# Nano Risk Assessment – An Introduction

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10 April 2012

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# Outline

- What is nano?
- Risk Assessment
  - Why risk assessment
  - Areas of risk assessment
  - Hazard and Exposure
  - Risk characterization
- Example: deterministic vs probabilistic
  - Deterministic risk assessment
  - Probabilistic risk assessment - IPRA

# What is nano?

Health & Consumer Protection
Directorate-General

Scientific Committee on Emerging and Newly Identified Health Risks

SCENIHR

OPINION ON

THE SCIENTIFIC ASPECTS OF THE EXISTING AND PROPOSED DEFINITIONS RELATING TO PRODUCTS OF NANOSCIENCE AND NANOTECHNOLOGIES

Scientific Committees

The SCENIHR adopted this opinion at the 21st plenary on 29 November 2007

22 pages on Scientific Basis for the Definition of the Term "nanomaterial"

***Nanostructure***

*Any structure that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less.*

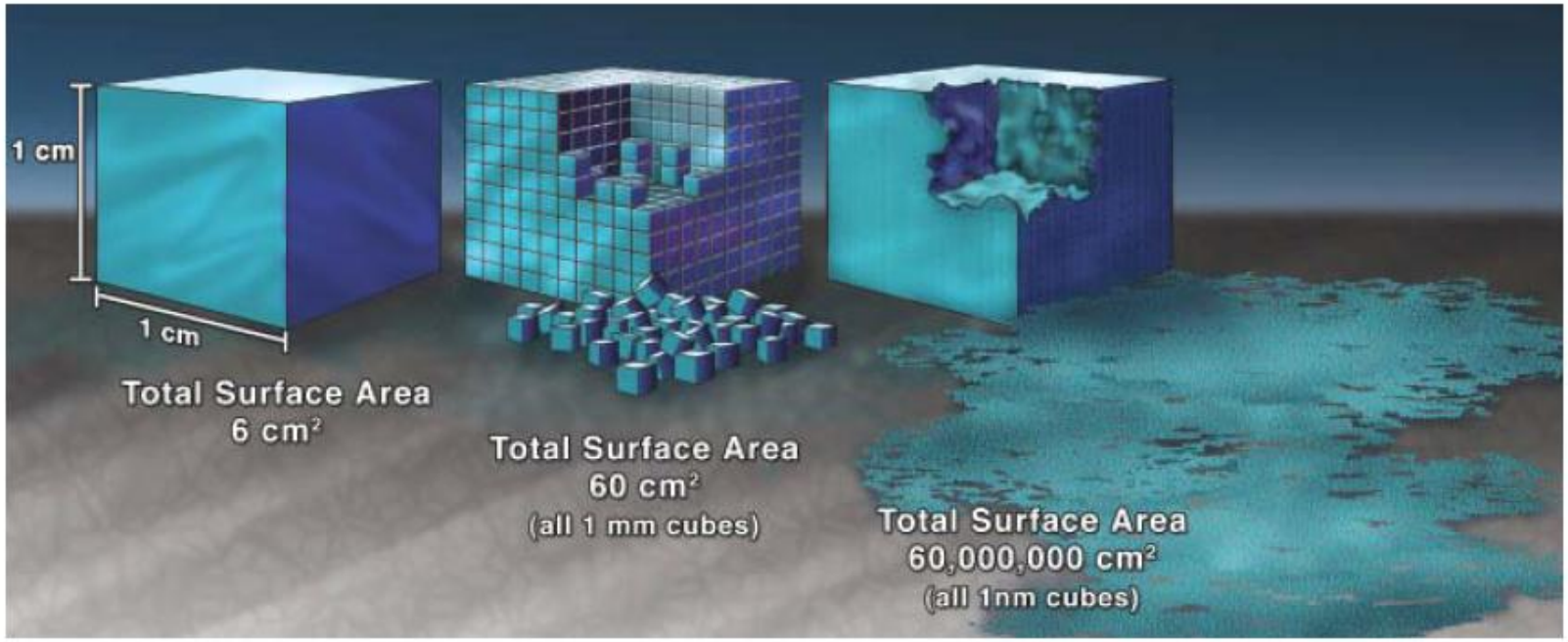
# Risk Assessment – Why?

A question of

**size...**


and

**Surface Area**

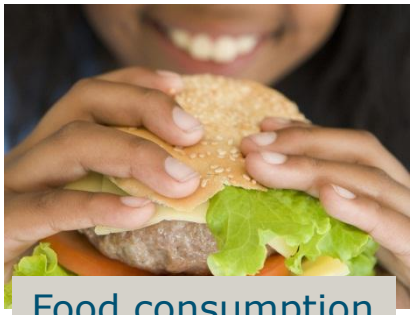



Bell, T.E. (2007)

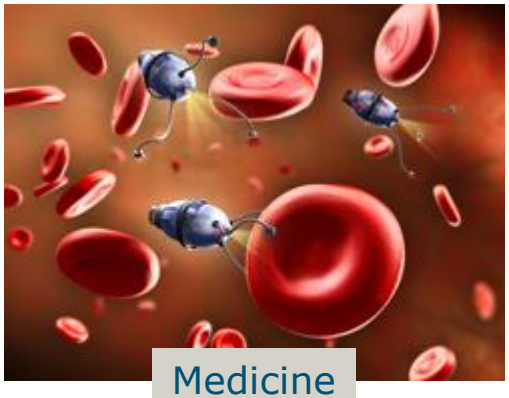
# Risk Assessment - Areas

- Human health risks

Occupational



Food consumption



Medicine

- Environmental risks
  - Exposure: water, soil, air
  - Effect on: aquatic life, plant life, animal life

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# Risk Assessment – Hazard and Exposure

- Hazard
  - Hazard identification
  - Hazard characterization
  - Dose-Response
- Exposure
  - Exposure assessment
  - Effect on: aquatic life, plant life, animal life

# Risk Assessment – Risk Characterization

**Definition**

A phase of risk assessment that integrates the results of the exposure and effects analyses to evaluate the likelihood of adverse effects associated with exposure to the stressor.

http://www.opentoxipedia.org/index.php/Risk_characterization

- Margin of Safety (MoS): $\frac{\text{no-effect-concentratation}}{\text{exposure}}$
- Margin of Exposure (MoE): $\frac{\text{no-effect-level}}{\text{exposure}}$
- Risk Quotient (RQ): $\frac{\text{exposure}}{\text{no-effect-concentratation}}$

deterministic

often worst case scenario

**vs**

probabilistic

- assess distribution of MoS/MoE/RQ
- uncertainty analysis

# Example – Nanosilica in food

"Presence and risks of nanosilica in food products" (Dekkers et al. 2011)

**Exposure – estimated worst case exposure**

Table II. Estimated intake of nanosilica based on consumption of food products analysed for their nanosilica (F1–F12) or silica (F13–F27) concentration.

| Code* | Food product | Mean concentration (mg nanosilica/g powder)** | Portion size (g powder/ portion) | Exposure per portion (mg nanosilica/portion) | Consumption (portion/day) | Exposure per day (mg nanosilica/day) |
|---|---|---|---|---|---|---|
| F1 | Mix for lasagne sauce | 0.3 | 32.5 | 8.5 | 0.2 | 1.7 |
| **F2□** | **Instant noodles** | 0.1 | 20 | 2.0 | 1 | 2.0 |
| F3 | Minced meat seasoning mix | 0.2 | 10 | 1.7 | 0.2 | 0.3 |
| F4 | Pancake mix | 0.1 | 133.3 | 13 | 1 | 13 |
| **F5⊠** | **Instant asparagus soup** | 0.2 | 20 | 4.2 | 1 | 4.2 |
| F6♦ | Spicy pepper rub | 0.1 | 3 | 0.39 | 0 | |
| F7♦ | Sweets sticky rub | 0.4 | 3 | 1.3 | 0 | |
| F8♦ | Steak house rub | 0.2 | 3 | 0.57 | 0 | |
| **F9♦** | **Roasted vegetable rub** | 0.6 | 3 | 1.7 | 0.2 | 0.3 |
| F10♦ | Seafood rub | 0.5 | 3 | 1.6 | 0 | |
| F11 | Burrito seasoning mix | 0.3 | 13.3 | 3.9 | 0.2 | 0.8 |
| **F12a◇** | **Coffee creamer (brand a)*** ** | 2.2 | 2.5 | 5.5 | 6 | 33 |
| F13⊠ | instant beef soup | 0.3 | 20 | 6.4 | 0 | |

# Example – Nanosilica in food

## Hazard – No-effect-level (critical-effect-dose)

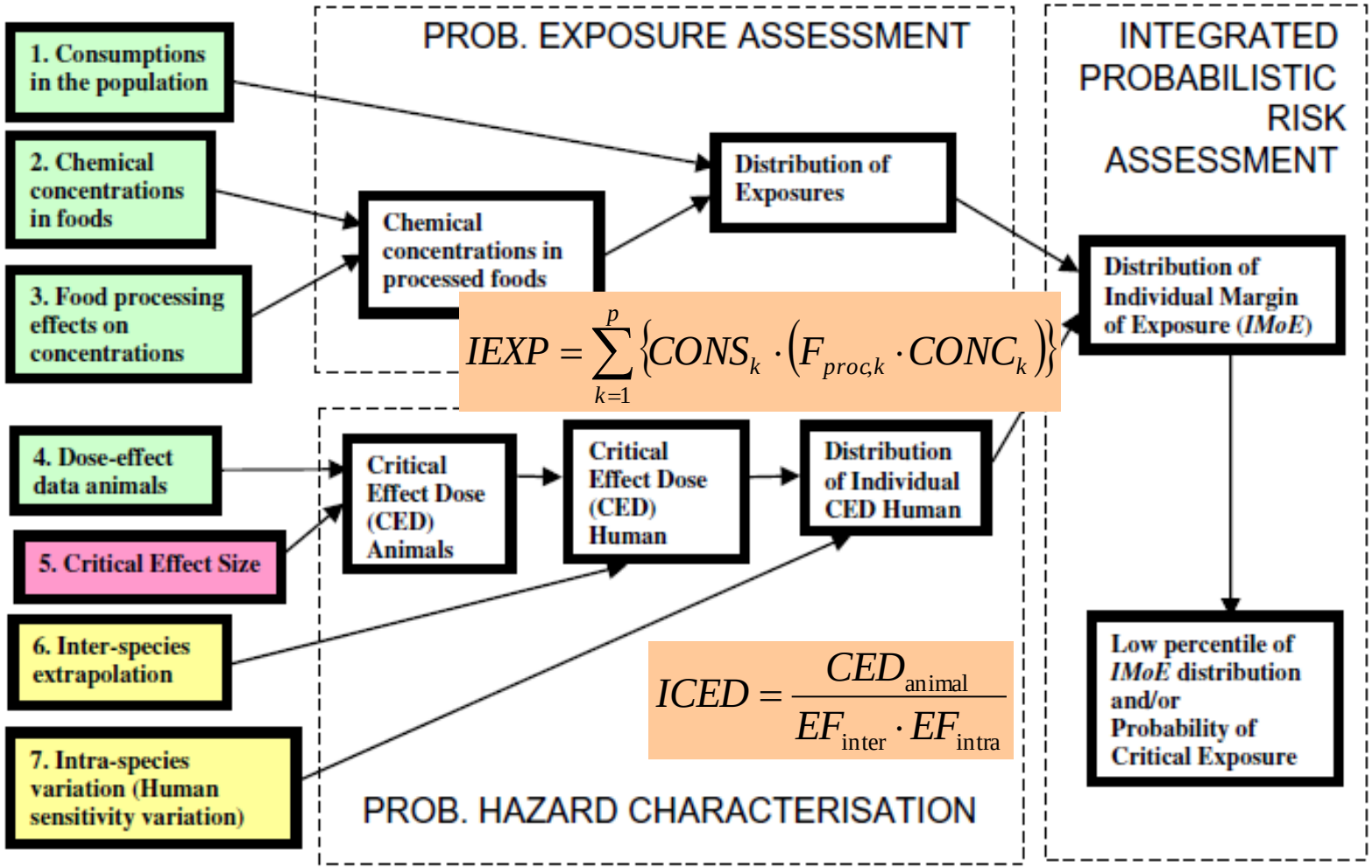
Animal study with mice being fed nanosilica (So et al. 2008)

Table III. Ratios between the NEL or LOAEL and the estimated exposure.

| Scenario | Dose metric | Estimated exposure[a] | NEL or LOAEL[b] | Estimated MOS |
|---|---|---|---|---|
| 1: Dissolved silica | mg/kg bw/d | 9.4 | 625 (NEL) | 66 |
| 2: Nanosilica particles | mg/kg bw/d | 1.8 | 1500 (LOAEL) | 850 |
| | **m2/kg bw/d** | 0.02–0.2 | 45–136 | 280–5600 |
| | **particles/kg bw/d** | $2 \times 10^{11} - 6 \times 10^{13}$ | $2 \times 10^{15}$–$5 \times 10^{16}$ | 31–250000 |

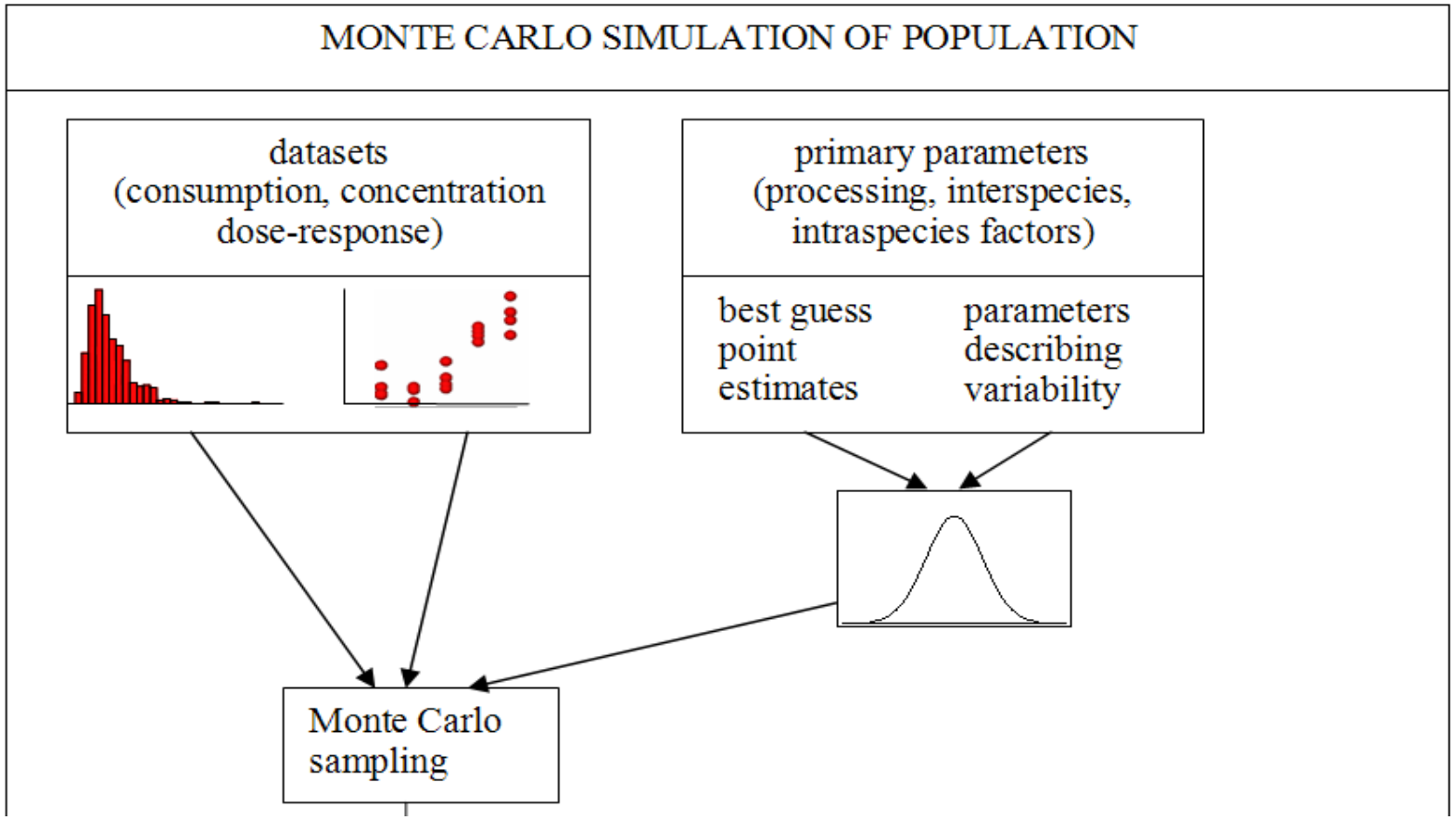
# Example - IPRA

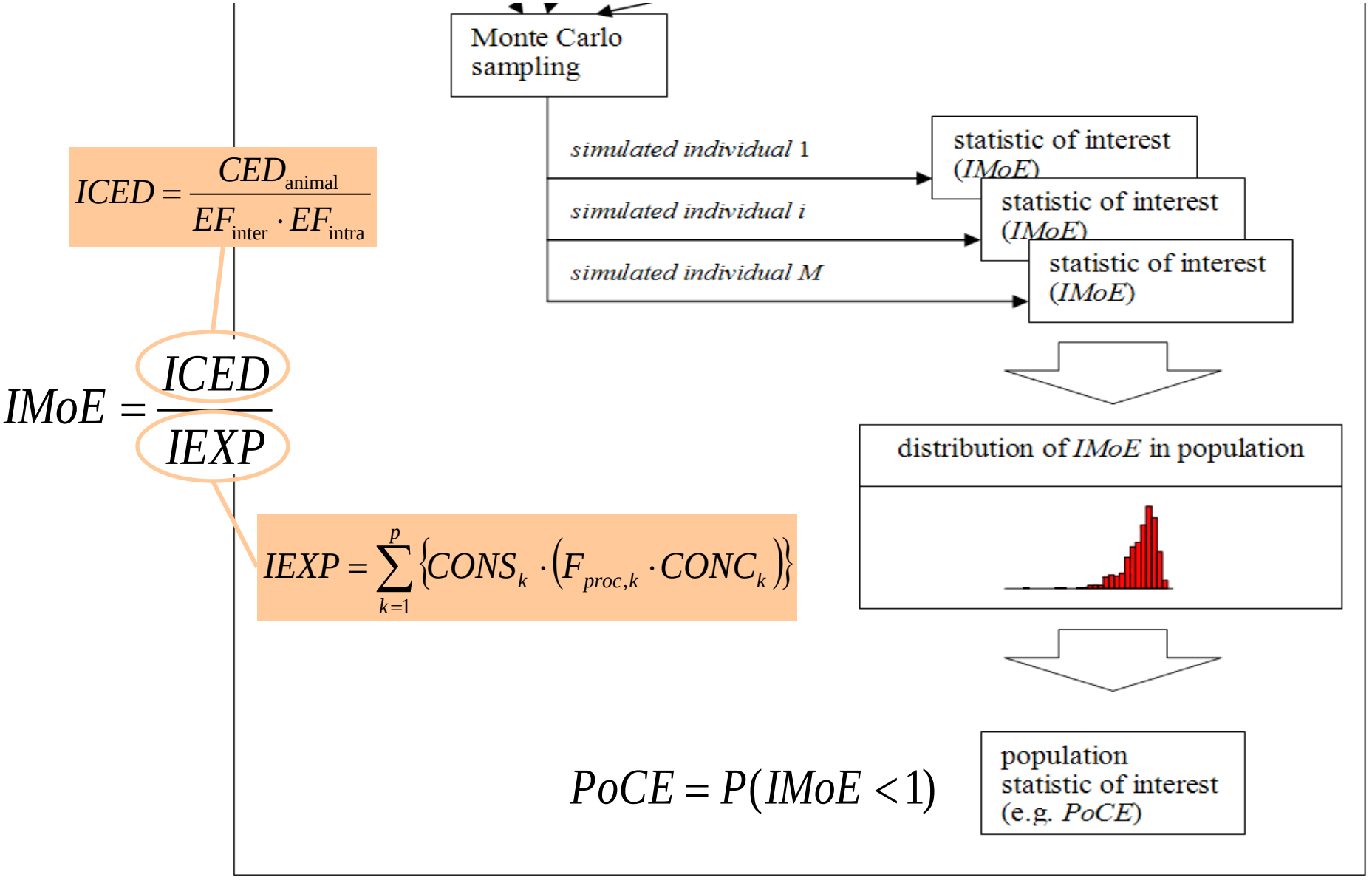
One possible probabilistic approach – IPRA (van der Voet et al. (2009))



# Example - IPRA

## Variability




Monte Carlo sampling
simulated individual 1
simulated individual i
simulated individual M
statistic of interest (IMoE)
statistic of interest (IMoE)
statistic of interest (IMoE)
distribution of IMoE in population
population statistic of interest (e.g. PoCE)
$ICED = \frac{CED_{animal}}{EF_{inter} \cdot EF_{intra}}$
$IMoE = \frac{ICED}{IEXP}$
$IEXP = \sum_{k=1}^{p} \{CONS_k \cdot (F_{proc,k} \cdot CONC_k)\}$
$PoCE = P(IMoE < 1)$

# Example - IPRA

**Variability**
- Truly existing differences between people
- Part of reality

**Uncertainty**
- Lack of knowledge
- Can be reduced (in principle)

Uncertainty in hazard characterisation:

- limited dose-response data
- interspecies factor
- intraspecies variation

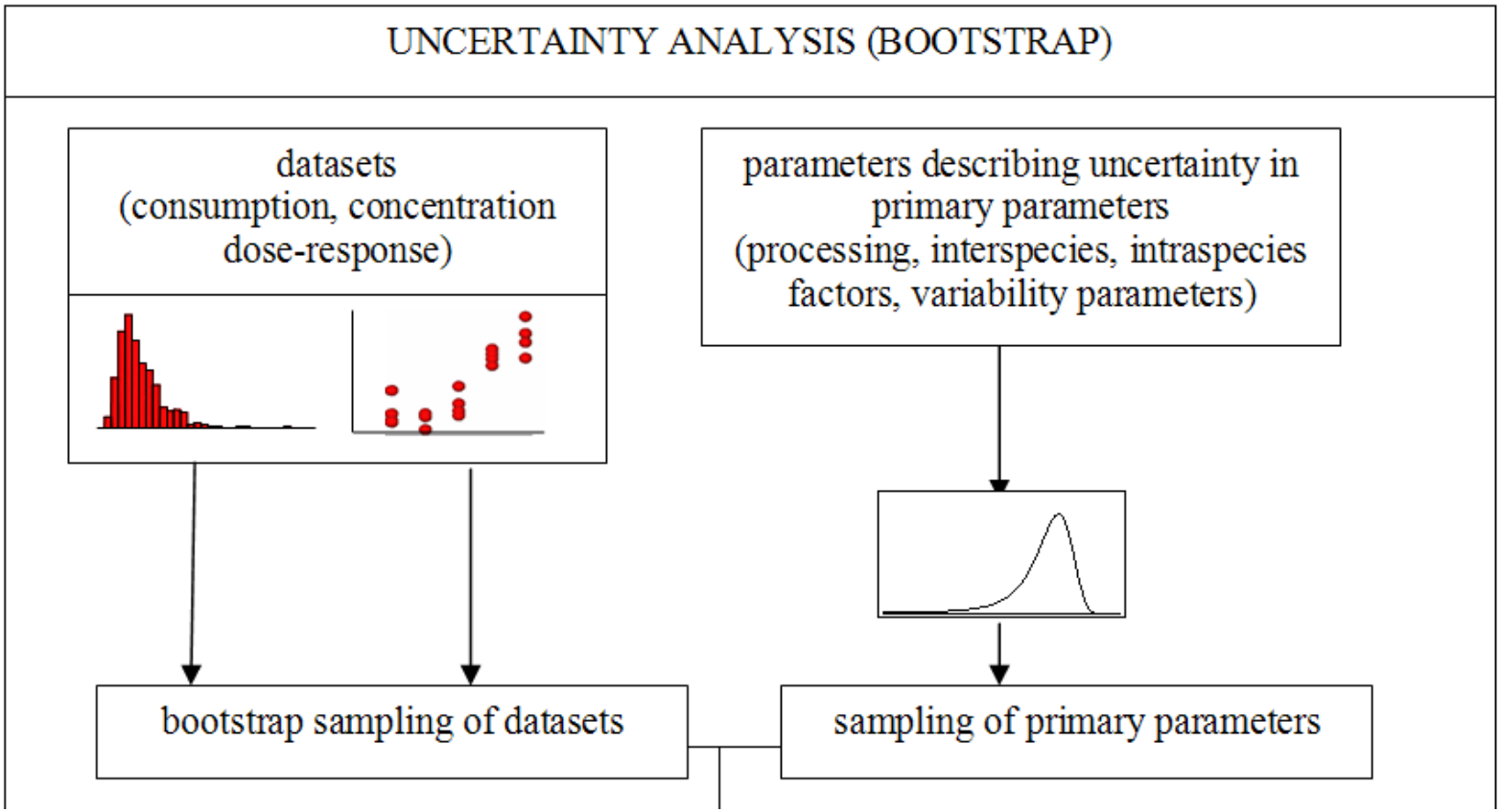
Uncertainty in exposure assessment:

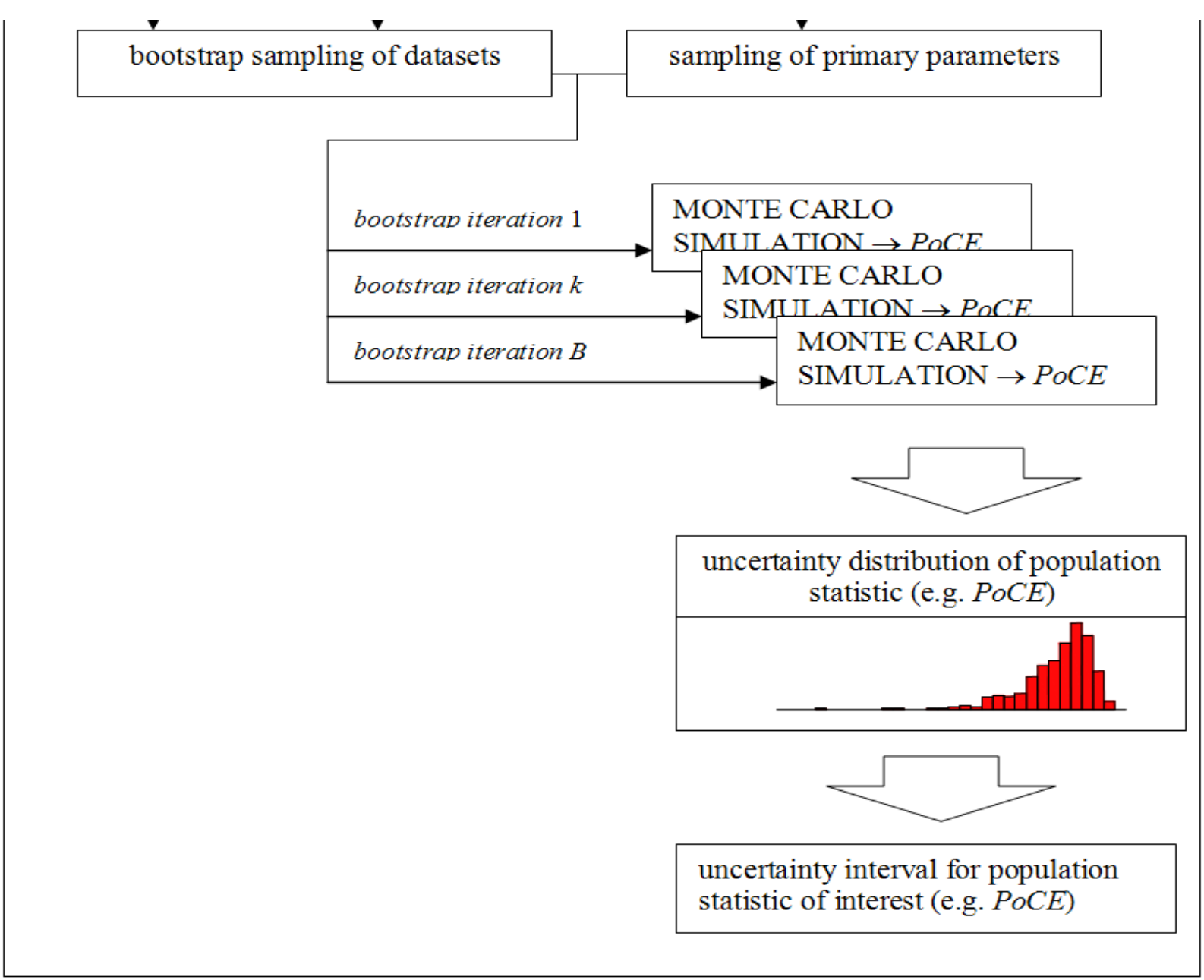
- limited consumption data
- limited concentration data
- processing factors and their variability

Computational: Monte Carlo approximation

# Example - IPRA

## Uncertainty




bootstrap sampling of datasets
sampling of primary parameters
bootstrap iteration 1
bootstrap iteration k
bootstrap iteration B
MONTE CARLO SIMULATION → PoCE
MONTE CARLO SIMULATION → PoCE
MONTE CARLO SIMULATION → PoCE
uncertainty distribution of population statistic (e.g. PoCE)
uncertainty interval for population statistic of interest (e.g. PoCE)

# References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- http://www.opentoxipedia.org/index.php/Risk_characterization

# Thank you

Questions?

Comments?

Suggestions?

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