CONSUMER EXPOSURE IN INHALATION RISK ASSESSMENT

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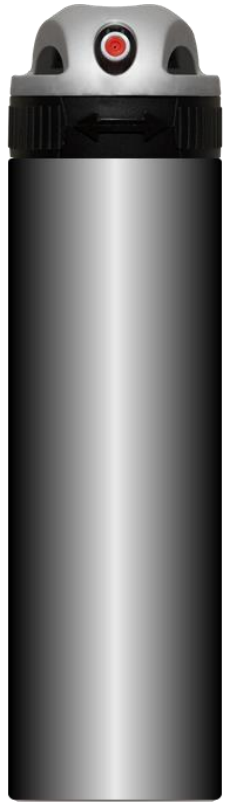
EVERYDAY LIFE INCLUDES THE USE OF SPRAY PRODUCTS

Household cleaning products



Anti-perspirant/ deodorant aerosols

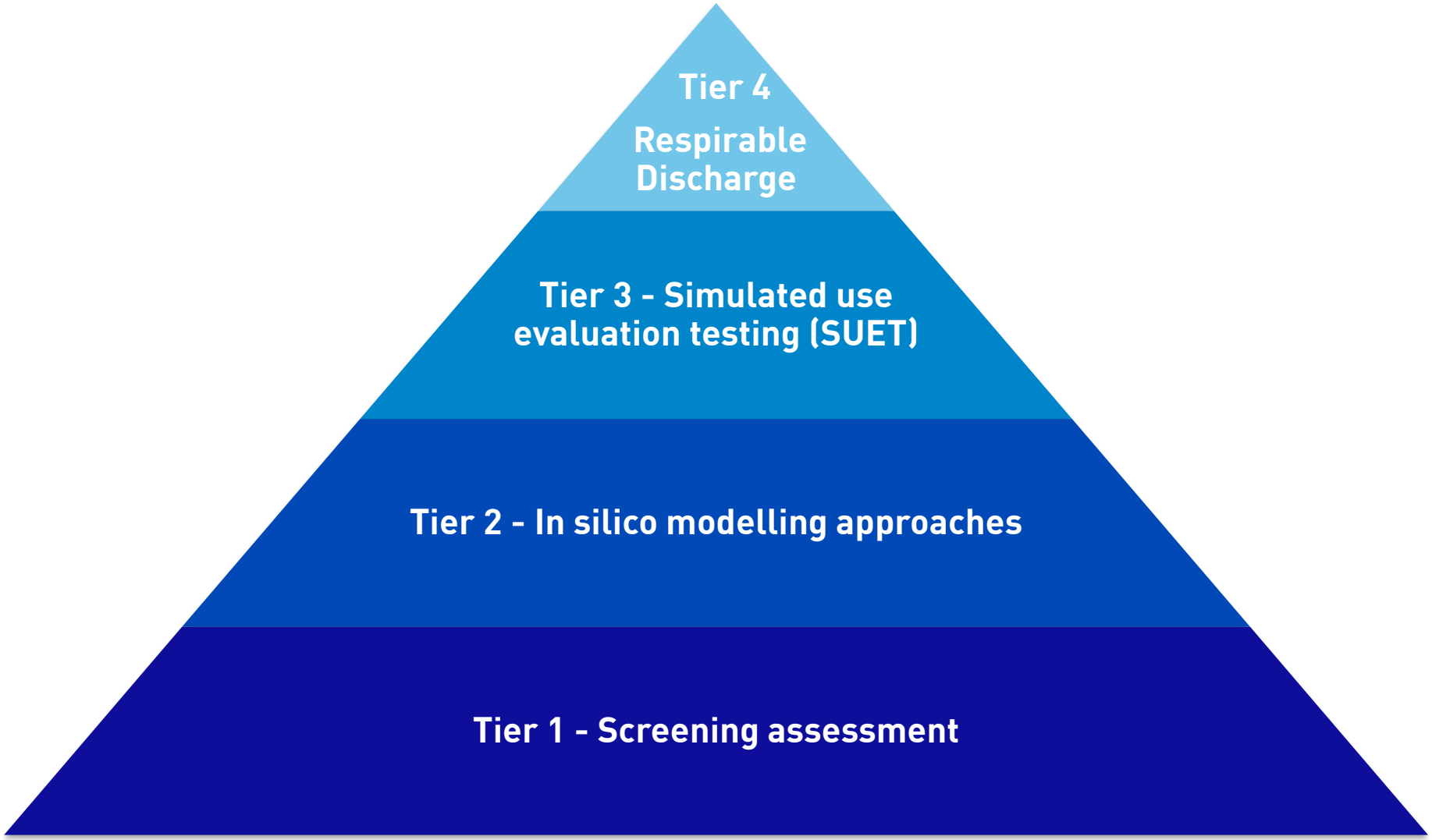
Hairsprays (pump and aerosol)

CAN WE USE AN INGREDIENT SAFELY?

- Can we safely use x% of ingredient y in product z ?

Inhalation exposure depends on product type and habits & practices

EXPOSURE ASSESSMENT- TIERED APPROACH



Steiling et al., 2014.Principle considerations for the risk assessment of sprayed consumer products. Toxicology Letters 227 (2014) 41–49

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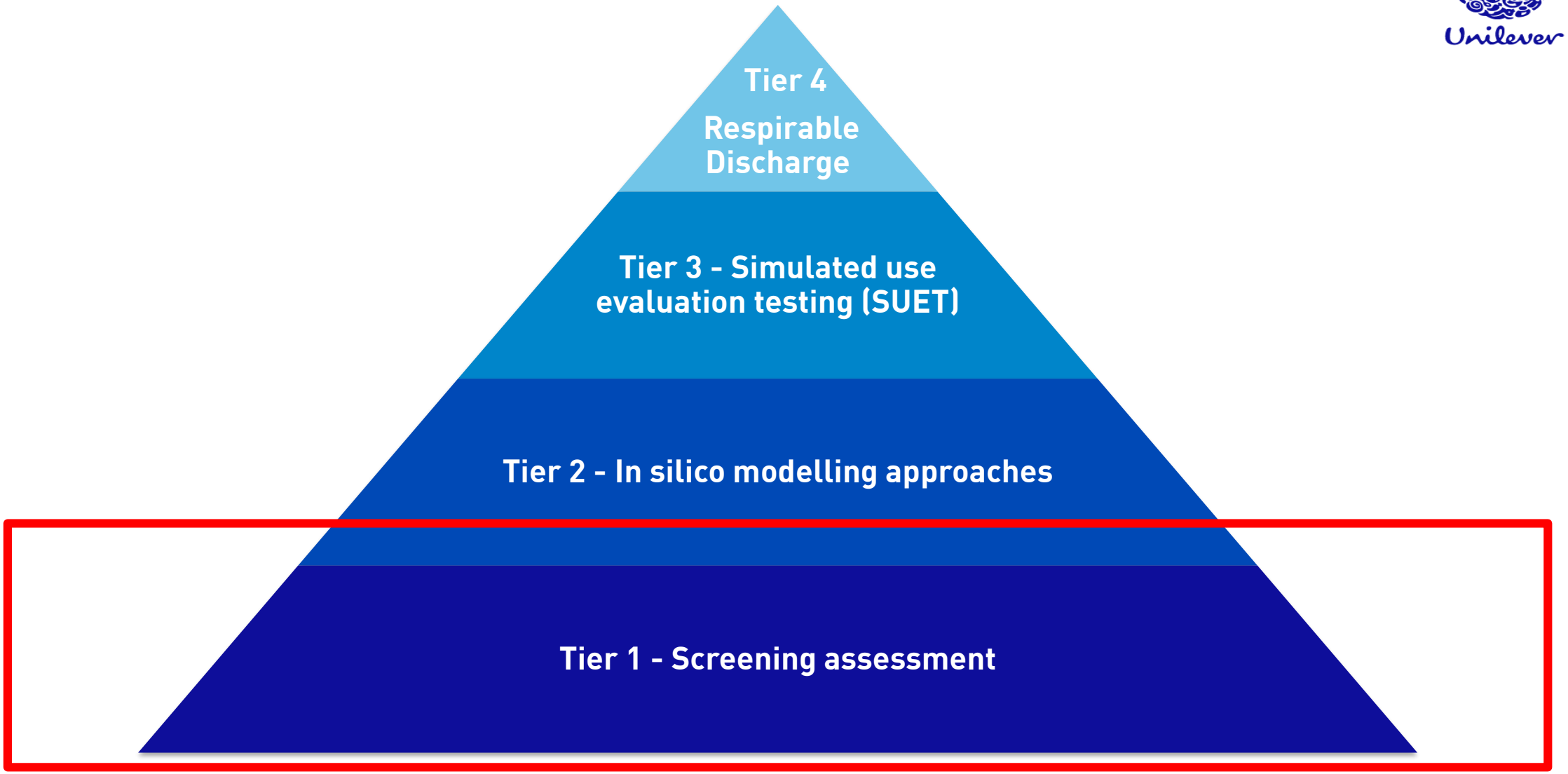

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TIER 1-SCREENING ASSESSMENT

This is a conservative approach that assumes that 100% of the substance in the consumer product or article will be released at once and homogenously into the room and there is no ventilation. The duration of exposure is 24 hours and all released material is 100% inhalable

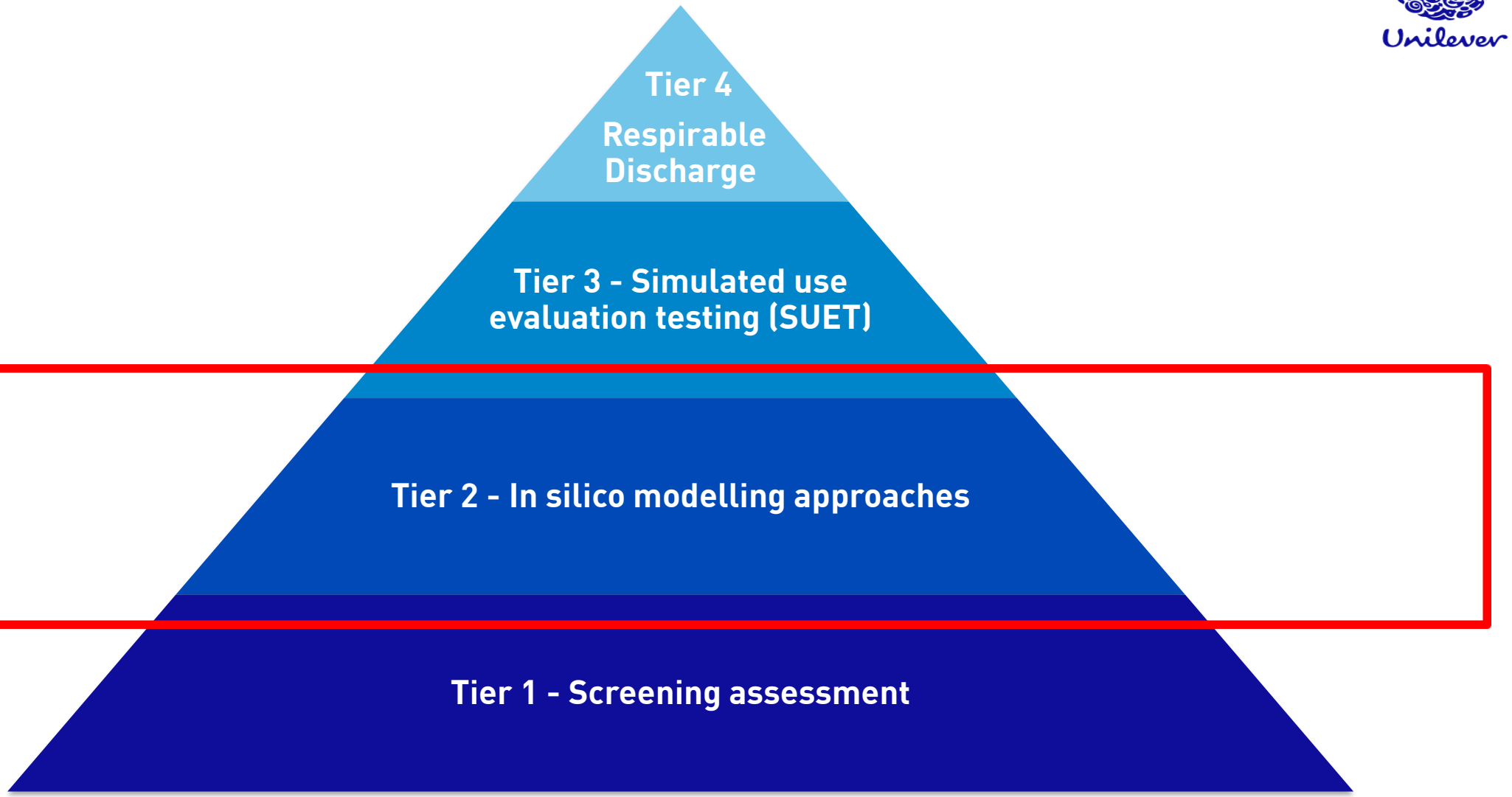
$$\text{Tier 1 Exposure} = \frac{\text{Weight of Ingredient in the Spray Formulation}}{\text{Volume}} \left[\frac{mg}{m^3}\right]$$

- Spray rate (g/s)
- % ingredient in formulation
- Duration of exposure

- Volume:
  - Room volume for a product sprayed away from consumer (e.g. air freshener); or
  - Consumer's breathing zone (2 m^3 for products sprayed at body and 1 m^3 sprayed at the head

1. Guidance on Information Requirements and Chemical Safety Assessment Chapter R.15: Consumer exposure assessment Version 3.0 - July 2016
2. Steiling et al., 2014. : Principle considerations for the risk assessment of sprayed consumer products. Toxicology Letters 227 (2014) 41–49

EXPOSURE ASSESSMENT



TIER 2-IN SILICO MODELLING APPROACHES TO INHALATION EXPOSURE

One-box
- BAMA/FEA
- **RIVM ConsExpo**
- BAuA SprayExpo

Two-box
- **RIFM 2-Box Indoor Air dispersion model**

Airborne concentration and internal dose (simple assumptions)

Multiple Path Particle Deposition (MPPD)

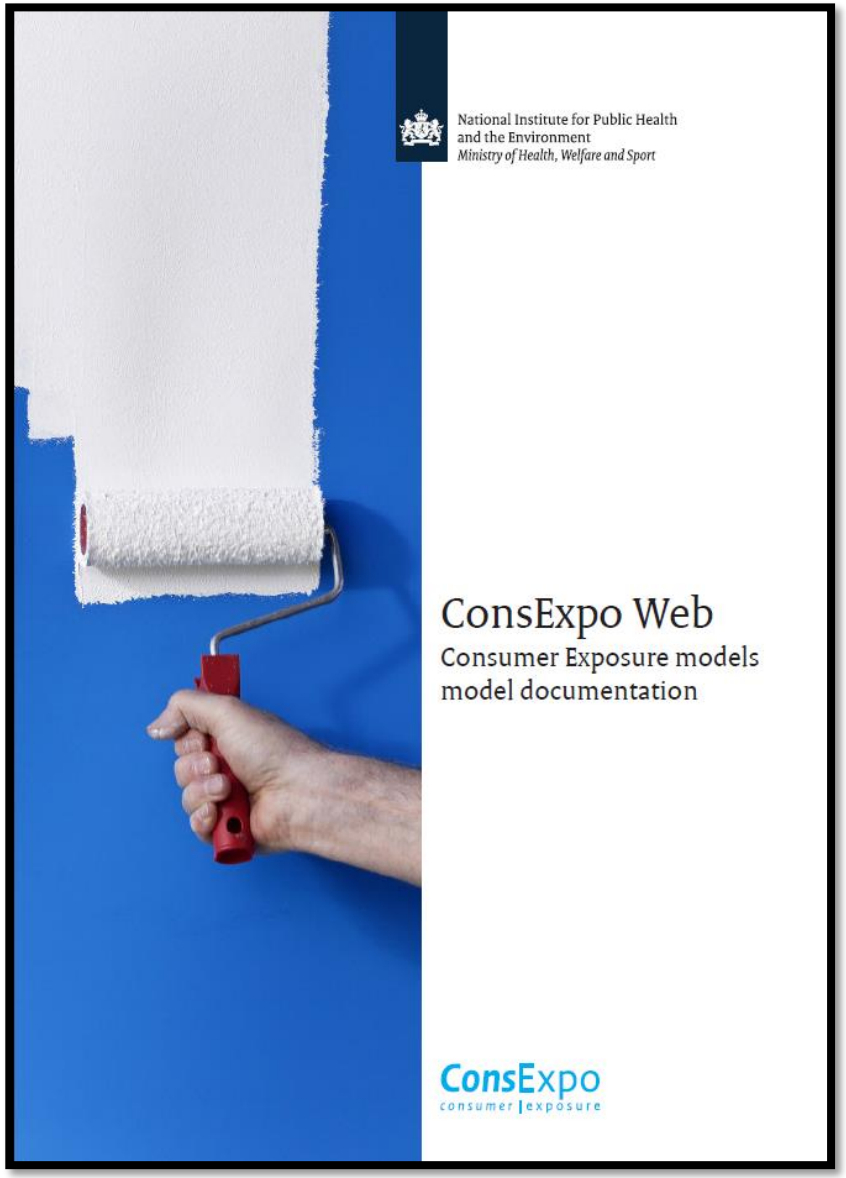
Computational Fluid Dynamics (CFD)

Airway deposition and clearance

Increasing complexity

PBPK modelling

Systemic Exposure



https://www.rivm.nl/en/Topics/C/ConsExpo

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Mini review

Principle considerations for the risk assessment of sprayed consumer products

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ABSTRACT

In recent years, the official regulation of chemicals and chemical products has been intensified. Explicitly for spray products enhanced requirements to assess the consumers'/professionals' exposure to such product type have been introduced.

In this regard the Aerosol-Dispensers-Directive (75/324/EEC) with obligation for marketing aerosol dispensers, and the Cosmetic-Products-Regulation (1223/2009/EC) which obliges the insurance of a safety assessment, have to be mentioned. Both enactments, similar to the REACH regulation (1907/2006/EC), require a robust chemical safety assessment. From such assessment, appropriate risk management measures may be identified to adequately control the risk of these chemicals/products to human health and the environment when used.

Currently, the above-mentioned regulations lack the guidance on which data are needed for preparing a proper hazard analysis and safety assessment of spray products.

Mandatory in the process of inhalation risk and safety assessment is the determination and quantification of the actual exposure to the spray product and more specifically, its ingredients. In this respect the current article, prepared by the European Aerosol Federation (FEA, Brussels) task force "Inhalation Toxicology", intends to introduce toxicological principles and the state of the art in currently available exposure models adapted for typical application scenarios. This review on current methodologies is intended to guide safety assessors to better estimate inhalation exposure by using the most relevant data.

Contents

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2-Box Indoor Air Dispersion model

Developed by the Research Institute for Fragrance Materials (RIFM) for use by their members

https://www.rifm.org/events-detail.php?id=95

RIVM CONSEXPO MODEL

One-box models are based on the assumption that particles/droplets are homogeneously distributed within the volume of the room or cloud. Loss of particles/droplets from air occurs by ventilation and gravitational precipitation.

3 different models available:

- Exposure to Vapour;
- Exposure to Spray;
- Emission from Solid Materials

→

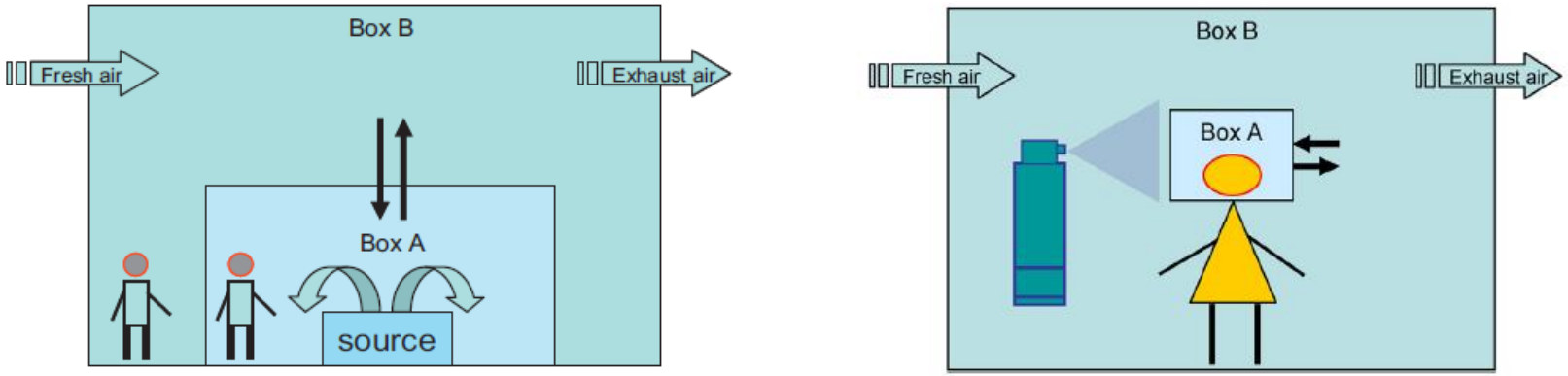
- Describes inhalation exposure to non-volatile or slowly evaporating compounds present in droplets that are released from an aerosol or trigger spray
- The model assumes only particles with a diameter < 10 µm are small enough to reach the alveolar region

Key outputs of the model: →

- **Air concentration (mg/m^3):** mean event concentration
- **External event dose (mg/kg)**: the amount potentially absorbed by inhalation per kg body weight during one event

https://www.rivm.nl/en/Topics/C/ConsExpo

2-BOX INDOOR AIR DISPERSION MODEL DEVELOPED BY RIFM

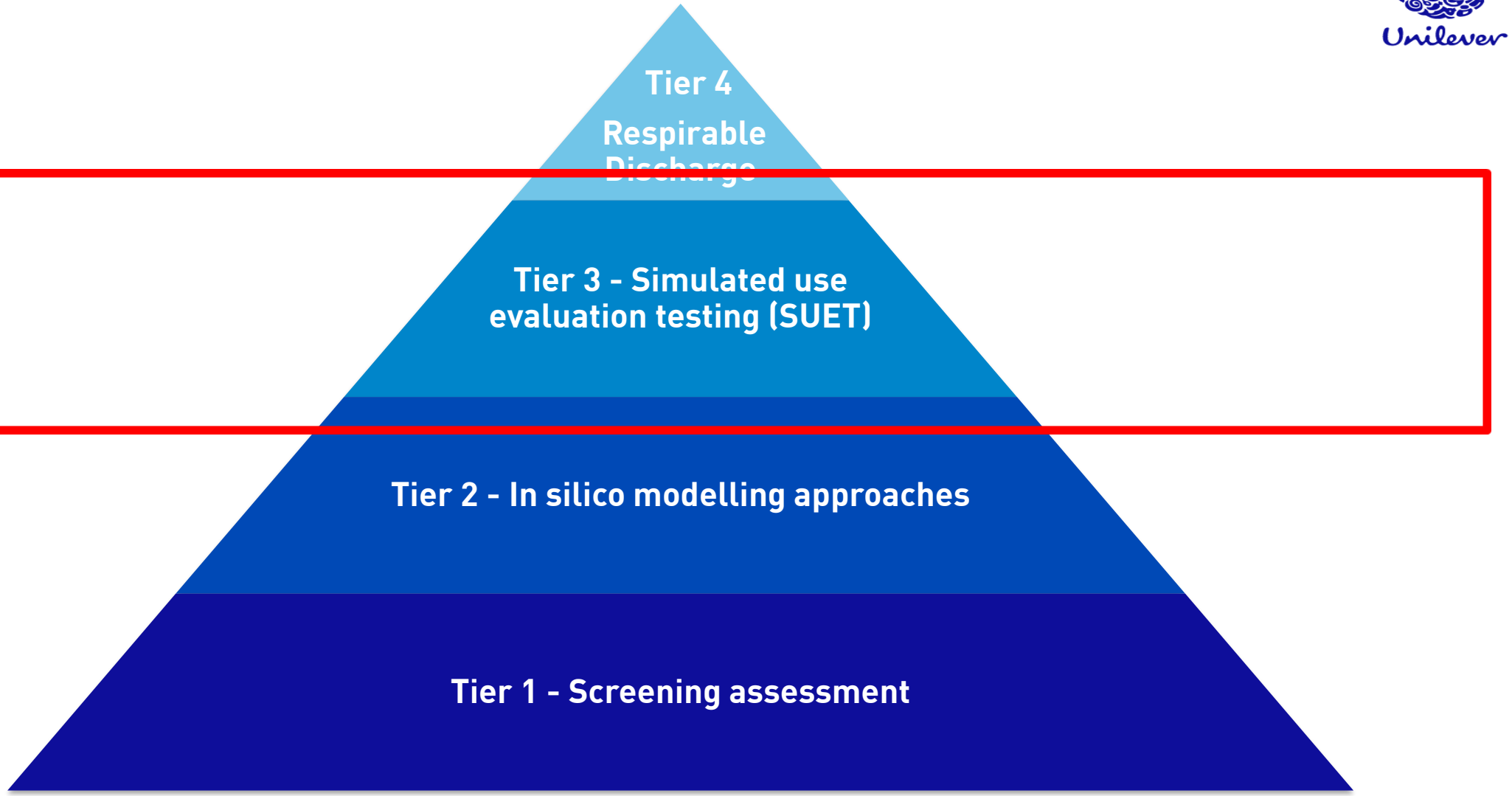


Images from: Steiling et al., 2014. Principle considerations for the risk assessment of sprayed consumer products. Toxicology Letters 227 (2014) 41–49

- Characterizes the homogenously dispersion of a single chemical inside two connected enclosed "boxes" and **calculates air exposure concentrations (mg/m^3) or total cumulative exposure (mg)** among others.
- The key parameters used to determine amount inhaled are:
  - Ingredient concentration in the individual boxes
  - Time spent in each box
  - Physiological minute ventilation of the exposed individual
  - Room volumes and airflow rates between boxes

http://www.rifm.org/uploads/Inhalation%20Modeling%202-Box%20Webinar%201.17.2012.pdf

EXPOSURE ASSESSMENT



TIER 3- SIMULATED USE EVALUATIONS

Estimation of.....

Respirable dose (RDose) (µg/sec spray)

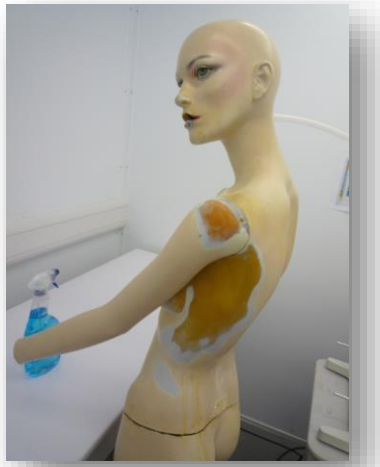
.....mass of non-volatile respirable material (<7µm) that has potential to be deposited in deep lung.....

Inhalable dose (IDose) (µg/sec spray)

.....mass of non-volatile inhalable material (<20µm) that has potential to be deposited anywhere in respiratory tract.....

Inhalable concentration (IConc)

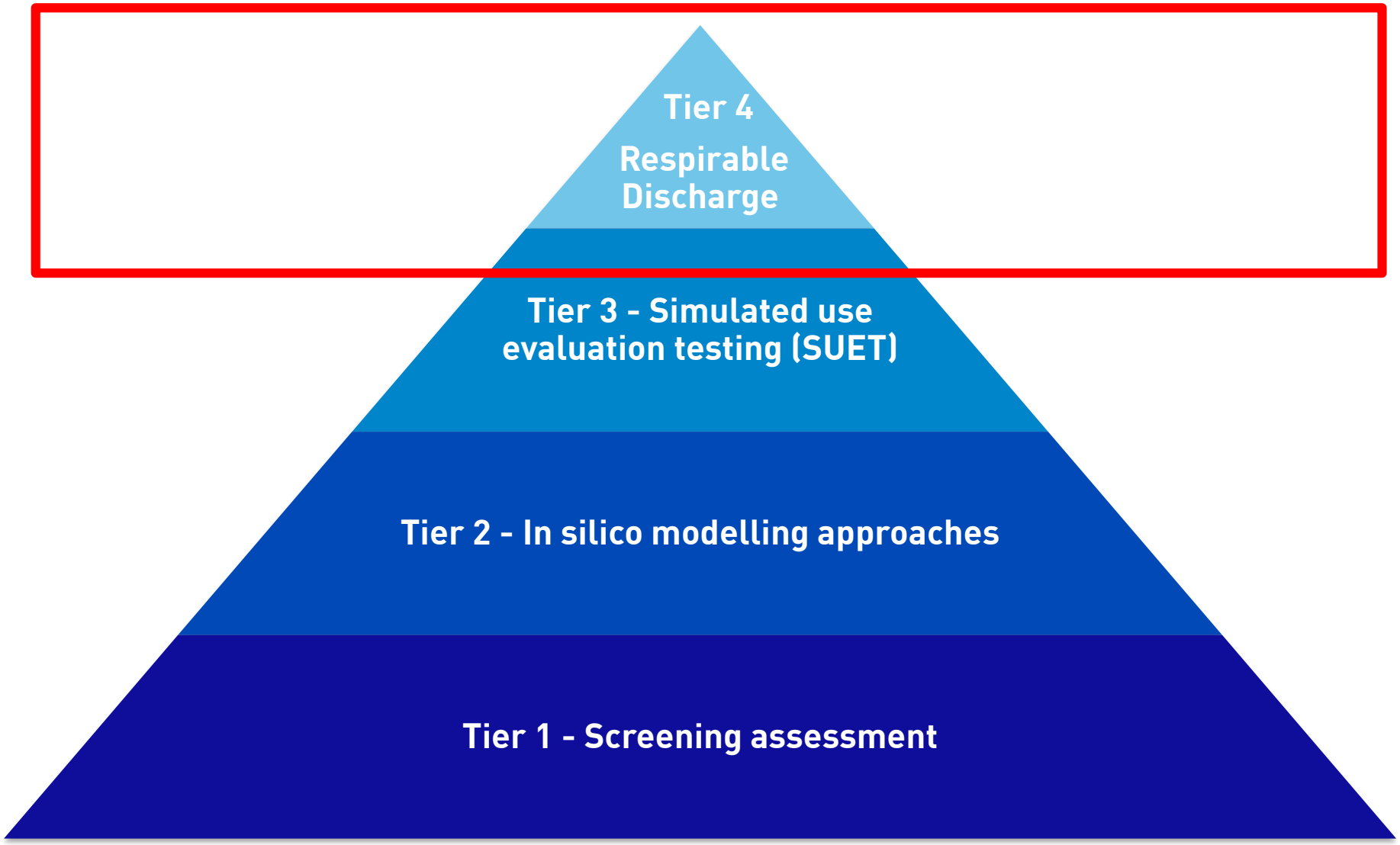
.....concentration (µg/m^3) of non-volatile inhalable material (<20µm) that has potential to be deposited anywhere in respiratory tract.....



SEAC

Tulum L et al., 2018. Airborne protein concentration: a key metric for type 1 allergy risk assessment-in home measurement challenges and considerations. 26;8:10 Clin Transl Allergy.

EXPOSURE ASSESSMENT



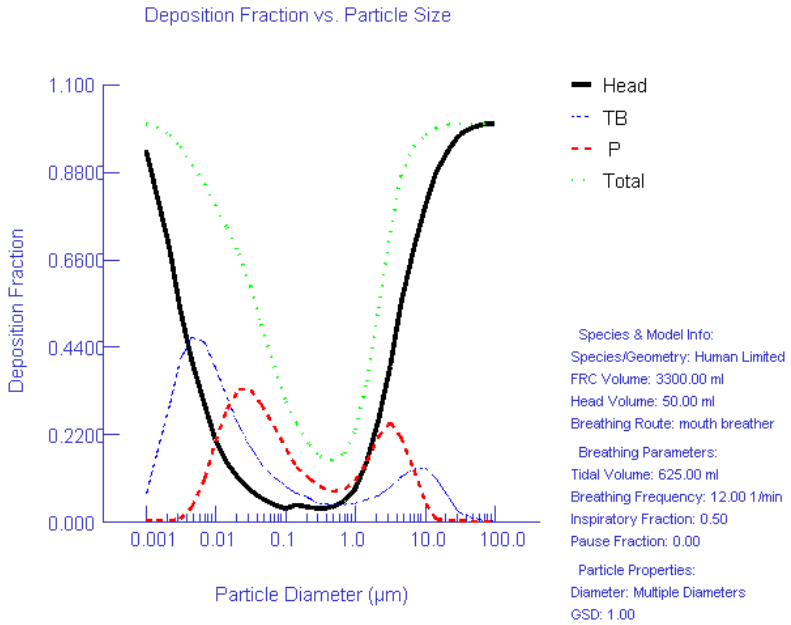
TIER4- RESPIRABLE DISCHARGE (RDIS)

- Estimation of mass of any individual ingredient (<7μm) that has potential to be deposited in deep lung if inhaled
- Used to refine Respirable dose
- Ingredient specific

Particles <7μm collected on impaction filter and sent for chemical analysis

1. Airborne concentration from consumer exposure scenario (screening assessment, in silico models, simulated use test)

2. Respiratory tract deposition by region (e.g MPPD)



3. Risk assessment depends on ingredient regional deposition and dosimetry:

- What are the possible **adverse outcomes of concern**? Different **toxicities** corresponding to **different regions of the lung**?
- What are the **most relevant cell types** to study the endpoint of concern?
- What are the key **in vitro dosimetry considerations** (p.e exposure device ≠ for powder vs liquid particles, particokinetics etc.)

CONCLUSIONS

- Understanding consumer exposure is key for the risk assessment of inhaled materials
- Simple models provide a good estimation of inhaled exposure in most instances…
- … However for certain ingredients and for novel exposure scenarios experimental approaches are needed
- Understanding the regional deposition of the material is key for designing the appropriate *in vitro* experiments for mode of action identification and risk characterisation.

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