# DoE 3: Exposure Modelling

ISES Europe Training Series

Natalie von Goetz, Wouter Fransman

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# Overview of All Training Videos

DoE 1) Basic Concepts and Principles in Exposure Science

DoE 2) Fundamentals of Environmental Chemistry and (Eco)Toxicology

**DoE 3) Exposure Modelling**

DoE 4) Exposure Monitoring

DoE 5) Exposure Assessment and Risk Characterisation

DoE 6) Risk Management and Sustainability Assessment

DoE 7) Relevant Legislative Frameworks

DoE 8) Risk Communication and Stakeholder Engagement

DoE 9) Statistics and Epidemiology

Access all videos via: **https://ises-europe.org/**

# Domain of Expertise (DoE) 3:
## Exposure Modelling

| | |
|---|---|
| Module 1 | Introduction, context&regulation, concepts for exposure modelling |
| Module 2 | Human exposure modelling: General concepts and worker |
| Module 3 | Human exposure modelling for the general population |
| Module 4 | Environmental exposure modelling |
| Module 5 | Validation&evaluation, advantages&limitations, conclusions |

# DoE 3: Exposure Modelling

## Module 3

## Human exposure modelling for the general population

**Dr. Natalie von Goetz**

# Presenter

**Meet Today's Presenter: Dr. Natalie von Goetz**

- **Current Role:**
  - Project Leader | Swiss Federal Office of Public Health (FOPH)
  - Lecturer | Federal Institute of Technology (ETH) Zurich
- **Previous Roles:**
  - Group Lead Human Exposure Modelling @ Safety and Environmental Technology Group | Federal Institute of Technology (ETH) Zurich
  - Expert for environmental fate of pesticides | BASF
- **Education:**
  - MSc Chemistry (Heidelberg University), PhD Natural Sciences (TU Braunschweig)
- **Special Expertise:** Exposure modelling

# Context and Disclaimers

## About This Lecture

This lecture provides an **introductory framework**, with some topics simplified for ease of understanding.

## Disclaimer

- The content presented herein does not necessarily reflect the opinions, views, or positions of the presenters' employer or any affiliated organizations.
- References to specific organizations, tools, or entities are for illustrative purposes only and do not imply endorsement or critique.
- While every effort has been made to ensure the accuracy of the information presented, errors or omissions may occur.

# Learning Objectives

- Understand principles and context of exposure modelling
- Understand formulae and necessary parameters
- Describe tiered approaches for general population exposure modelling
- Explain validation of exposure models using human biomonitoring

# Content

1. **Human Exposure Modelling for the General Population**
2. Key Factors for Product Exposure Assessment
3. Assessment of Overall Exposure
4. Methods and Tiered Approach
5. Uncertainty Assessment and Validation
6. Summary

# Human Exposure Modelling for the General Population: Definitions

Exposure modelling for the general population includes all exposures that are not workplace related (non-occupational exposures), namely exposures from environmental media and consumer exposure

- Sometimes the term "**General population exposure modelling**" is used to describe only human exposure to substances via the environment (unintentional exposure, secondary exposure), which other authors describe as "**environmental exposure**"
- The term "environmental exposure" is both used for human exposure via the environment or for organisms in the environment. In a specific context it is important to explain, which is meant. Ideally the term "environmental exposure" should not be used to describe human exposure
- **Consumer exposure modelling** covers the exposure via substances in consumed products or food.

# Non-occupational versus Occupational Exposure Assessment

- Even more diversity in exposures of the general population than for workers
- Exposure normally at lower concentrations
- Ingestion exposure of higher importance

→ **Different methods are being used for assessing general population exposure compared to occupational exposure.**

→ **For the general population exposure modelling is more important, specific exposure monitoring is less often available**

# Single Substance Assessment as Starting Point

- Risk assessment firstly focuses on the assessment of a single chemical substance
- Therefore, also exposure assessment starts with single substance assessment
- Models for general population exposure assessment are e.g. ConsExpo or Ecetoc TRA (Consumer exposure module)

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# Assessment of Product Exposure

(Consumer) Product:

- sum of **chemical substances**
- tied together by **chemical/ physical forces**
- meant for a specific **use**
- by specific **people**

## Risk Assessment is focused on substances

Reduction of complexity: Focus on **chemical substance** with

- highest percentage in product
- highest toxicity
- highest release rate

# Product Exposure

## Extent of substance release from products depends on:

- **Matrix**
  - Liquid (pesticide solutions, shampoo, household cleaner)
  - Solid (pesticide granules, furniture)
  - Polymer (plastics)
- **Bond type**
  - Physical Bonds (Pesticide formulation, polymers with “solved” ingredients like plasticizers)
  - Chemical Bonds: covalent bonds, H-bridges

# Exposure from Multiple Products

| | Secondary source<br>**Direct Source** | Primary source<br>**Indirect Source** | **Substance class** |
|---|---|---|---|
| Oral | Food | Processing<br>Agriculture<br>Packaging | Additives<br>Pesticides<br>Migrating compounds |
| Inhalation | Dust | Furniture<br>Carpets<br>Cleaning chemicals .... | Biocides<br>Flame retardants<br>Fragrances<br>Solvents ... |
| Dermal | Cosmetics | Personal Care Products<br>Decorative Cosmetics<br>Sunscreens | Preservatives<br>Dyes<br>UV absorber |
| | Textiles | Agriculture<br>Textile Finishing<br>Preserving | Pesticides<br>Dyes<br>Flame retardants<br>Biocides |

Aggregate exposure
From multiple products

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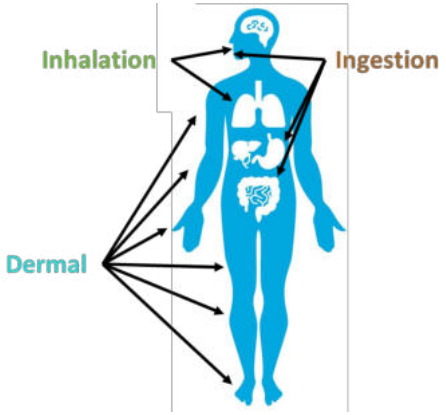
# Different levels of summing up exposure

Different **routes of exposure**

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Different **sources of exposure**

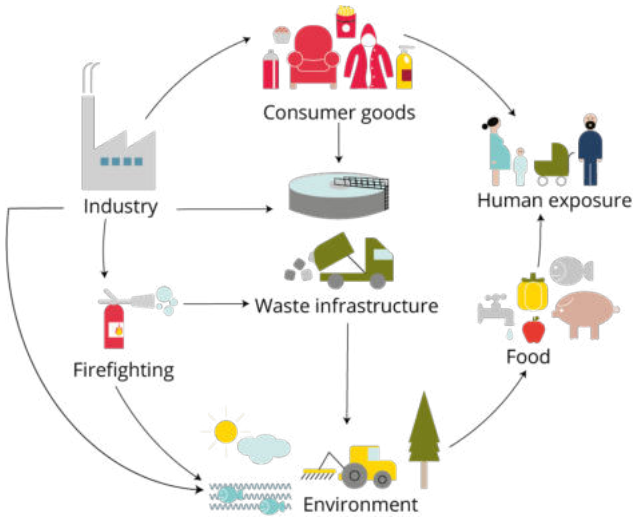


**Image credit: EEA** https://eea.europe.eu

Different **substances**

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# Definitions for Summarized Exposure

## Aggregate exposure

Exposure to **one agent** from **different exposure sources**, via different exposure pathways and/or exposure routes

## Total exposure

If **all routes and sources** have been considered, the aggregate exposure is equivalent to "total exposure" to a **specific agent or stressor**.

## Cumulative exposure/Combined exposure

Total or aggregate exposures (or doses) for **multiple chemicals or stressors** evaluated together.

**Heinemeyer et al., 2021 JESEE** https://doi.org/10.1038/s41370-021-00390-w

# Aggregate Exposure Modelling

Aggregate exposure assessment examines exposures to a **single substance** across **multiple sources** (e.g. occupational, consumer, environmental) and **multiple routes** (ingestion, inhalation, dermal contact), via **multiple pathways** (e.g. water, air, dust, and diet)

- Risks can be underestimated if all sources and routes are assessed separately
- Occupational, non-occupational and environmental exposure assessments have historically been conducted separately, in part due to different regulatory silos
- Current regulatory attention (EFSA, ECHA)
- **No current harmonized methodology or guidance for aggregated exposure assessment to chemicals in the general population**

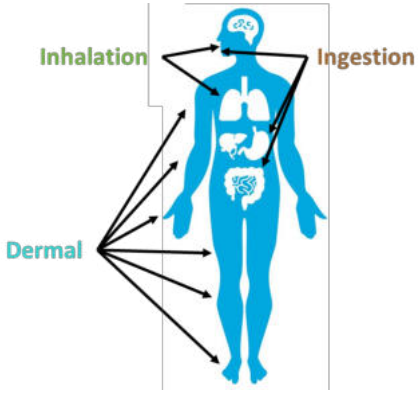


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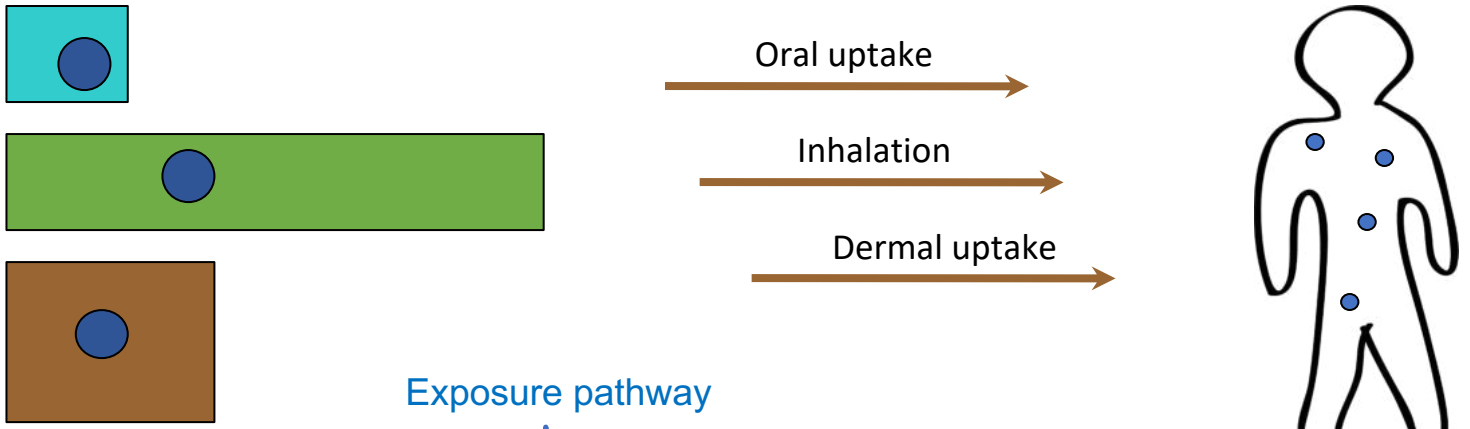
**Image credit: NIH** https://epi.grants.cancer.gov

# Aggregate Exposure Modelling




$$D_{xy} = \frac{C_x * q_{xy}}{bodyweight} * r_y$$

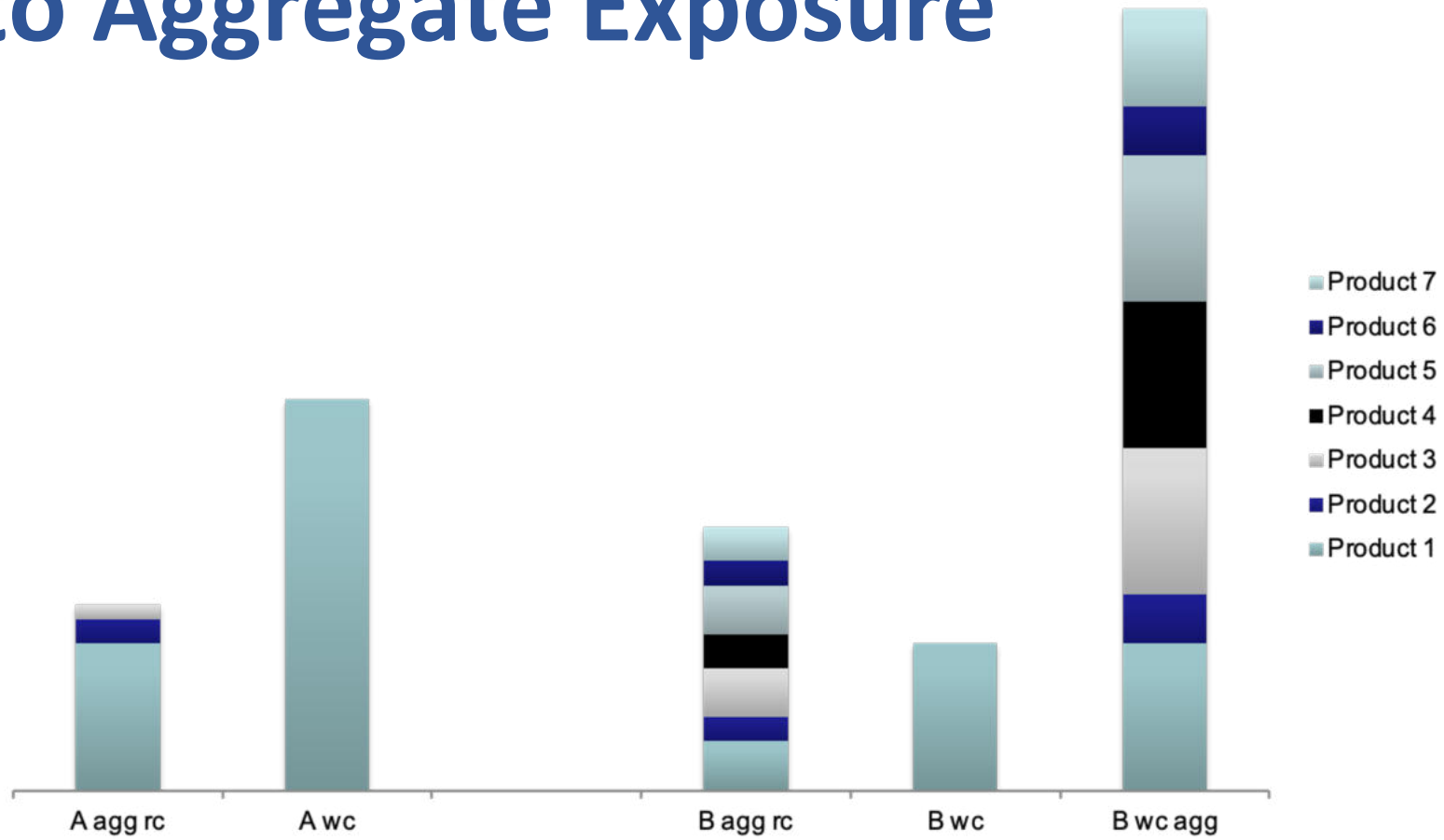
**Single source exposure**

D: dose (internal exposure)
C: concentration in source x
q: quantity of x taken up
r: uptake fraction via y

$$D_{agg} = \sum D_{xy}$$

**Aggregate exposure**

# When to Aggregate Exposure




**Substance A:**
used in large amounts in one product

**Substance B:**
used in small amounts in many products

→ **importance of realistic cases!!**

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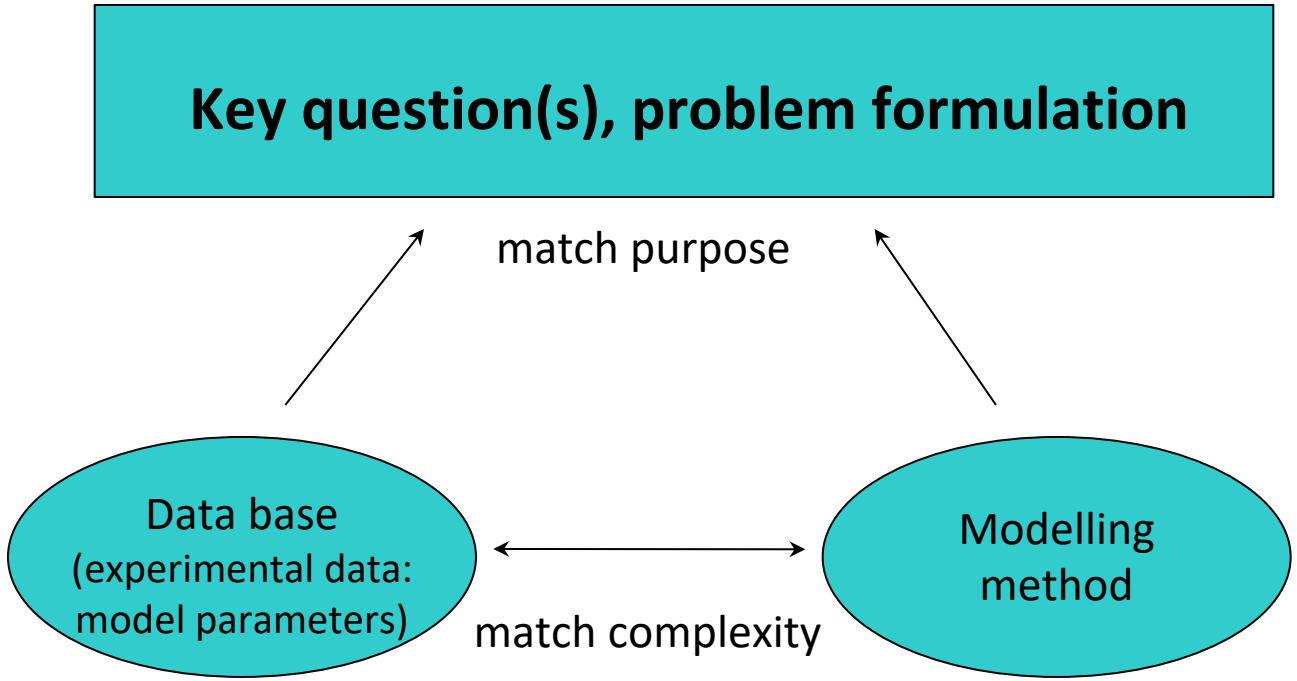
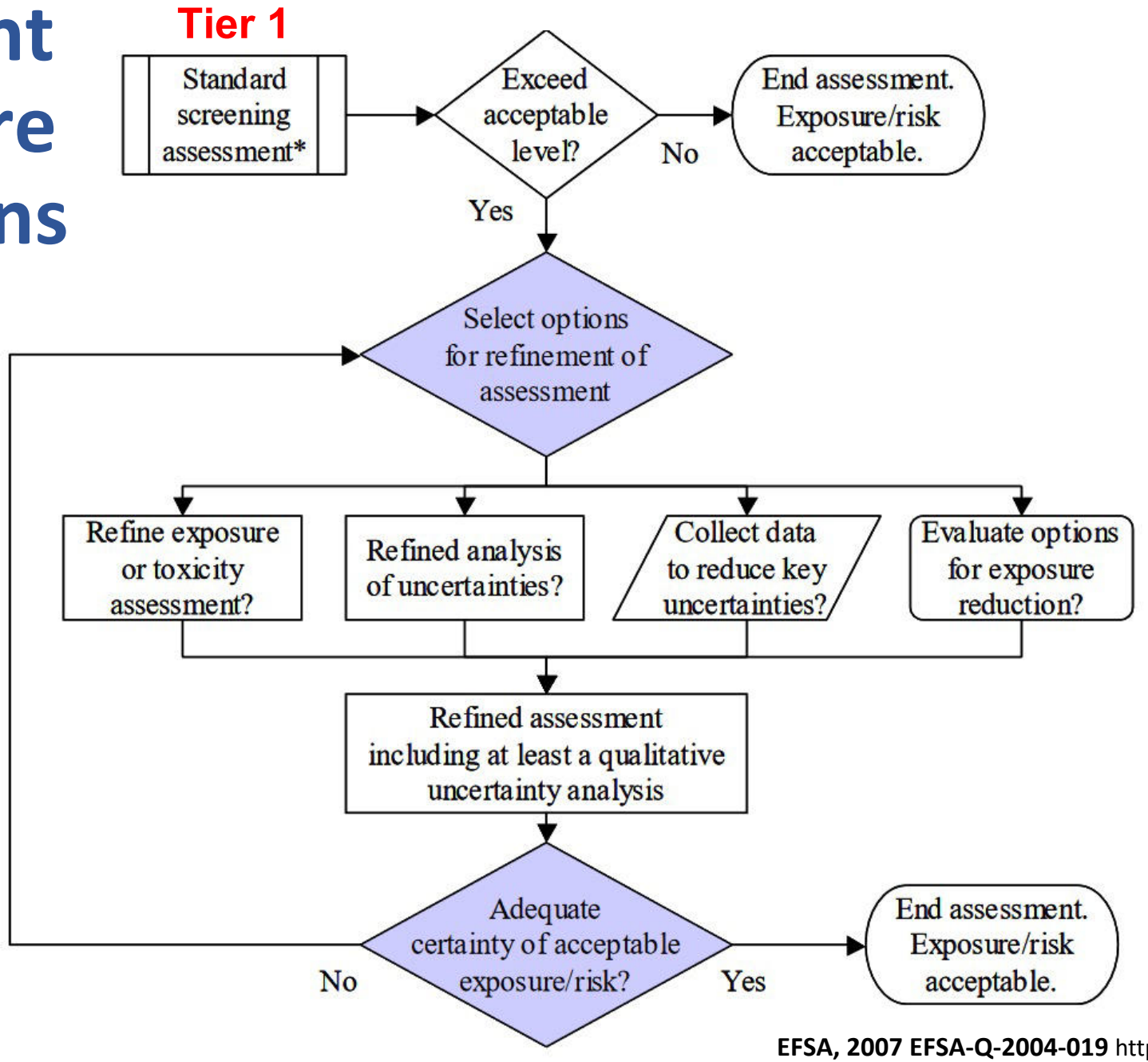
# Choice of Methods for Exposure Modelling



# Refinement of Exposure Calculations




**Tier 2**
**Tier 3**

**EFSA, 2007 EFSA-Q-2004-019** https://doi.org/10.2903/j.efsa.2007.438

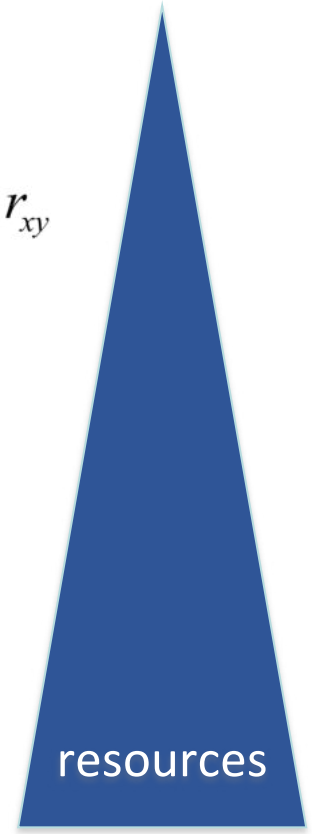
# Tiers by Method Selection

- Deterministic assessment: mean or worst-case parameters (point values)

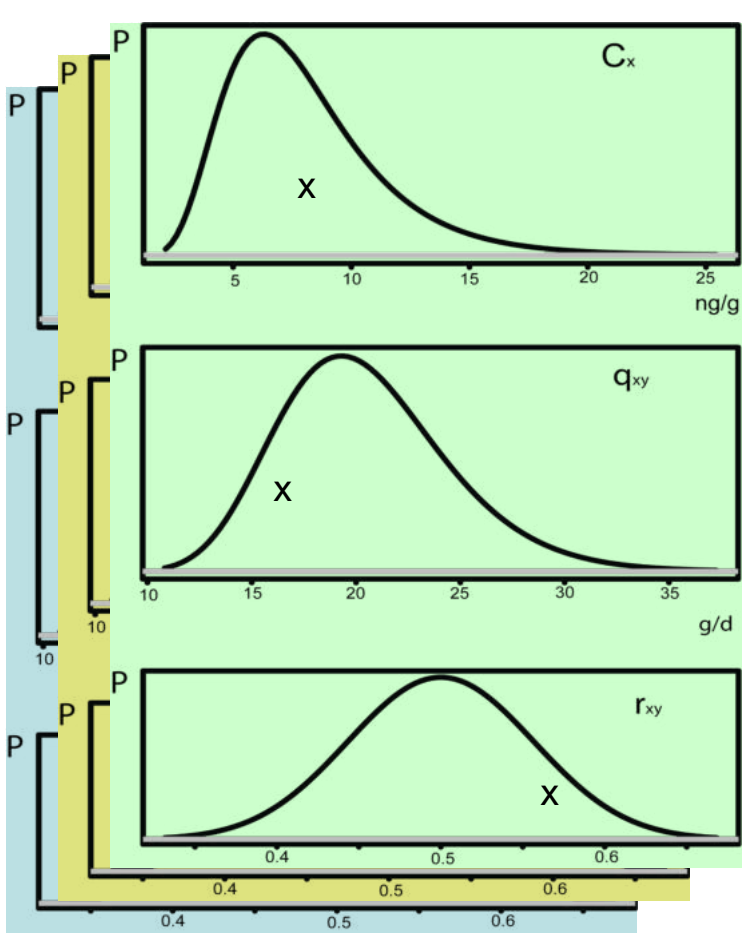
$$D_{xy} = \frac{C_x \cdot q_{xy}}{bw} \cdot r_{xy}$$

- Probabilistic assessment: distribution represent each parameter

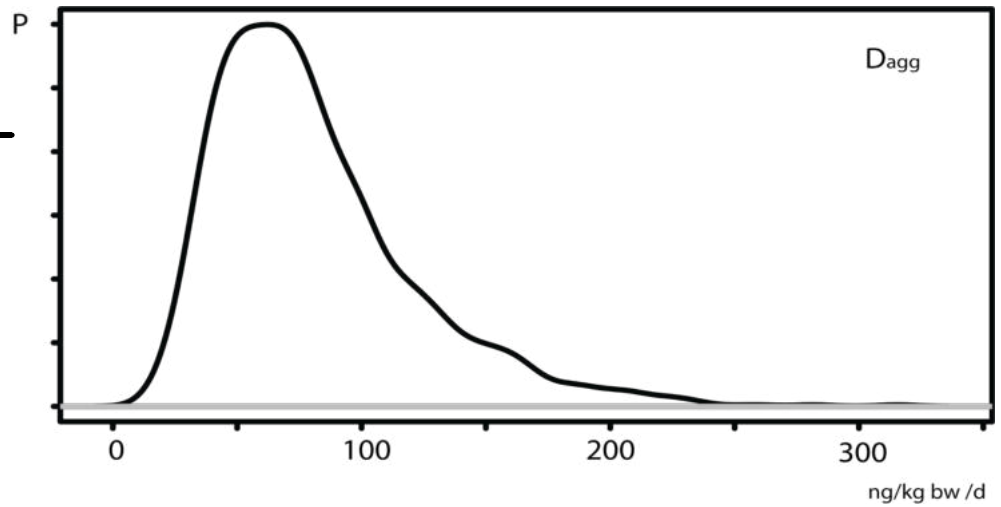
- Individual-based assessment (includes co-exposure)



# Probabilistic Modelling: Monte Carlo Approach

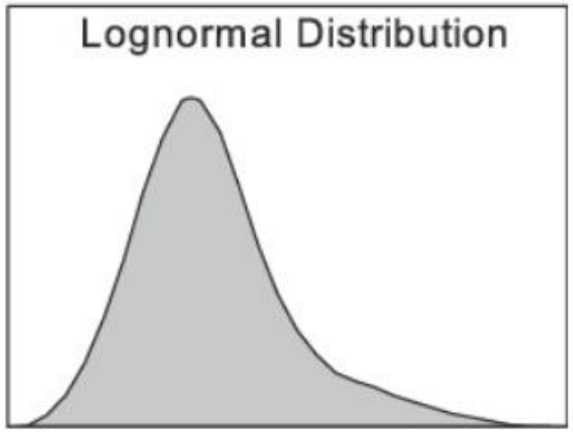



$$D_{xy} = \frac{C_x \cdot q_{xy}}{bw} \cdot r_{xy} \qquad D_{agg} = \sum D_{xy}$$

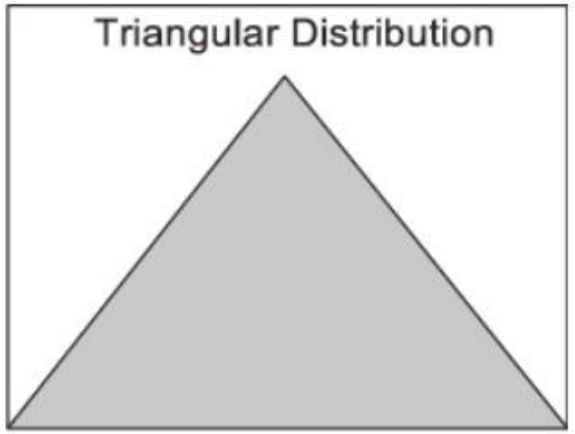


# Types of Distributions

**Lognormal distribution**
e.g. concentrations



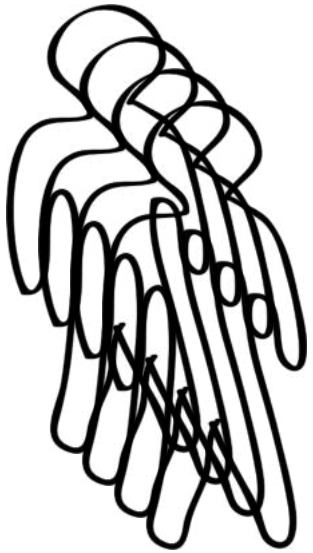

**Triangular distribution**



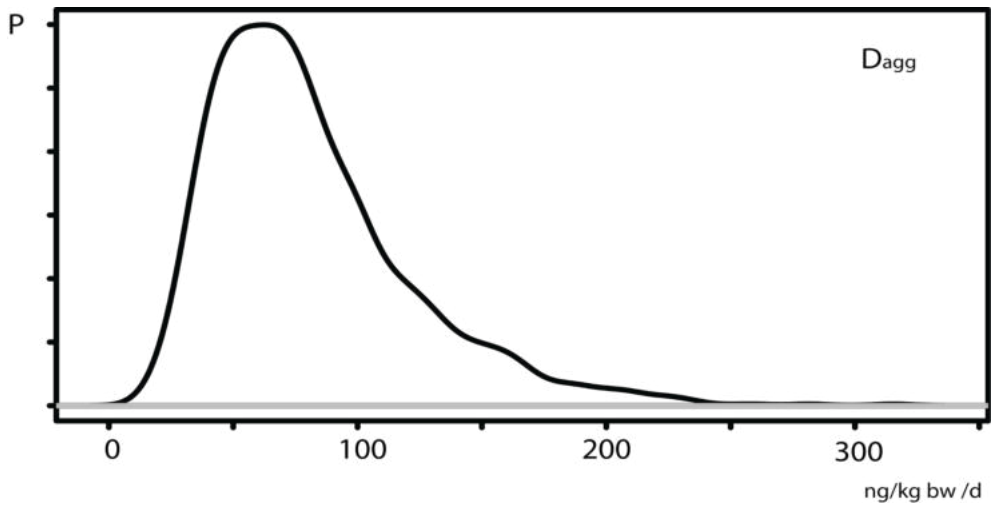

**Uniform distribution**
e.g. only a range is known


**Nam et al., 2014 Resources Processing** https://doi.org/10.4144/rpsj.61.10

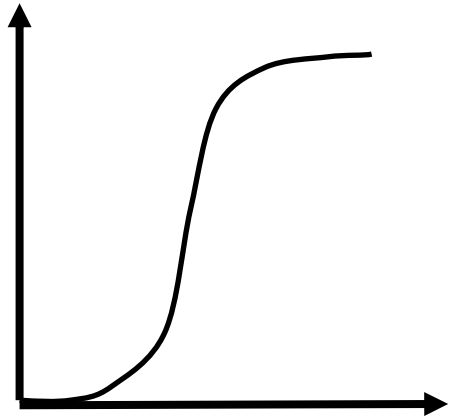
# Individual-based Exposure Modelling



$$D_{xy} = \frac{C_x \cdot q_{xy}}{bw} \cdot r_{xy} \qquad D_{agg} = \sum D_{xy}$$



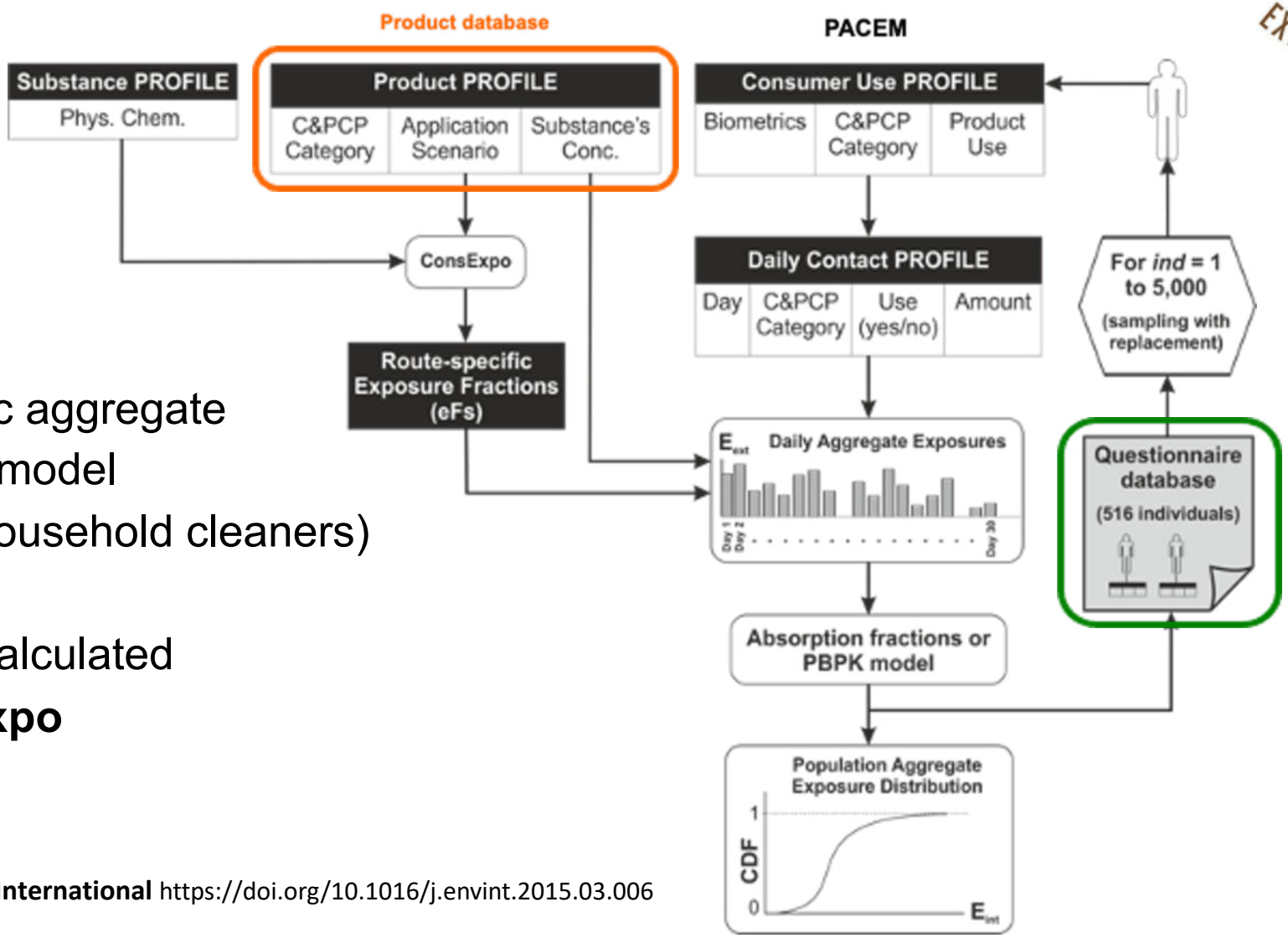

Exposure distribution



Cumulative distribution function (CDF)

Advantage: Improved modelling of co-exposure to multiple products

# Individual-based Modelling in PACEM




**PACEM**: probabilistic aggregate consumer exposure model (for cosmetics and household cleaners)

Exposure fractions calculated externally in **ConsExpo**

**Dudzina et al., 2015, Environment International** https://doi.org/10.1016/j.envint.2015.03.006

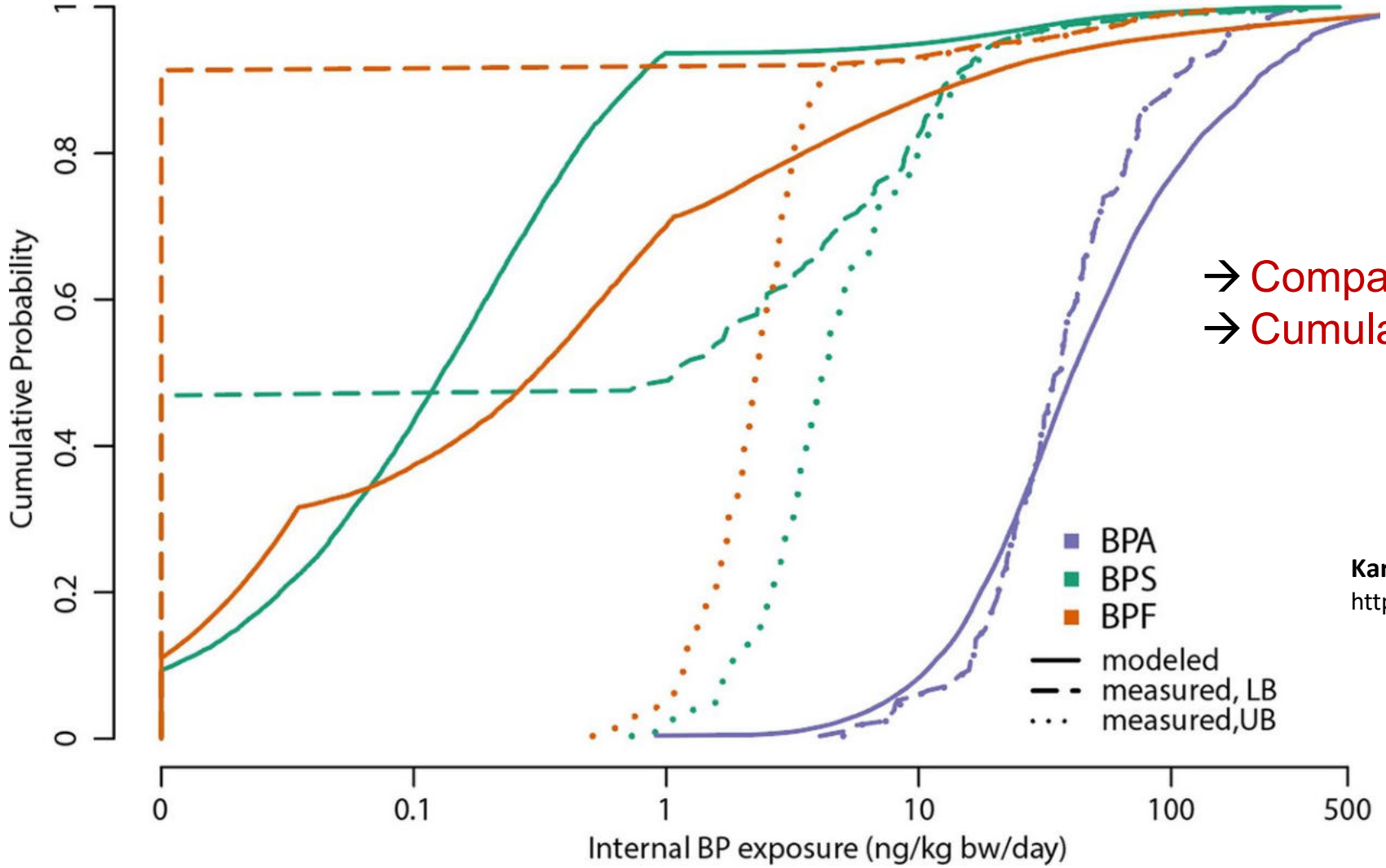
# Use Pattern Parameters for Higher Tier Modelling

**Assessment by questionnaires, interviews, and/or experiments**

- **Frequencies** by questionnaire/interview:
  How often do you use a shampoo
  How often do you wash your hands, etc
- **Use amounts** e.g. by pictures in surveys or by dedicated studies with weighing before and after use

**Image credit: Biesterbos et al., 2013, Food and Chemical Toxicology** https://doi.org/10.1016/j.fct.2012.11.014

# Individual-based Modelling for Bisphenols BPA, BPF, BPS




→ Comparison of BPs
→ Cumulative exposure assessment

**Karrer et al., 2020 Environment International**
https://doi.org/10.1016/j.envint.2019.105397

# Example Models/Tools for Consumer Exposure Modelling

**Methods**

- Technical Guidance Document on Risk Assessment (EU)
- REACh guidance chapters (e.g. R15, R16, R19)

**Models for single exposure (one product, one route: one pathway)**

- ECETOC-TRA (Tier 1)
- ConsExpo (Tier 2)
- LifeLine (Tier 2)
- RiskofDerm etc.

$$D_{xy} = \frac{C_x * q_{xy}}{bodyweight} * r_{uptake}$$

**Models for aggregate exposure (one substance, several pathways), all Tier 2 / Tier 3**

- ConsExpo
- Research models (e.g. ETH Zurich)
- PACEM (cosmetics, household cleaning)
- CRÈME (food, food packaging, cosmetics)

$$D_{agg} = \sum_{x=1}^{n} \sum_{y=1}^{m} D_{xy}$$

# Selecting parameters for Consumer Exposure Modelling

$$D_{xy} = \frac{C_x * q_{xy}}{bodyweight} * r_{uptake}$$

**1. Concentration $C_x$**

- Food: Total Diet studies (representative sampling); literature search
- Cosmetics: SCCS Opinions, literature search
- Other non-food sources: if available national surveys; literature search

**2. Exposure quantities $q_{xy}$**

- Behavioural surveys
- EPA Exposure factors handbook (2011)
- ExpoFacts (European data) → CPDC
- Default values

**EPA Exposure factors handbook:**
https://www.epa.gov/expobox/exposure-factors-handbook-2011-edition
**ExpoFacts:** https://joint-research-centre.ec.europa.eu/scientific-tools-and-databases-0/expofacts-european-exposure-factors-sourcebook_en

**3. Uptake fraction**

- In vitro models (skin, gut)
- Conservative default values (e.g. 50% for cosmetics if no data submitted)

**4. Bodyweight**

- Statistical data (e.g. national data)
- Default values

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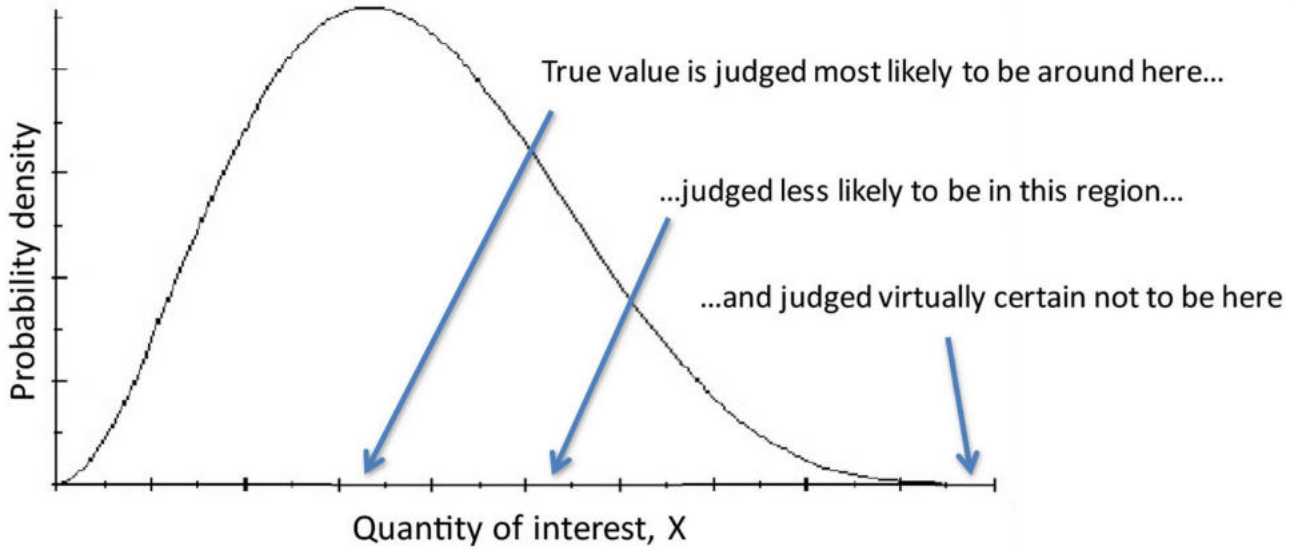
# Uncertainties in Exposure Modelling

- Model uncertainty
- Parameter uncertainty

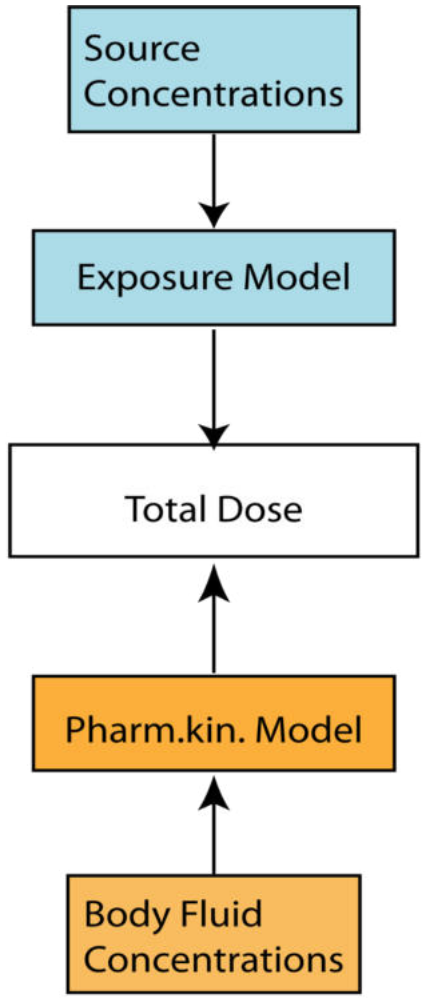



→ Modelling always involves uncertainties, so that it is not possible to determine the true value as a point value. Identifying the extent and influence of uncertainties helps to assess the most likely true value

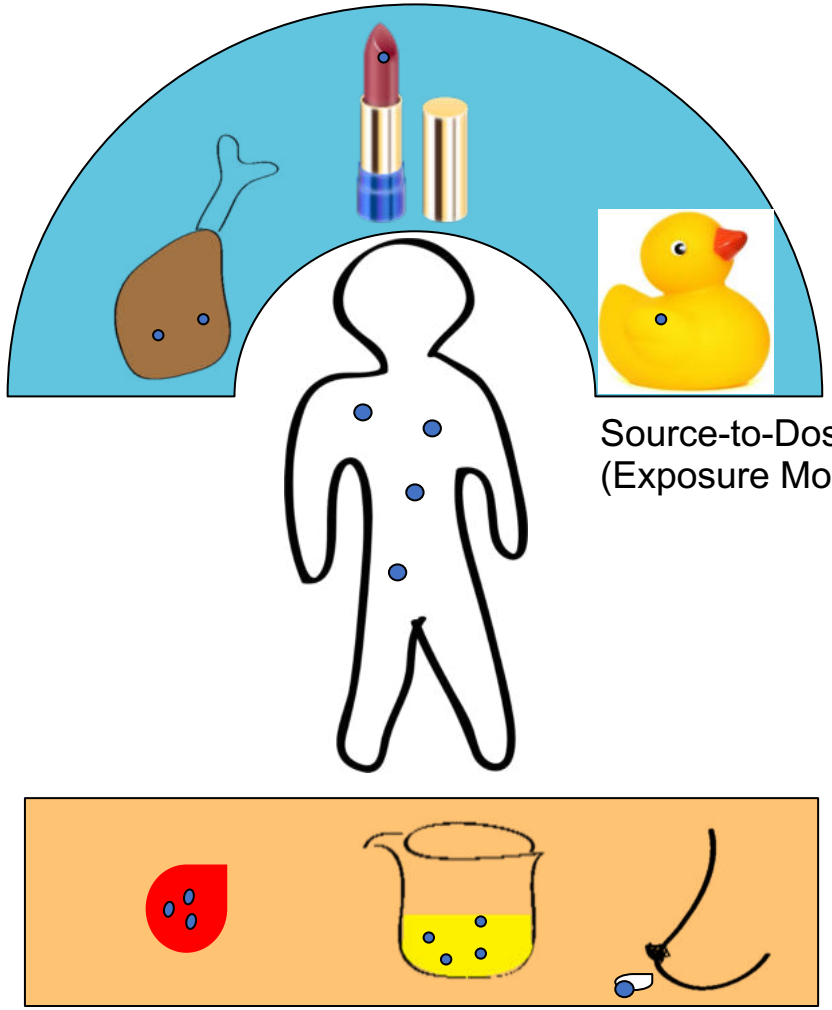
→ Uncertainty assessment is an important part of modelling to reflect how reliable the estimations are

**EFSA, 2018 EFSA-Q-2013-00738** https://doi.org/10.2903/j.efsa.2018.5123

# Validation of Exposure Modelling with an Alternative Assessment Method (Human Biomonitoring - HBM)




*Comparison: Validation/evaluation*



Source-to-Dose Modelling (Exposure Modelling)

HBM

# EFSA Opinion on Bisphenol A: Source-to-dose modelling compared to Humanbiomonitoring

**Table 2**
Comparison of forward and backward exposure modeling estimates for selected age groups (see EFSA CEF Panel, 2015b for all age groups).

| Consumer groups | Average internal exposure (ng kg bw$^{-1}$ d$^{-1}$) | | | | High internal exposure (ng kg bw$^{-1}$ d$^{-1}$) | | | |
|---|---|---|---|---|---|---|---|---|
| Sources | Infants, breast-fed 0–3 m | Toddlers 1–3 y | Children 3–10 y | Women 18–45 y | Infants breast-fed, 0–3 m | Toddlers1-3 y | Children 3–10 y | Women 18–45 y |
| Oral: Dietary | 165 (30[a]) | 375 | 290 | 132 | 600 (80[a]) | 857 | 813 | 388 |
| Oral: Dust | 8.8 | 7.3 | 2.9 | 0.6 | 14.6 | 12.2 | 4.9 | 1 |
| Oral: Toys | 0.2 | 0.01 | NA | NA | 0.6 | 0.01 | NA | NA |
| Inhalation: Air | 0.7 | 0.7 | 0.4 | 0.2 | 1.4 | 1.1 | 0.6 | 0.3 |
| Dermal: Thermal paper | NA | NA | 6.9 | 5.9 | NA | NA | 55 | 54.2 |
| Dermal: Cosmetics | 2.4 | 1.4 | 1.1 | 1.0 | 4.7 | 2.8 | 2.1 | 2 |
| **Multi-route agg. exposure, forward modeling**[b] | **177 (42[a])** | **384** | **301** | **140** | **621 (101[a])** | **873** | **876** | **446** |
| Age group Biomonitoring (BM) | Infants, 1-2 m | Toddlers 3-5 y | Children, 5-10 y | Women 18-52 y | Infants, 1-2 m | Toddlers,3–5 y | Children, 5-10 y | Women 18-52 y |
| **Multi-route agg. exposure, backward modeling** | **<10** | **107** | **49** | **36** | **161** | **676** | **380** | **234** |

Exposure Modelling

Biomonitoring

[a] Formula-fed, 0–6 months, agg.: aggregate, m: months, y: years NA: not applicable, since exposure scenario is not expected.
[b] "Average internal exposure to total BPA summed up over routes for comparison with biomonitoring" according to EFSA, 2015b.

**von Goetz et al.,** Reg Tox Pharm; http://dx.doi.org/10.1016/j.yrtph.2017.02.004

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# Summary

- For aggregate exposure modelling all routes and sources of exposure need to be considered
- For overall risk assessment the calculation of aggregate exposure is necessary, often spans several different legislations
- Tiered approach is followed and depends on factors like level of concern, data availability, model availability etc.
- Validation of models important, but often difficult

# Consequent Modules

**Module 4**:

- Environmental exposure modelling

**Module 5**:

- Validation & evaluation, advantages & limitations, conclusions

**Future training videos**:

- Additional details may be covered by ISES Europe in specialized training videos.

# Thank You!

## We appreciate your participation and attention

## We encourage you to explore other ISES Europe training videos for deeper insights and broader understanding

Access all videos via: **https://ises-europe.org/**

# Further Reading

**Exposure factors handbook**

*US Environmental protection agency (EPA)*

https://www.epa.gov/expobox/exposure-factors-handbook-2011-edition

**Uncertainty and data quality in exposure assessment (2008)**

*WHO/IPCS  Harmonization project*

https://www.who.int/publications/i/item/9789241563765

**EFSA Guidance on Uncertainty Analysis in Scientific Assessments (2018)**

*EFSA Scientific Committee*

https://doi.org/10.2903/j.efsa.2018.5123

**Aggregation of food and non-food sources for Bisphenol A (2016)**

Von Goetz N et al.

http://dx.doi.org/10.1016/j.yrtph.2017.02.004

**The probabilistic exposure model PACEM used in a tiered approach (2015)**

Dudzina et al.

https://doi.org/10.1016/j.envint.2015.03.006