protection Act

Otte PF et al. (2001) RIVM-report 711701021

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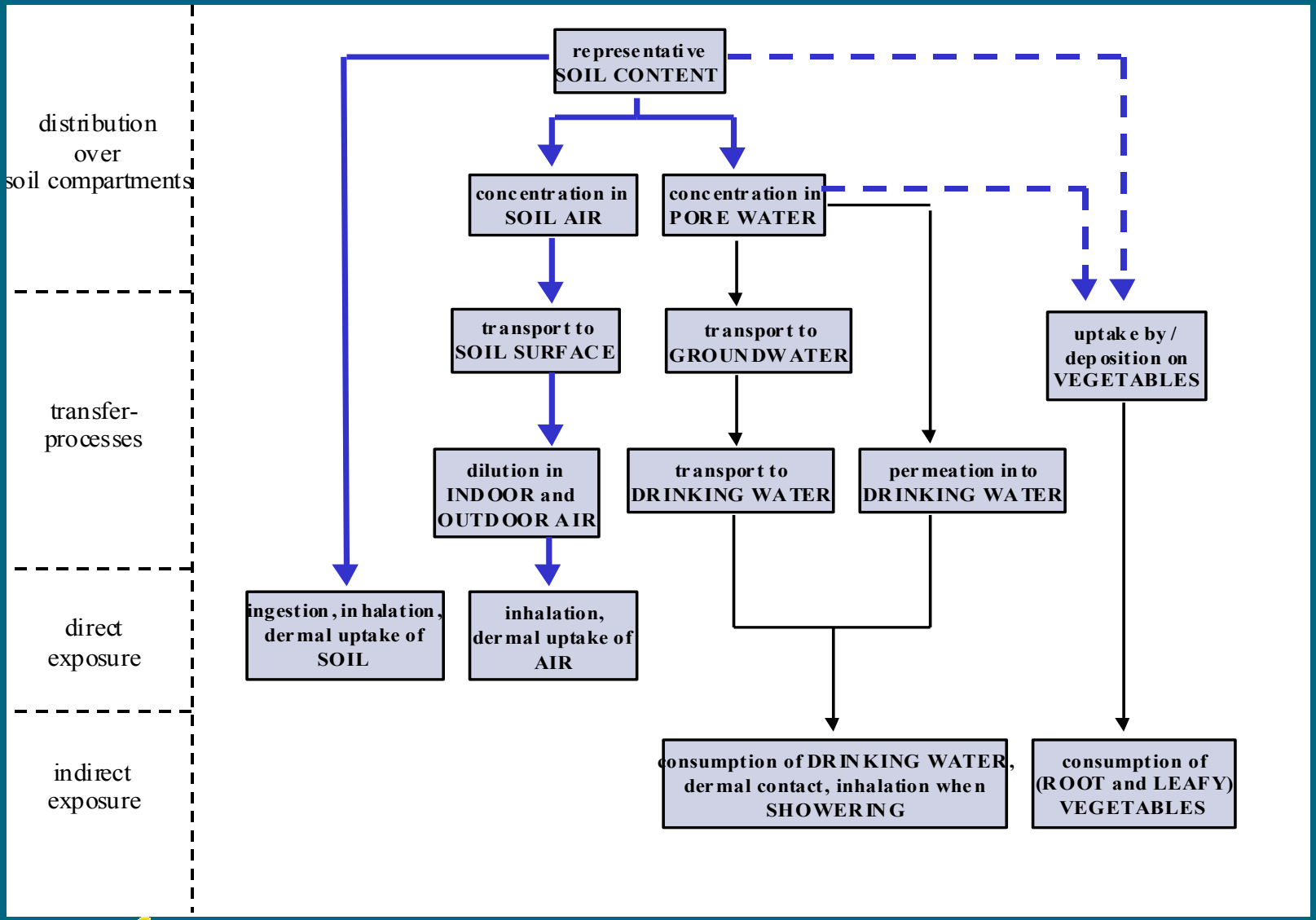
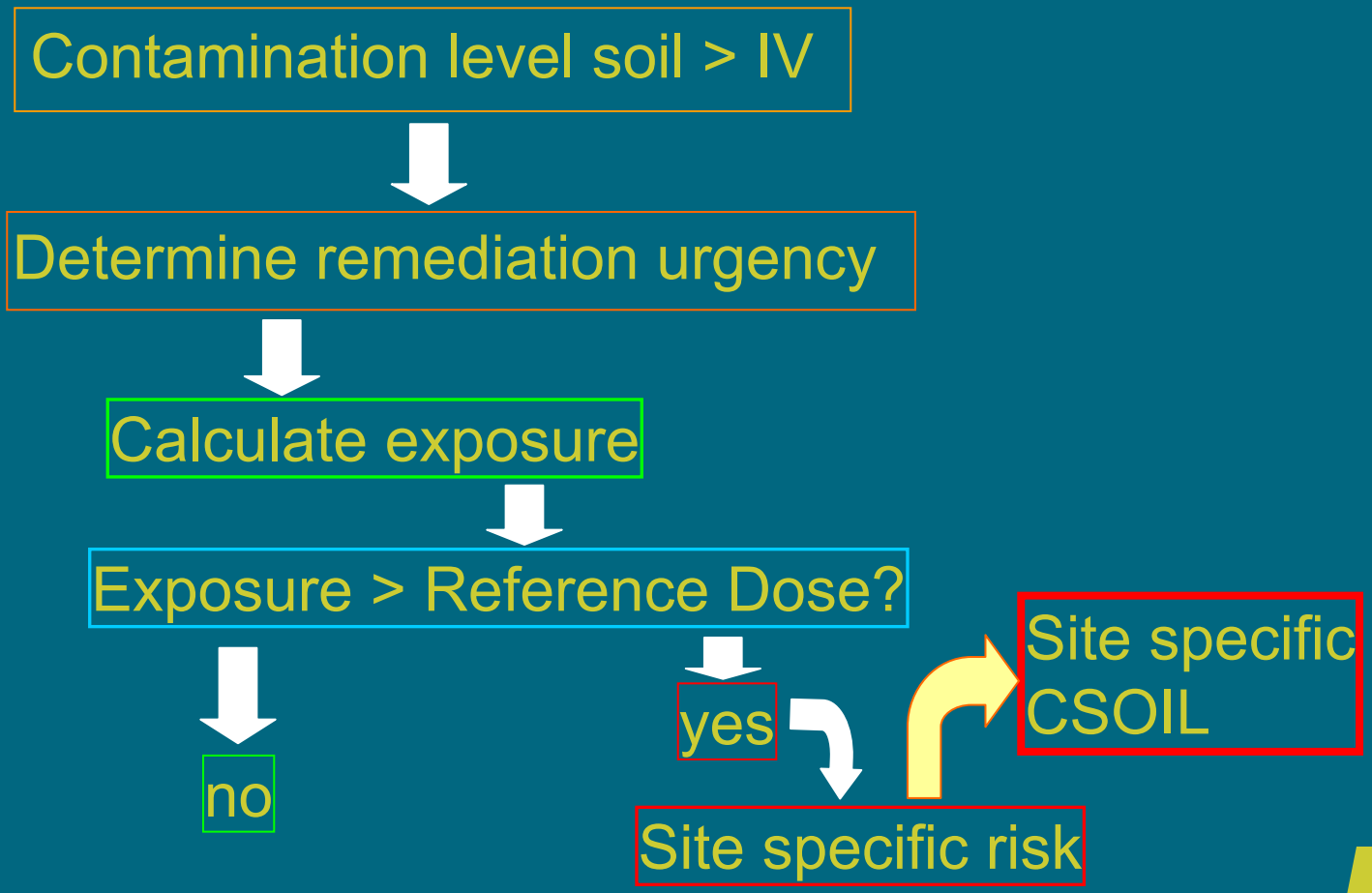
CSOIL


distribution over soil compartments
transfer-processes
direct exposure
indirect exposure
representative SOIL CONTENT
concentration in SOIL AIR
concentration in PORE WATER
transport to SOIL SURFACE
transport to GROUNDWATER
uptake by / deposition on VEGETABLES
dilution in INDOOR and OUTDOOR AIR
transport to DRINKING WATER
permeation into DRINKING WATER
ingestion, inhalation, dermal uptake of SOIL
inhalation, dermal uptake of AIR
consumption of DRINKING WATER, dermal contact, inhalation when SHOWERING
consumption of (ROOT and LEAFY) VEGETABLES

SUS


Contamination level soil > IV
Determine remediation urgency
Calculate exposure
Exposure > Reference Dose?
no
yes
Site specific risk
Site specific CSOIL

Present/future Dutch policy

In 2023 all remediaton actions finished

Tempo is by a factor 4 too slow (risk assessment)

Policy makers try to overcome these hurdles by:

More regional responsibility

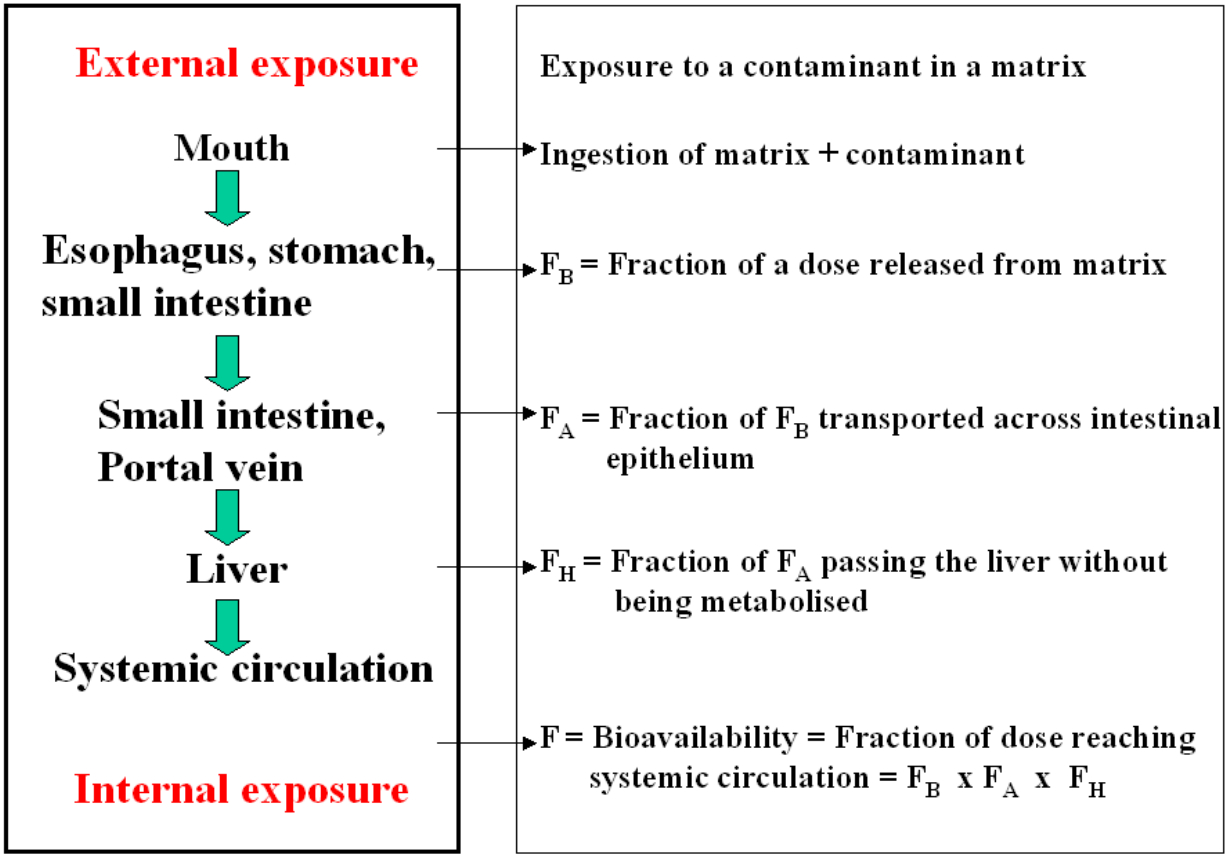
Cost efficient: Fitness for use, *in vitro* models

New tiered approach instead of SUS/CSOIL

Human risk assessment in CSOIL

- One of the routes of exposure is ingestion - oral bioavailability (F_{soil})
- F_{soil} is assumed to equal F from matrices studied in toxicity studies underlying Reference Dose (RfD)
- CSOIL does not assume 100% F from soil
- *Relative* F is assumed to equal 100% in CSOIL

Bioavailability - our definition -



Relative F

$$F = F_b \times F_a \times F_h$$

- F_a and F_h are supposed to be compound specific and not depending on matrix of ingestions;
- information on $F_a \times F_h$ can be derived from studies using drinking water or olive oil as matrix
- *Relative* F is described by bioaccessibility from certain soil sample compared to bioaccessibility from matrix used in RfD-studies

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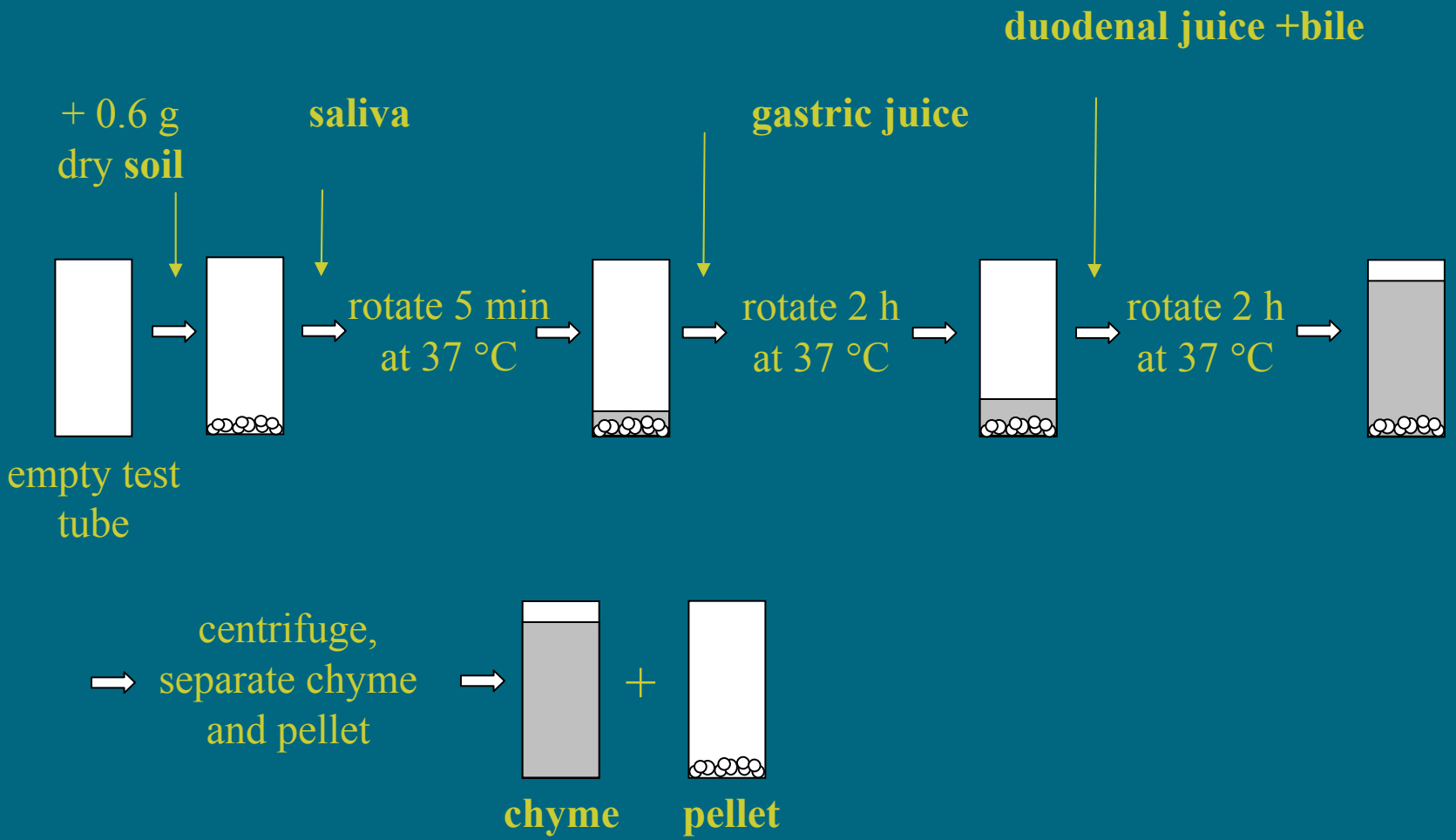
In vitro digestionmodel



BARGE = Bioavailability Research Group Europe

Aim:

Comparison of *in vitro* digestion models (5) - round robin studies

Gaining insight in critical factors in those models - factorial designs

Comparison with *in vivo* data (from Maddeloni *et al.)* - one study in man available

Development:

more participants also outside of Europe

experiences from BARGE serve as input for ISO guideline

Oomen et al. 2002 Environ. Sci. Technol., Maddeloni et al. 1998 Environ. Health Perspect.

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Bottlenecks BARGE

- financing
- only metals studied
- only one solid human *in vivo* study performed for validation

BARGE - wishes for the future

- New round robin studies, based on factorial design yield
  - insight in factors influencing results of bioaccessibility tests
  - better interpretation of existing data
- New round robin studies for organic compounds, based on factorial design
  yield
  - insight in factors influencing results of bioaccessibilty tests concerning organic compounds
  - better interpretation of existing data

BARGE - wishes for the future

- New *in vivo* studies in man for various soil types and for organic as well as inorganic compounds yield
  - sound proof for vitro validation
  - better interpretation of existing data
- Better interaction between european and american/canadian groups specialized in bioaccessibility testing (e.g. annual workshop ?) yield
  - collaboration in research (shared research programme?)
  - bringing together various expertises involved

Description five digestion models

- (BGS, UK): static gastric model
- (Bochum, Germany): static gastrointestinal model
- In vitro digestion model (RIVM, NL): static gastrointestinal model
- (Ghent University, B): static gastrointestinal model
- (TNO, NL): dynamic gastrointestinal model

Table: Characteristics in vitro digestion models

	SBET	*DIN*	*RIVM*	*SHIME*	*TIM*
pH stomach	1.5	2.0	1.1	4.0	5.0 decreasing to 2.0 in 90 min
Incubation time stomach	1 h	2 h	2 h	3 h	Gradual secretion at 0.5 ml/min
Solid-to-fluid ratio stomach	1:100	1:50	1:38	1:2.5	1:30
pH intestine	-	7.5	5.5	6.5	6.5-7.2
Incubation time intestine	-	6 h	2 h	5 h	Gradual secretion at 1 ml/min
Conc bile	-	4.5 g/l	0.9 g/l	1.5 g/l	Variable
Solid-to-fluid ratio intestine	-	1:100	1:98	1:4	1:51
Separation chyme and pellet	0.45 μm filter	Centrifugation 7000g	Centrifugation 3000g	Centrifugation 7000g	Hollow fiber membrane

Results

Bioaccessibility of As, Cd, and Pb after digestion of Montana 2711 (n=3)

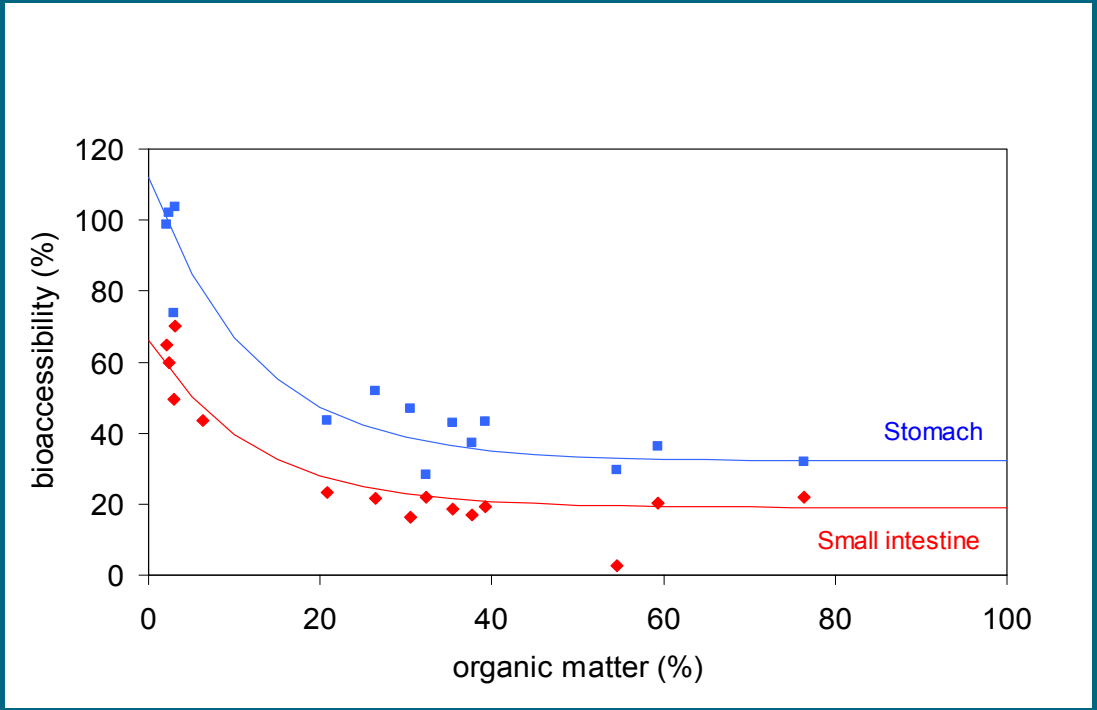
	Bioacc As (%)	*Bioacc Cd (%)*	*Bioacc Pb (%)*
SBET	59 ± 2	99 ± 4	90 ± 2
DIN*	50 ± 1	79 ± 8	68 ± 2
DIN-WM*	41 ± 2	45 ± 3	46 ± 2
RIVM	59 ± 1	40 ± 2	11 ± 2
SHIME	10 ± 0.4	6 ± 0.3	3 ± 0.3
TIM	50 ± 1 (n=2)	58 ± 1 (n=2)	17 ± 3 (n=2)

* DIN and DIN-WM represent a DIN digestion with and without milk powder, respectively.

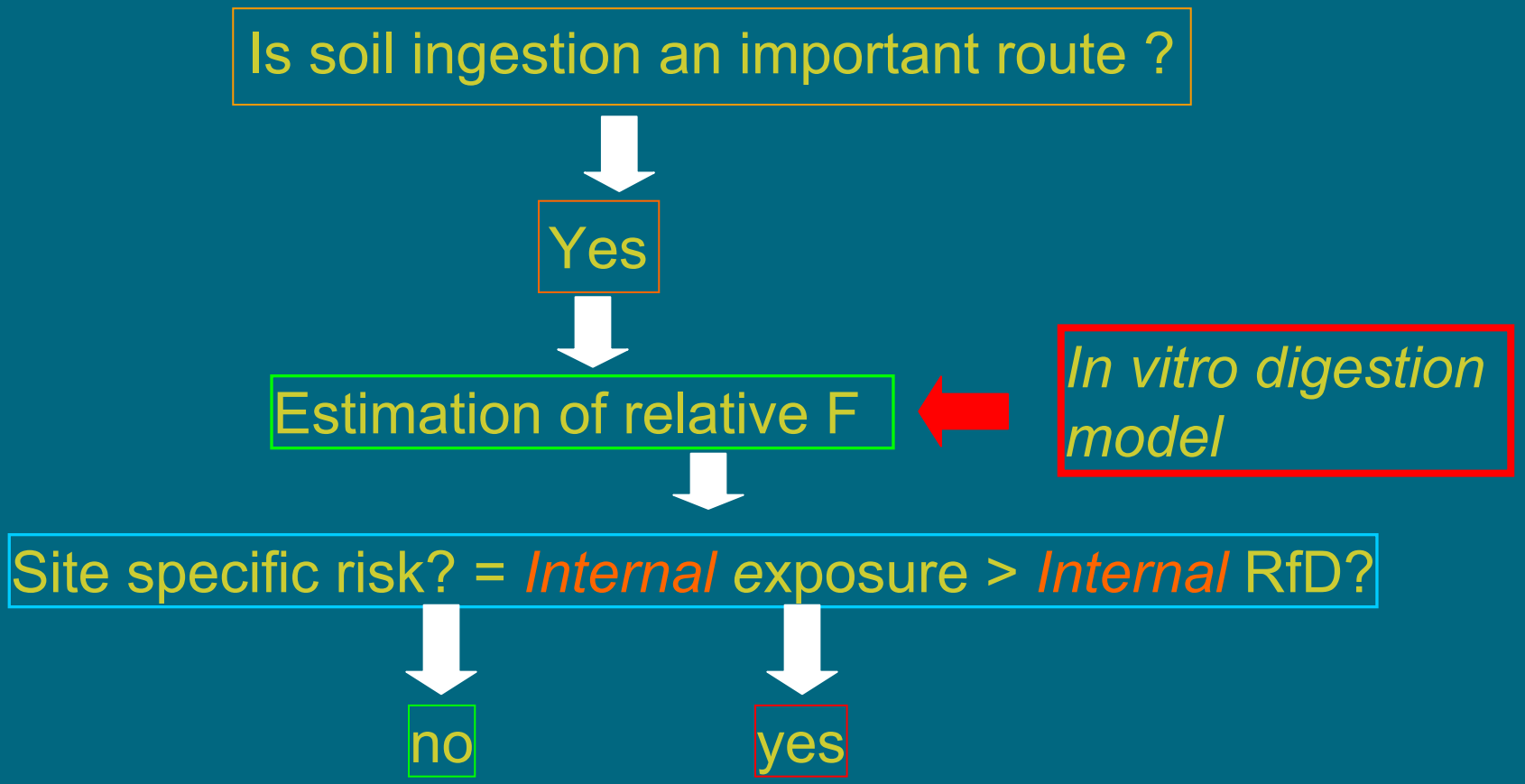
Other soils: Flanders, Oker 11, Bunker Hill

Oomen et al. 2002, Environ. Sci. Technol. 36, 3326-3334.

Bioaccessibility and organic matter content



Future perspectives towards SUS



Result: reduction of contaminated sites with high remediation urgency

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SUS new style offers

- Site specific risk assessment
- When soil ingestion is the most important route of external exposure, then determining *relative* F can be beneficial
  e.g. not beneficial for pesticides, DDT, DDE, dioxines
  e.g. beneficial for PAH's except naphtalene or di-benz(a,h)anthracene

Lijzen et al. RIVM report 711701 023 Technical evaluation of the Intervention Values for Soil/sediment and Groundwater. 2001

RIVM colleagues involved

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