Exposure based safety assessment of cosmetics

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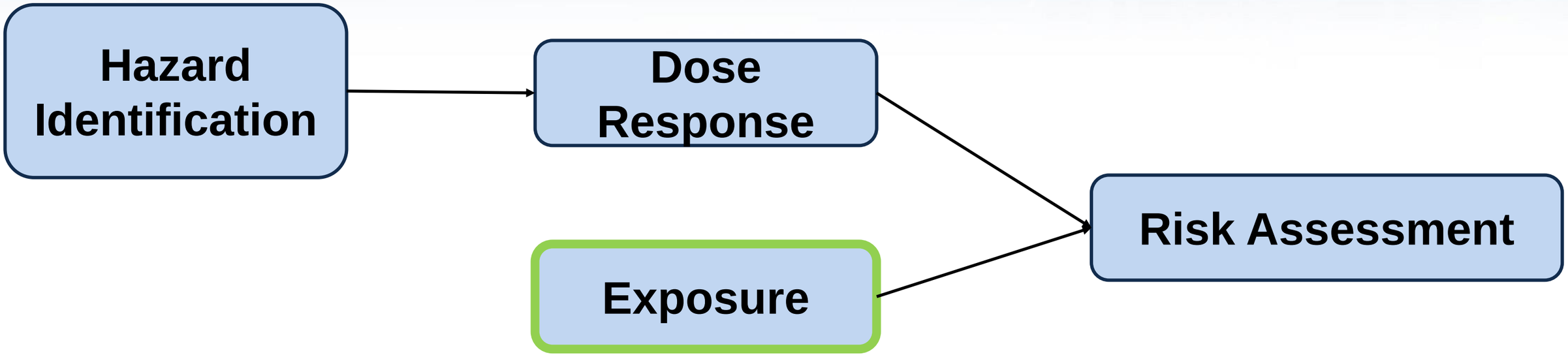
Human Safety
Ensuring Safe Products

AFSA
Non-Animal Cosmetic Safety Assessment Workstream

Risk Assessment Framework



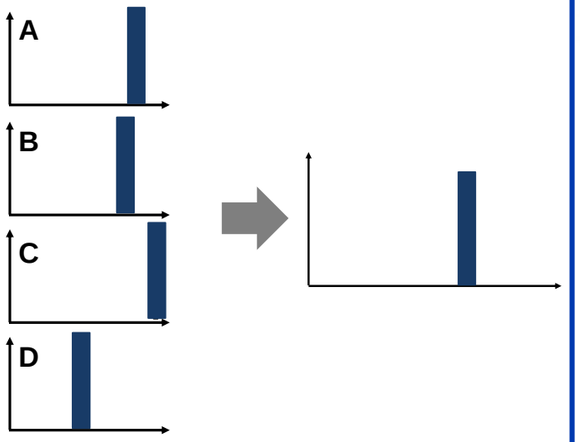
Exposure assessment is the process of specifying the exposed population, identifying potential exposure routes, and measuring or estimating the magnitude, duration and frequency of exposure to a chemical.

Tiered Exposure Assessments

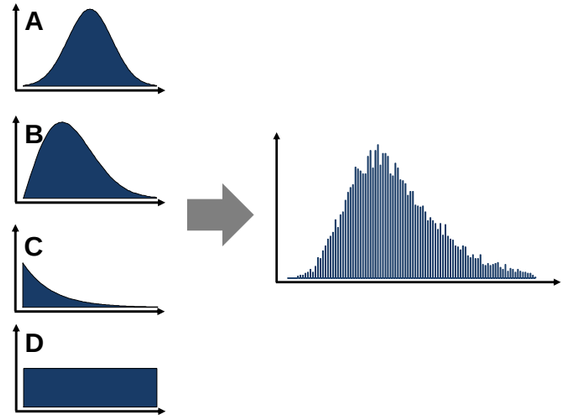
External

Single product

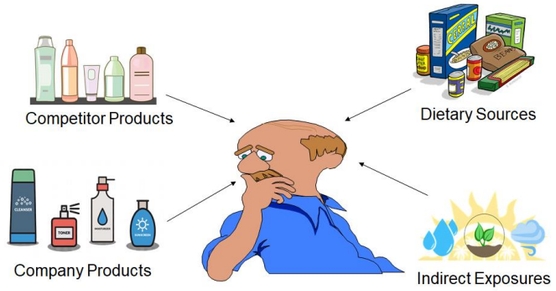
Deterministic



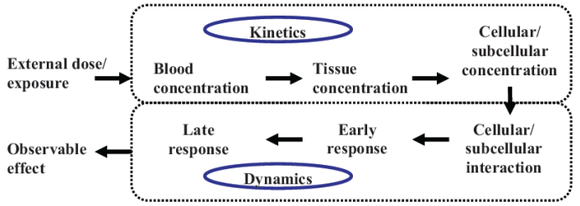
Probabilistic



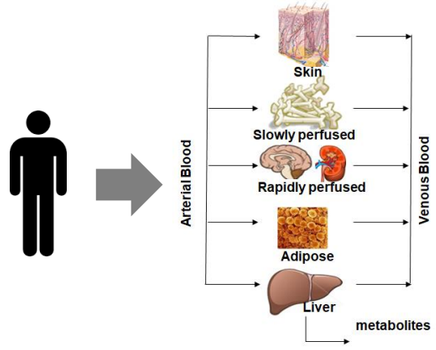
Aggregate



Internal



Physiologically Based Kinetics



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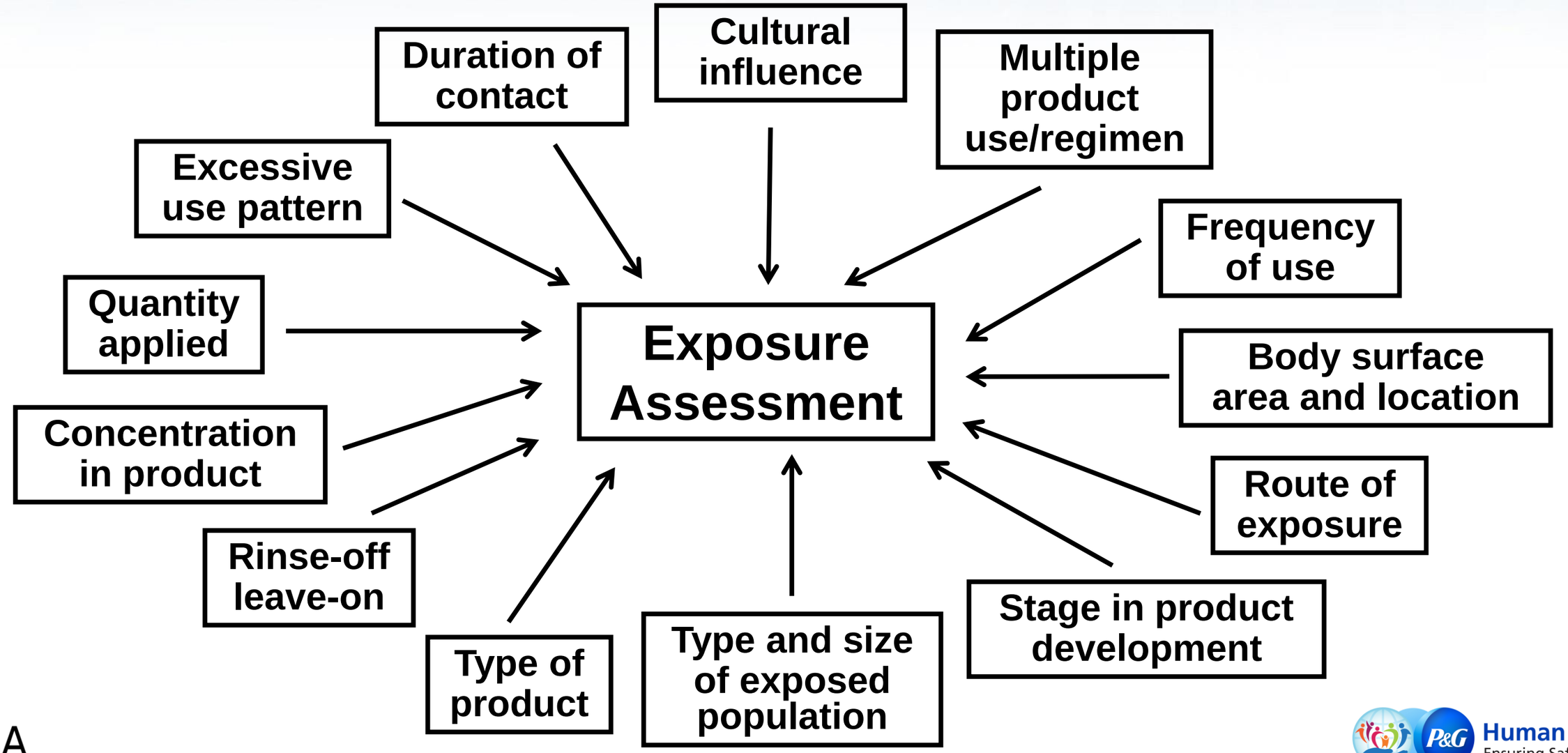
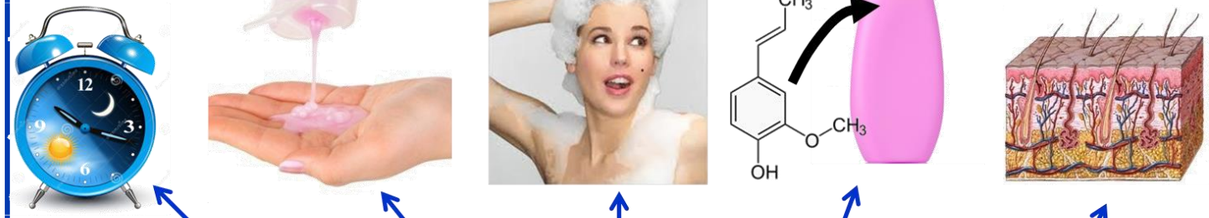
Exposure is Based on Habits and Practices for the Product



Exposure Algorithm Defines Data Needs

Systemic exposure (mg/kg/day)



$$Exp = \frac{Frequency \times Amount \times Retention \times Concentration \times Penetration}{Bodyweight}$$

Local exposure (ug/cm2/day)

$$Exp = \frac{Frequency \times Amount \times Retention \times Concentration}{Surface\ Area}$$

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Resources for H&P Data and Exposure assessment tools

Examples of External Data Sources

- National Health and Nutrition Examination Survey (NHANES)
- US EPA Exposure Factors Handbook
- ECETOC Human Exposure Assessment Tools Database (HEATDB)
  - Also contains list of external tools

    https://www.rivm.nl/en/consumer-exposure-to-chemical-substances/exposure-models
- SCCS Notes of Guidance
- RIVM Cosmetics Fact Sheet

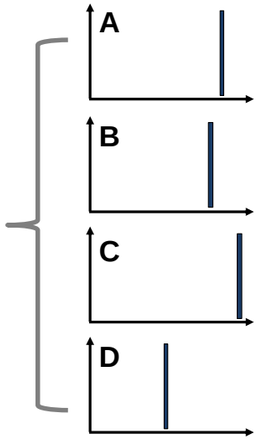
Product type	*Estimated daily amount applied* q_x *(g/d)*	*Relative daily amount applied*[1] q_x *(mg/kg bw/d)*	*Retention factor*[2] F_{ret}	*Calculated daily exposure* $E_{product}$ *(g/d)*	*Calculated relative daily exposure*[1] $E_{product}$ *(mg/kg bw/d)*
Bathing, showering					
Shower gel	18.67	279.20	0.01	**0.19**	**2.79**
Hair care					
Shampoo	10.46	150.49	0.01	**0.11**	**1.51**
Hair styling products	4.00	57.40	0.10	**0.40**	**5.74**
Skin care					
Body lotion	7.82	123.20	1.00	**7.82**	**123.20**
Face cream	1.54	24.14	1.00	**1.54**	**24.14**
Hand cream	2.16	32.70	1.00	**2.16**	**32.70**

Deterministic vs Probabilistic Exposure Approaches

$$Exp = \frac{Frequency \times Amount \times Retention \times Concentration \times Penetration}{Bodyweight}$$

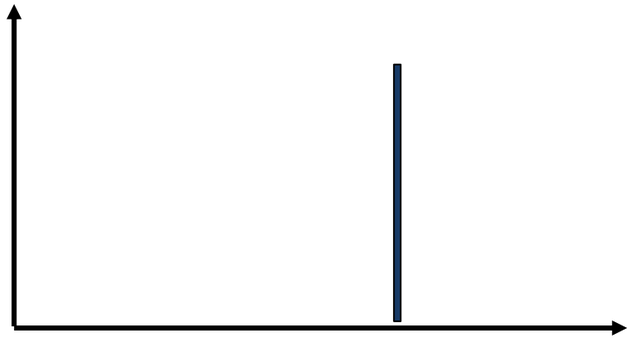
Deterministic Approach

Input parameters



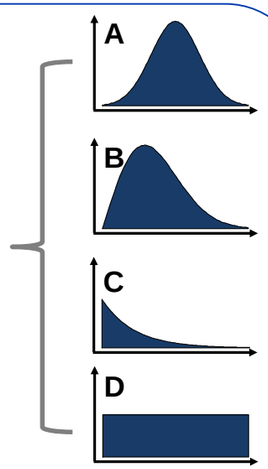
Exposure model

Exposure Estimate



Probabilistic Approach

Input parameters

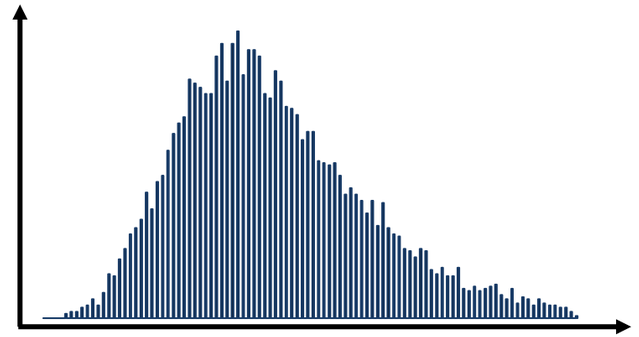


Exposure model

+

Statistical model

Exposure Estimate



Deterministic vs Probabilistic Exposure Approaches

	Deterministic	Probabilistic
Pros	Less data intensive Easier to conduct and interpret Approach commonly accepted	Takes into account all information & scenarios in one go Provides an estimate of the probability Allows more refined risk decisions
Cons	Large amounts of information are overlooked Point estimate is not necessarily the central tendency Often based on (realistic) worst case	More complex and resource intensive Risk management and decision making is more complex Draws focus to the (less likely) extremes of the distribution

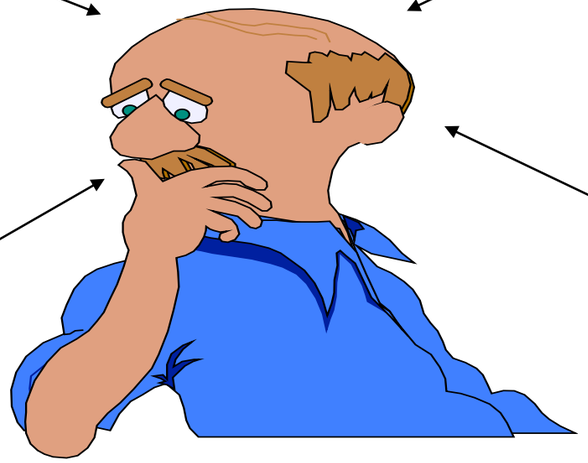
Aggregate Exposure

Considers ALL sources of exposure to the chemical

- Other products marketed within a company (within and across product categories)
- Other products marketed by competitors (including those in other categories)
- Indirect exposures via environmental media

Competitor Products

Dietary Sources



Company Products

Indirect Exposures

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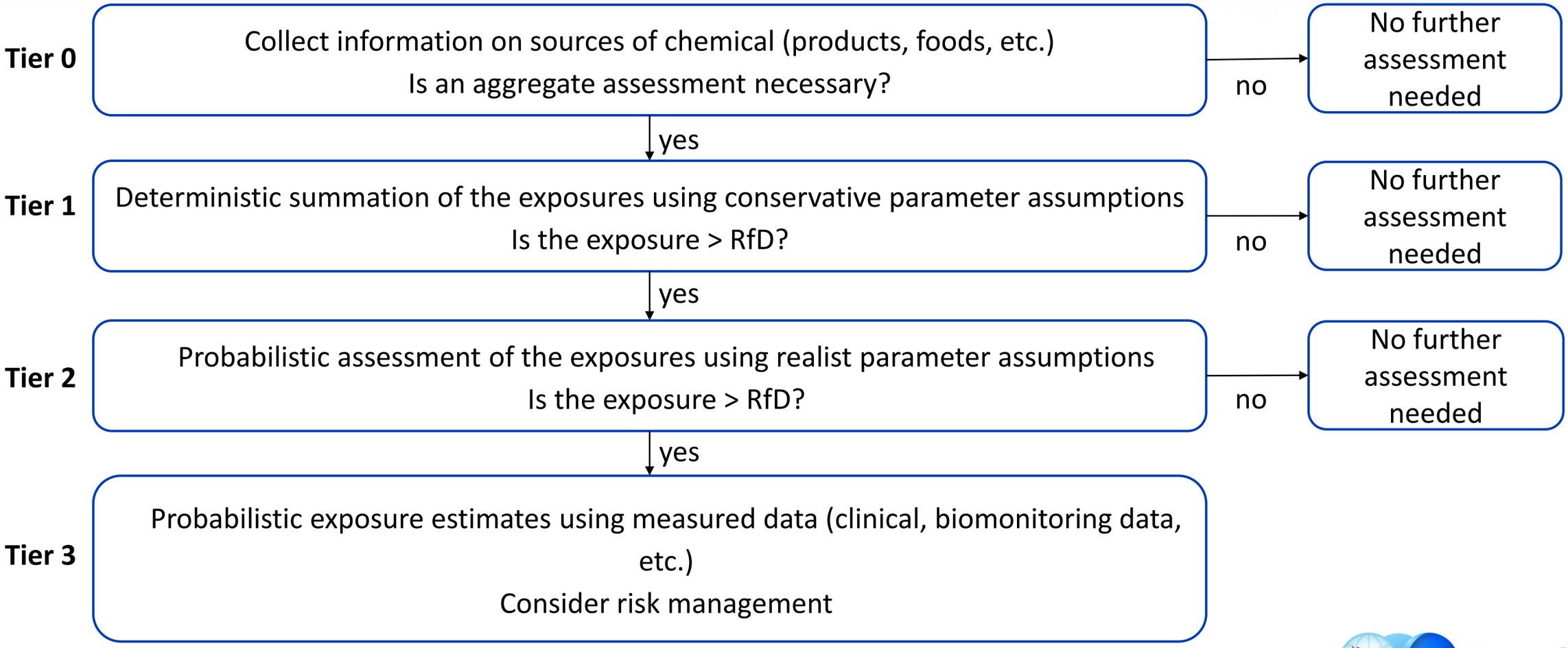
Tiered Aggregate Exposure



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Internal Exposure

- Toxicity depends on the concentration of reactive species reaching target site
- Pharmacokinetics (PK) determines the internal exposure for a chemical
- An understanding of PK enables a better understanding of overall toxicological profile and risk assessment
- PK is an opportunity to refine a risk assessment

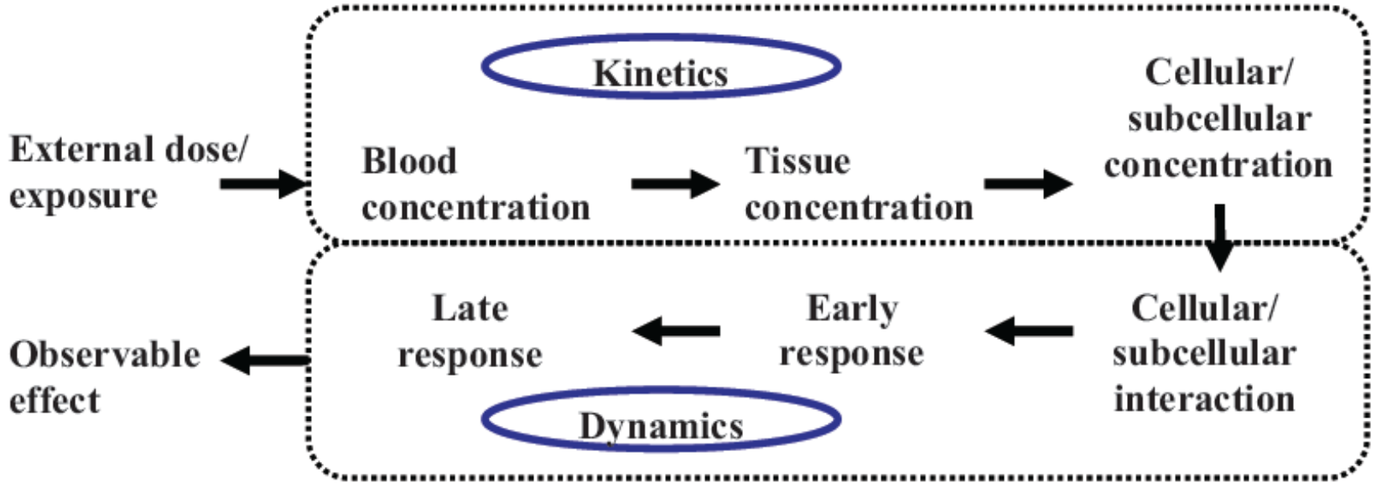
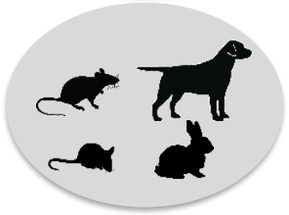
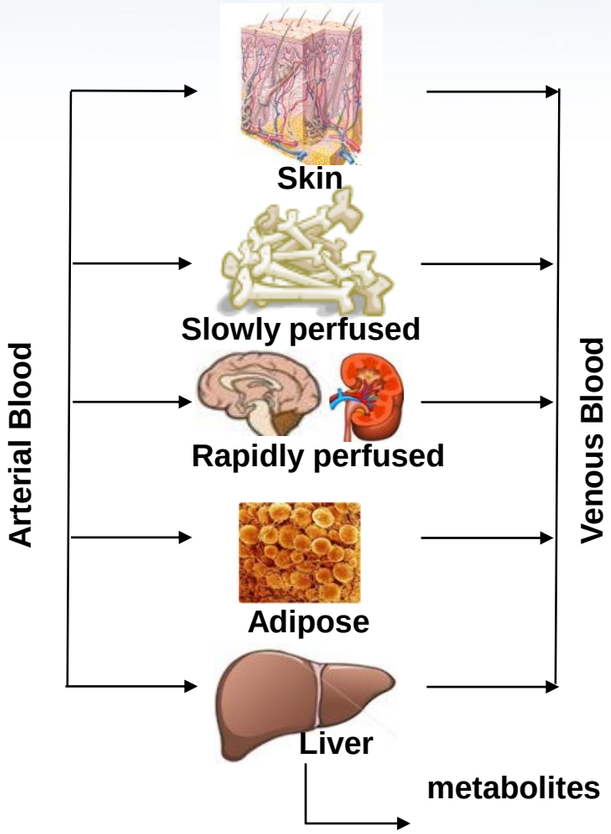


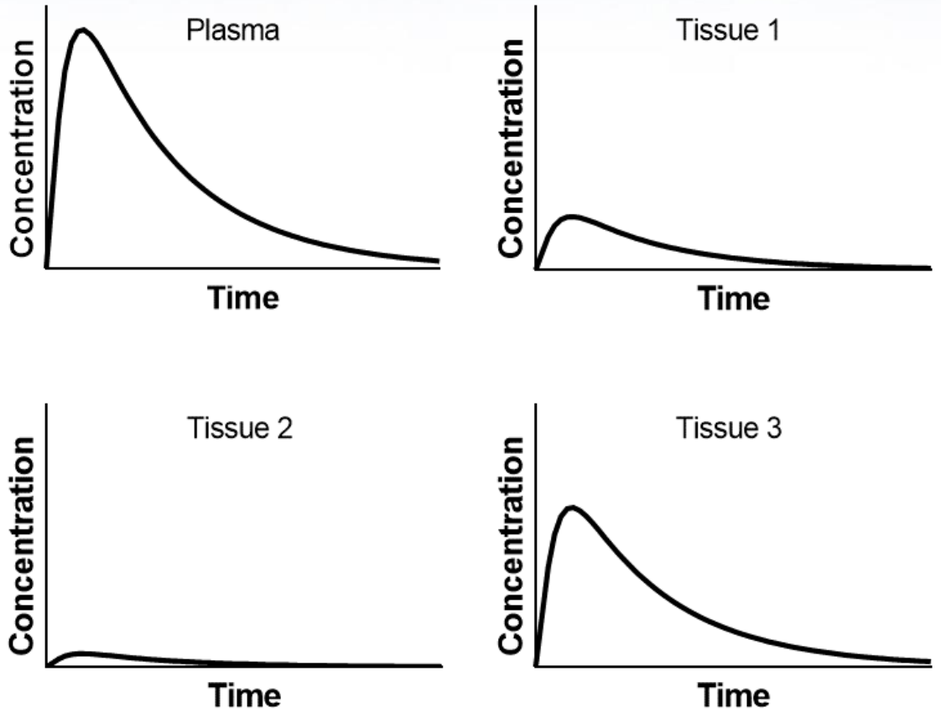
Figure A1: Schematic representation of some key elements of the MOA for the critical dose–response relationship for a chemical.

Source: IPCS (2010) Characterization and application of physiologically based pharmacokinetic models in risk assessment

Physiologically Based Kinetic (PBK) Modeling







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Building Blocks of a PBK Model

Organism properties

Anatomy & physiology
- Organ volumes
- Tissue composition
- Blood flow rates

Chemical properties

Phys-chem
- Lipophilicity
- Molecular weight
- pKa/pKb

Chemical biological properties
- Plasma protein binding
- Metabolism
- Permeability
- Partition coefficients

Exposure scenario

Administration
- Study design
- Dose
- Frequency

Exposure route

Formulation

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Summary

- Risk = Hazard x Exposure
- Exposure is an important part of a human safety risk assessment
- A tiered approach can be used for the exposure assessment, starting with conservative default assumptions and moving towards refined more realistic conditions
- Exposure calculations can estimate external and/or internal exposures

- “The dose makes the poison” – *Parcelsus*