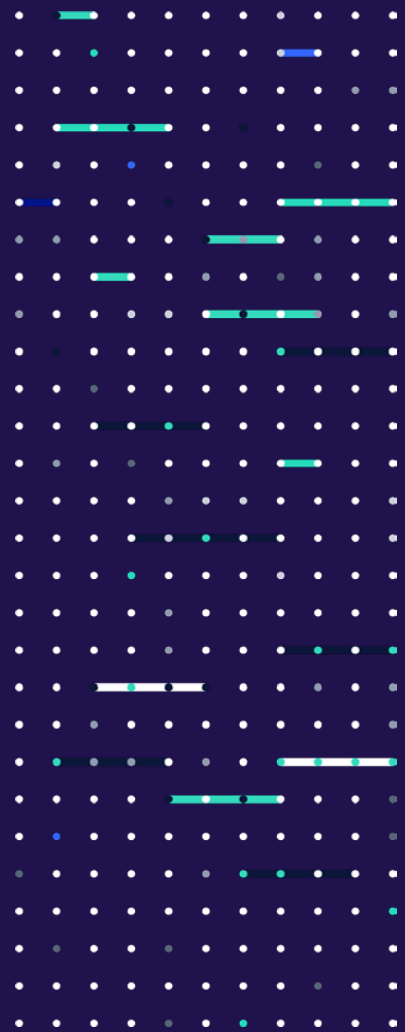


▶ **Creme Global**

*Novel and Integrated Approaches to modelling aggregate exposures to chemicals across different conditions of use and routes of exposure*

TERA Workshop: Beyond Science and Decision Making, Feb 19 2020

**Dr. Clare Thorp, SVP North America**  
Creme Global  
[clare.thorp@cremeglobal.com](mailto:clare.thorp@cremeglobal.com)





# About Us

We are a Scientific Modelling, Data Analytics and Computing Company.

# Our Mission

To enable better decision-making in a complex world.



# Some of our clients

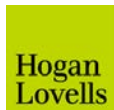
## Services

## Food

## Cosmetics & Fragrances

## Chemical

## Gov & Academia

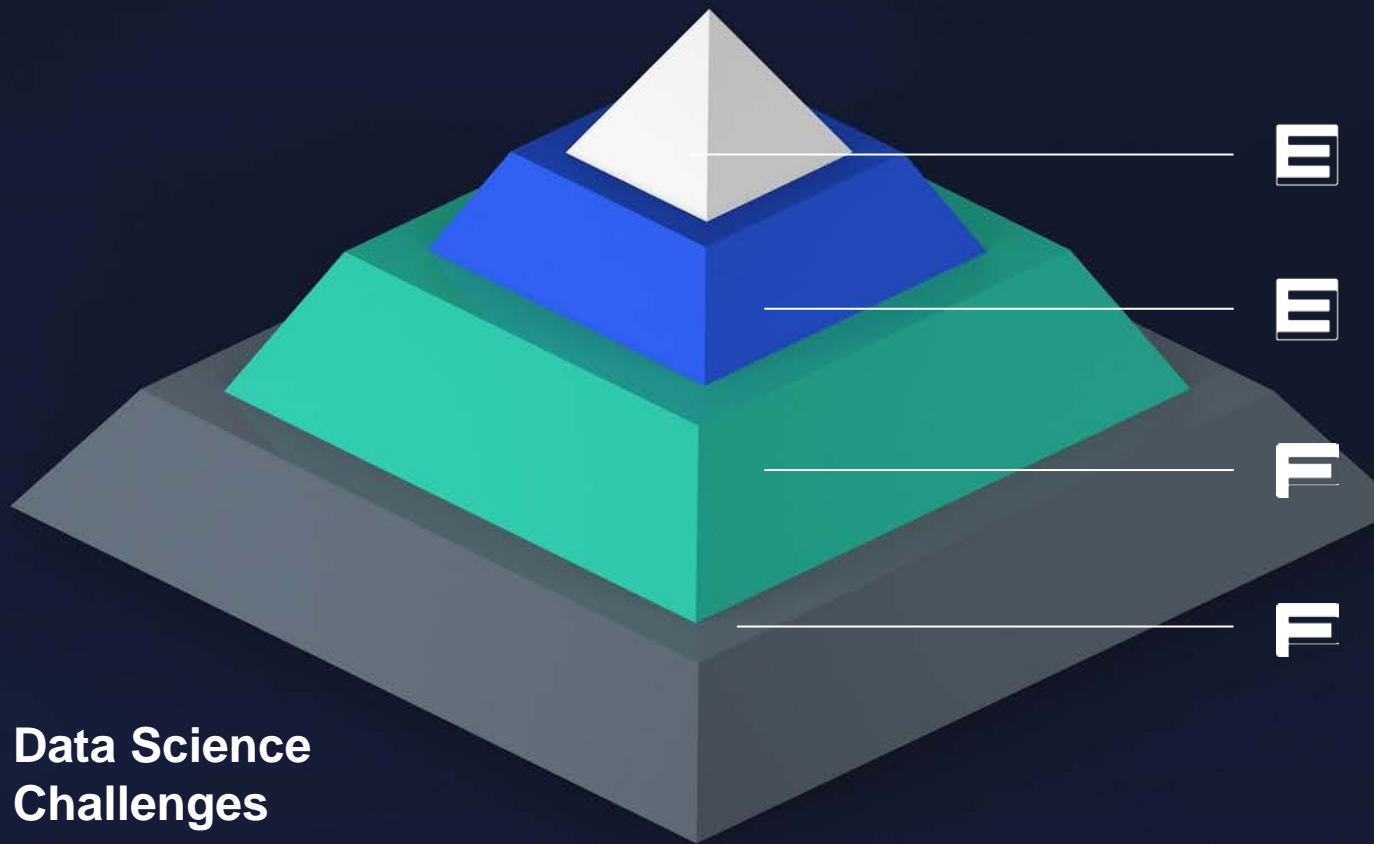


Bayer CropScience



## Associations





### **Foresight**

Developing Predictive Models



### **Insight**

Analysing and Visualising the Data



### **Understanding**

Structuring, Validating and Sharing



### **Gathering Data**

Collect the Data

**Data Science  
Challenges**

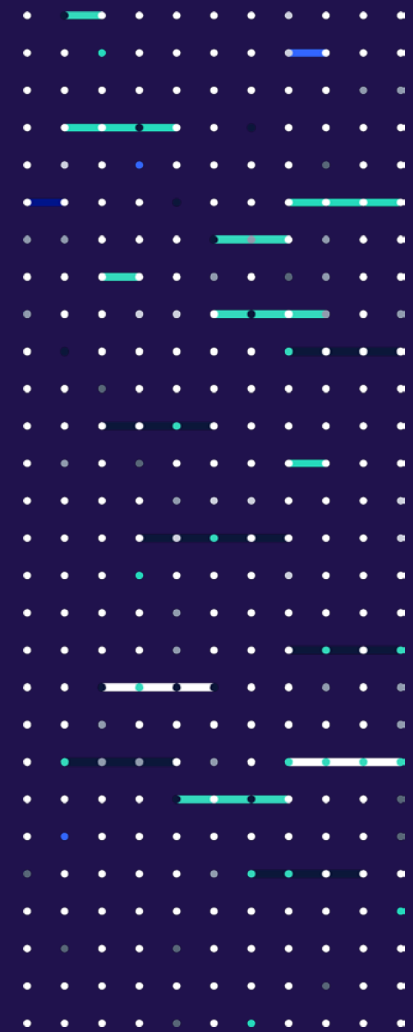
## ► Creme Global

*Novel and Integrated Approaches to modelling aggregate exposures to chemicals across different conditions of use and routes of exposure*

## Some of The Challenges:

1. Data, or lack thereof
2. Data, confidentiality
3. Data, from multiple sources

## CASE STUDY: RIFM



# Case Study

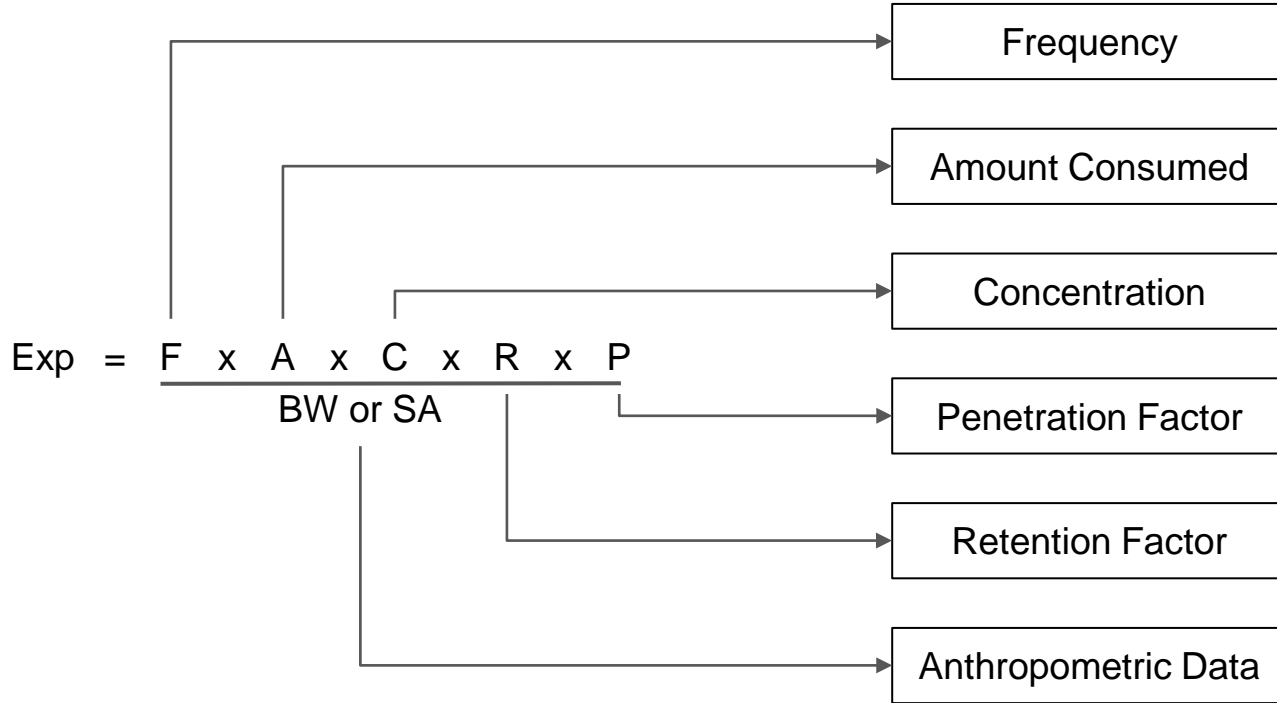
## Creme RIFM Model

**A tool to estimate aggregate exposure from consumer product ingredients.**

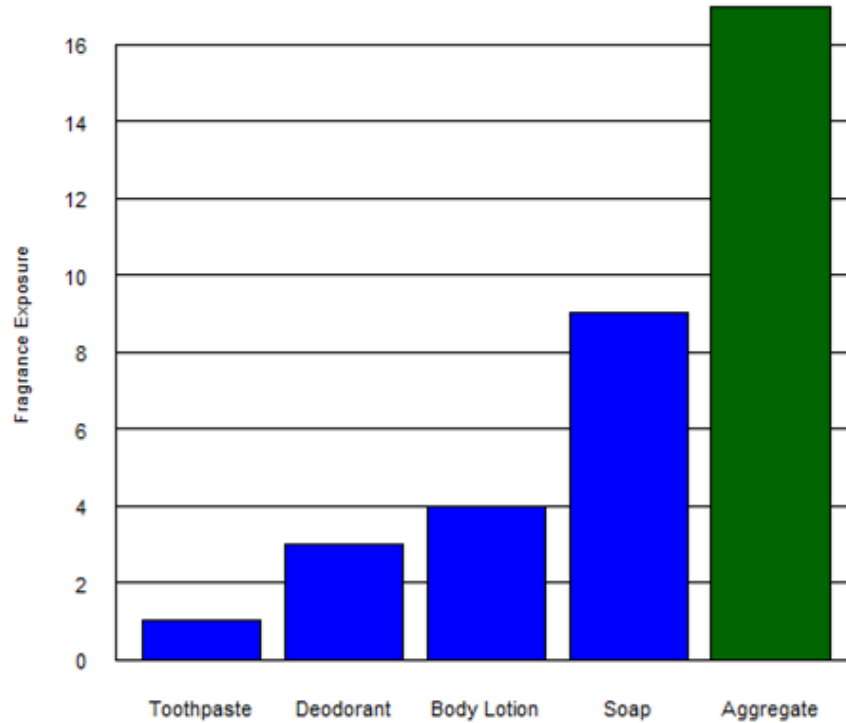
- Cosmetics, personal care products, air care products and household cleaning products.
- United States and Europe populations.
- Systemic, Dermal, Inhalation, Ingestion.
- Probabilistic model based on real world data.
- Flexible and customizable.



# What Are the Data needs?

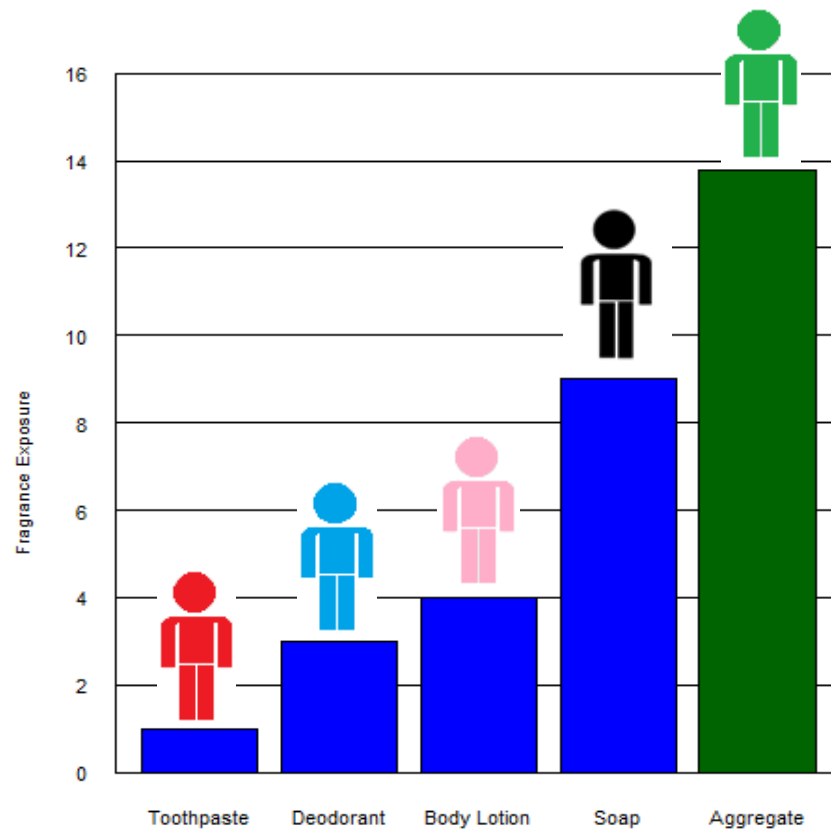


# Deterministic Method





# Percentile Exposure



## The Solution

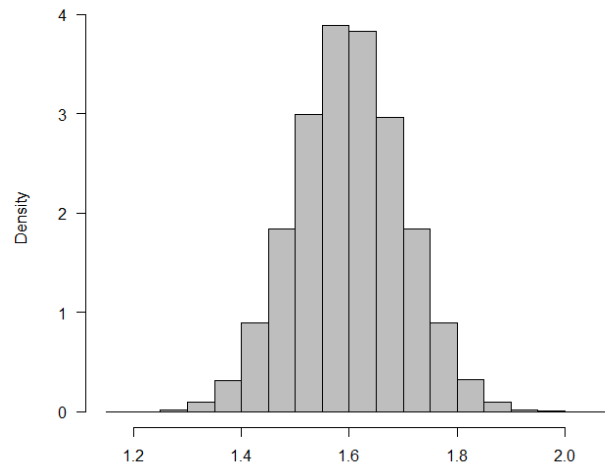
Aggregate exposure based on actual product consumption surveys and distributions of data provided is more realistic.

E.g. Amount of Toothpaste consumed

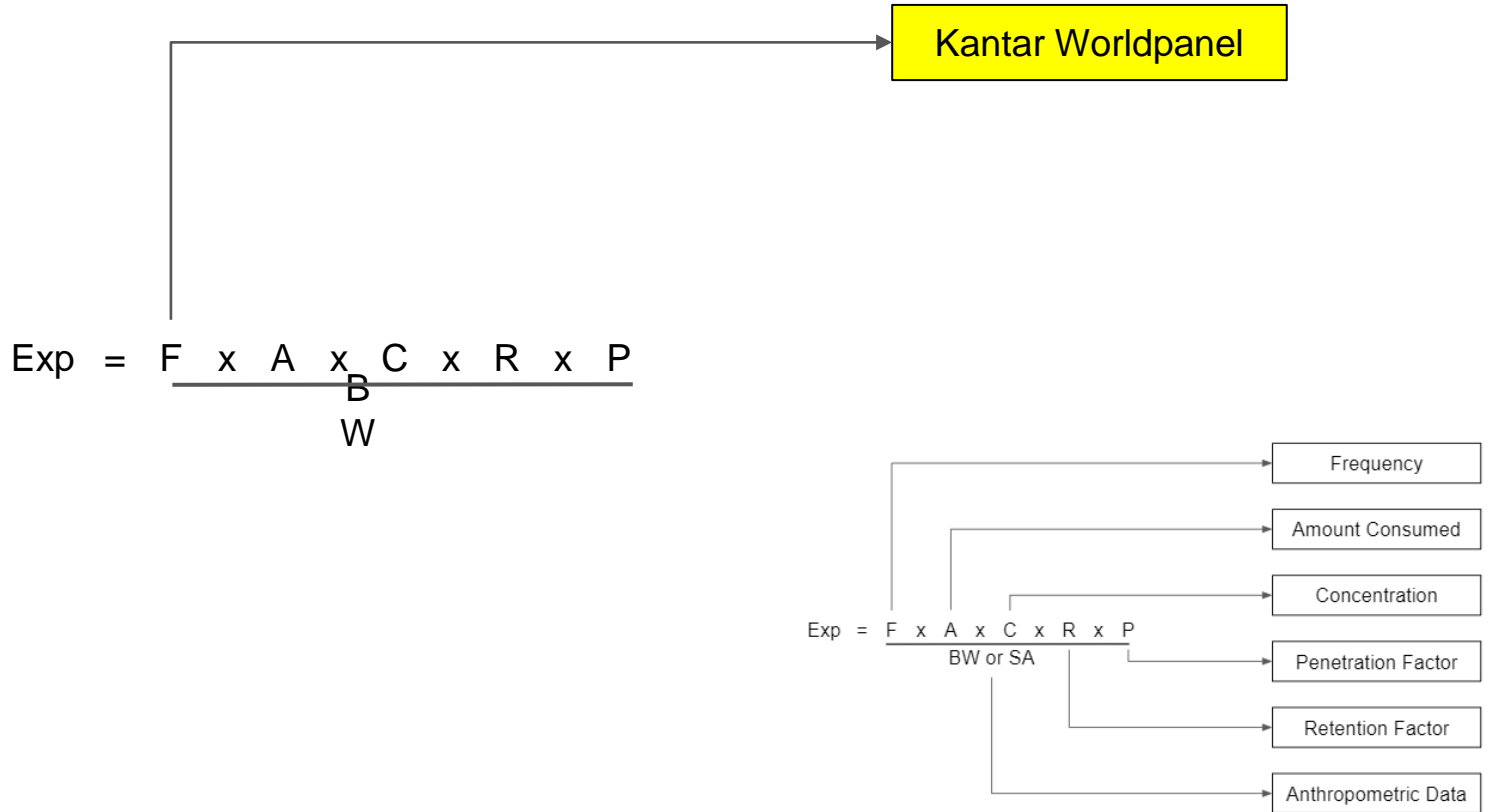
2g



VS.



# Frequency of Use

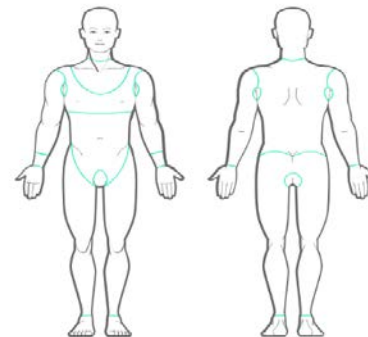


# Kantar - Online Consumption Diaries

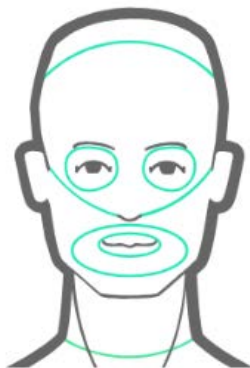


## Body

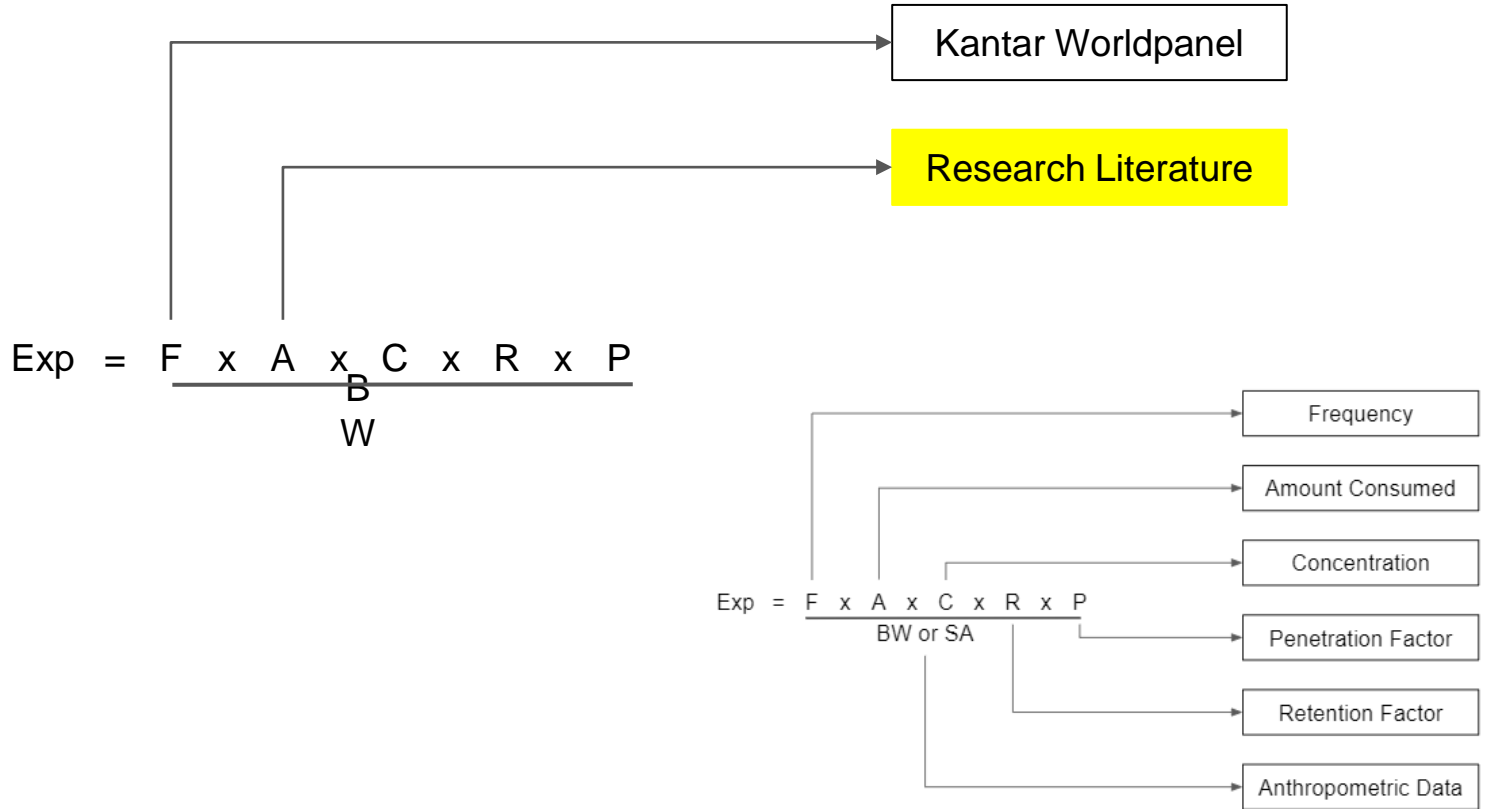
- Decolletage
- Outer Chest
- Stomach
- Back
- Underarms
- Arms
- Wrists
- Back of Hands
- Palms
- Intimate Parts
- Legs
- Feet



- Scalp
- Upper Face
- Eyes
- Lower Face
- Lips
- Inside Mouth
- Behind Ears
- Front of Neck
- Back of Neck



# Amounts Used



# Amounts Used

Europe  
2011)

→ COLIPA (Hall *et al.*, 2007;

→ Ficheux *et al.*, 2016

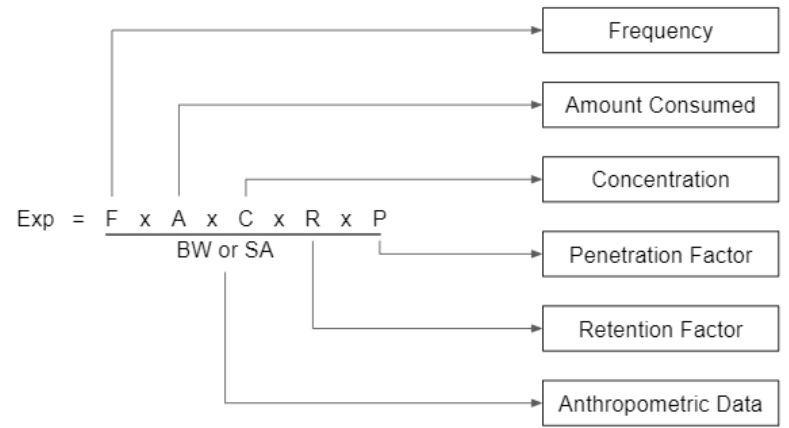
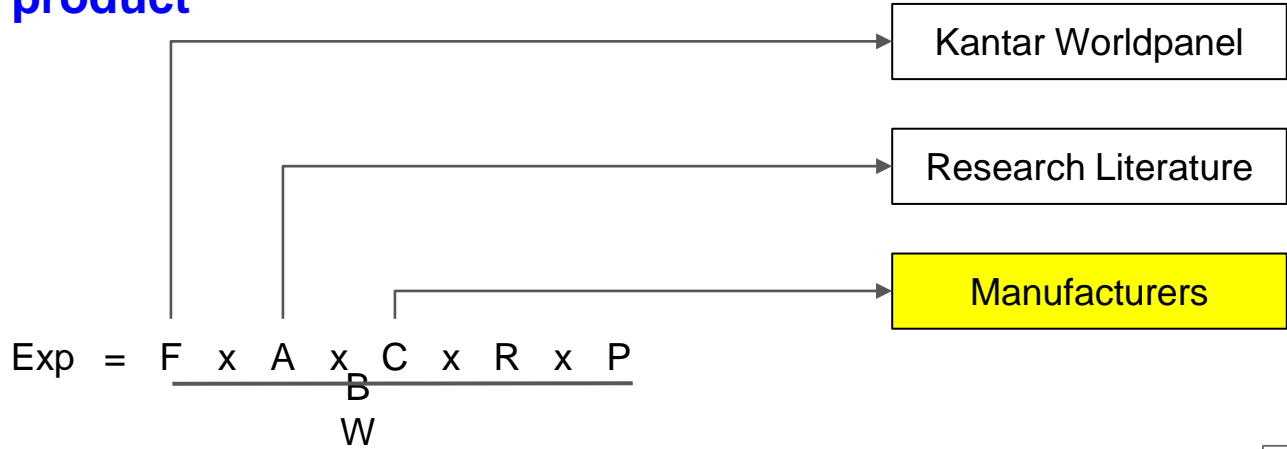
USA  
2006; 2008)

→ CTFA (Loretz *et al.*, 2005;

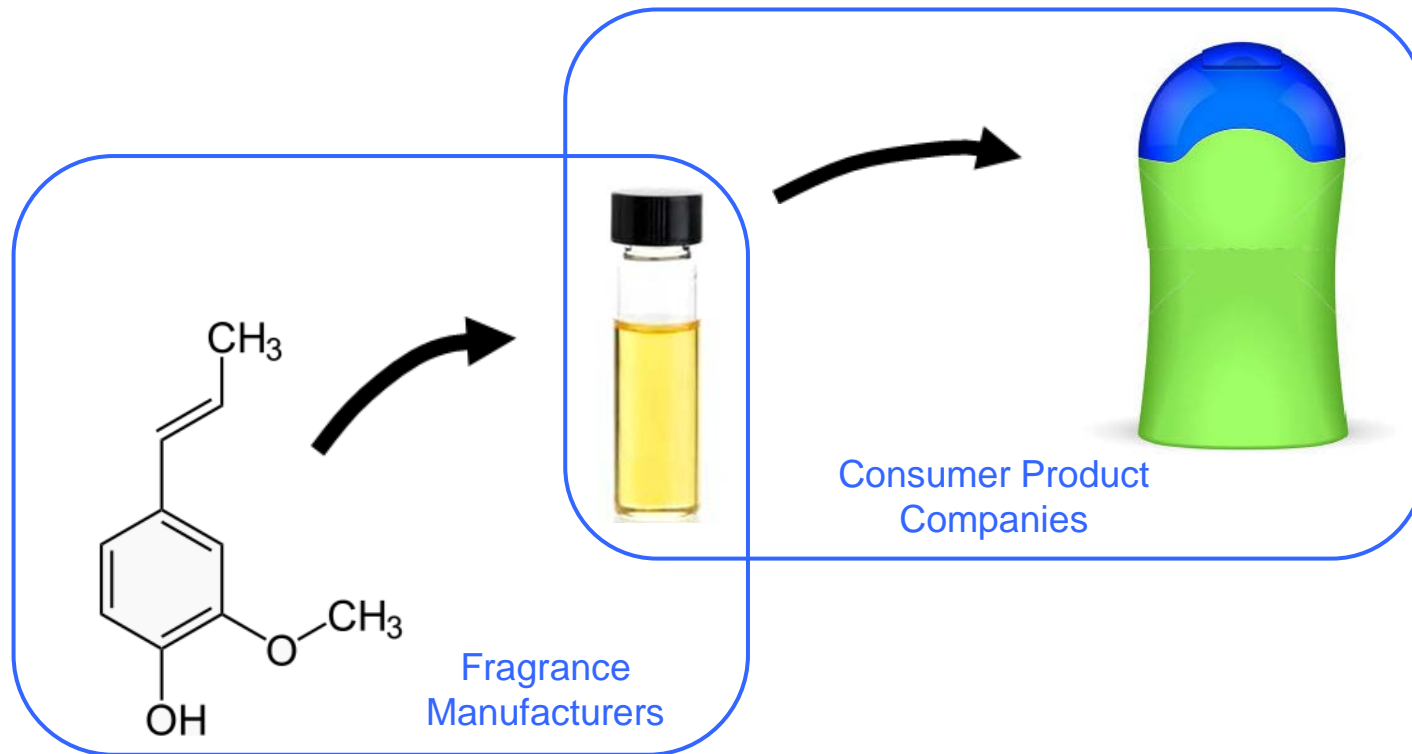
Hydroalcoholics → Tozer *et al.*, 2004



# Concentration of the fragrance chemical in the final product

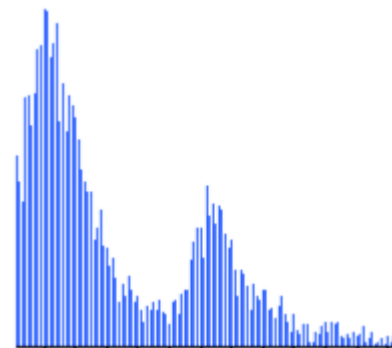
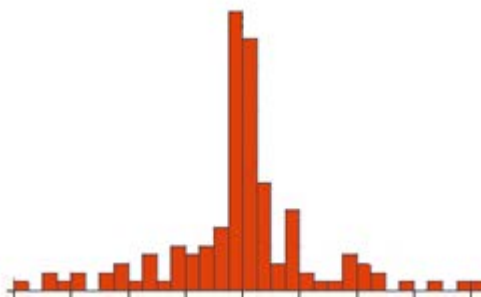
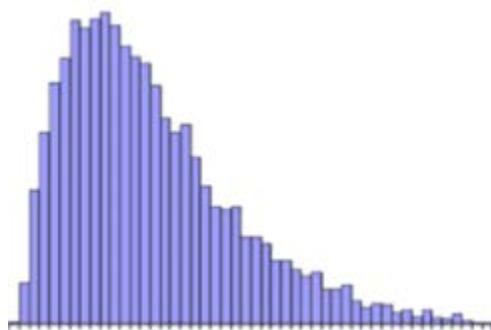
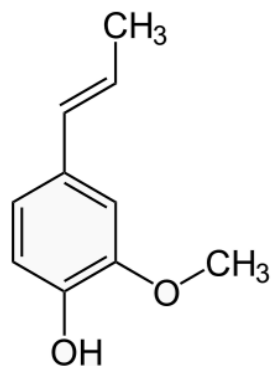


# Fragrance Concentration

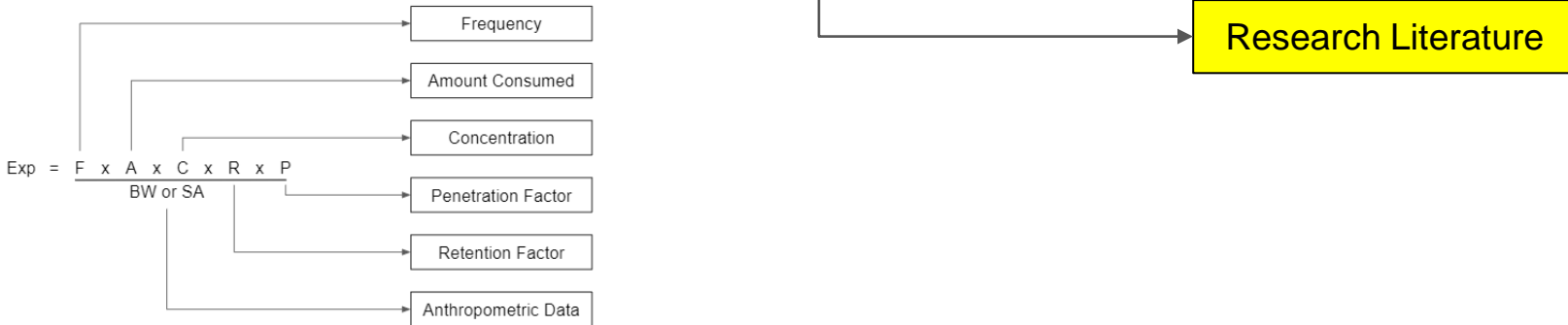
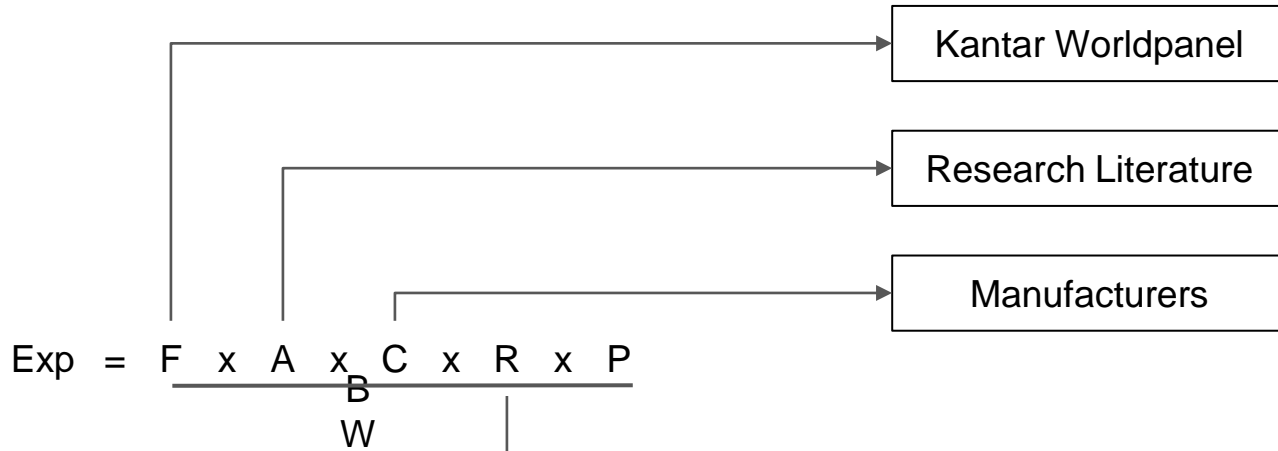




# Two-level Concentrations



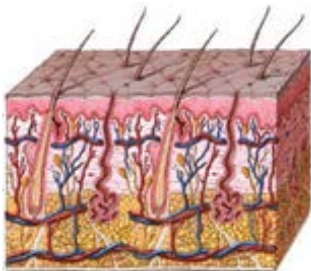
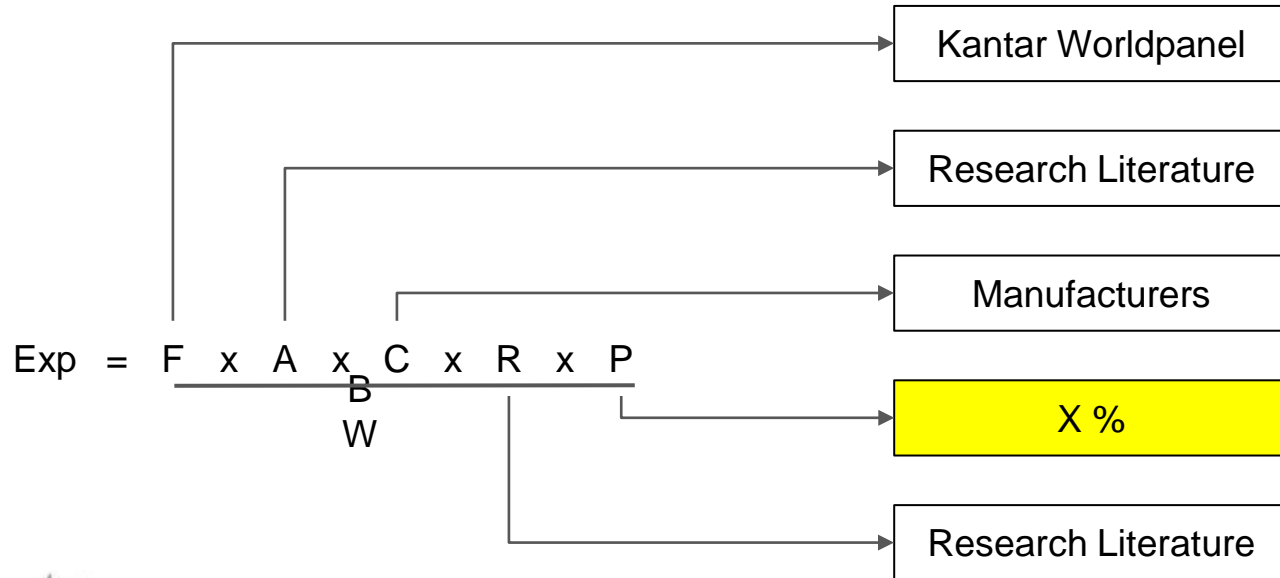
# Retention Factor



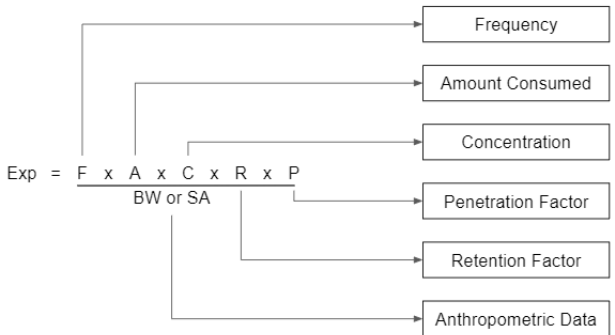
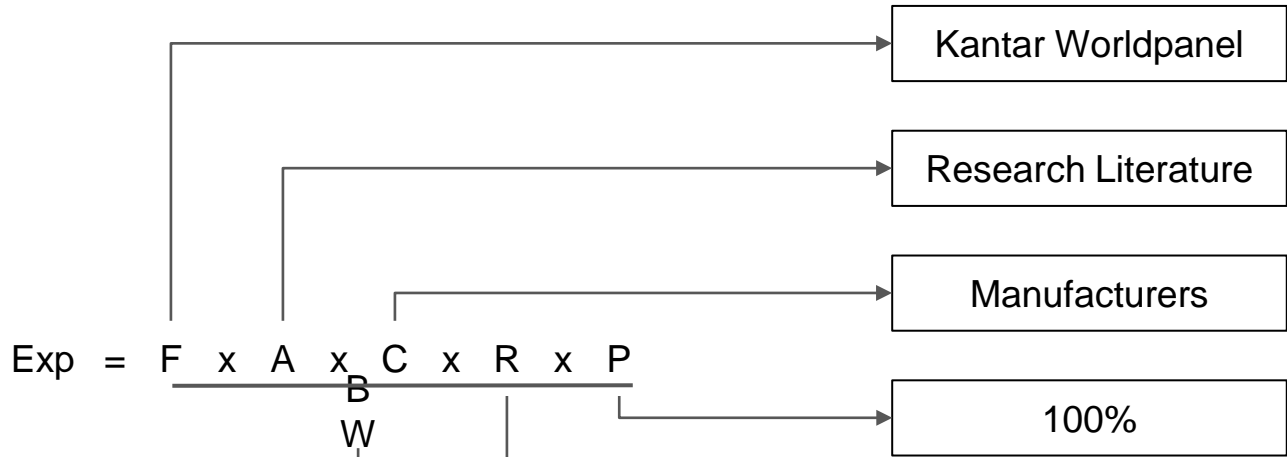
## Retention Factors (Examples)

	<b>Dermal</b>	<b>Ingestion</b>	<b>Inhalation</b>
<b>Body Lotion</b>	1		
<b>Shampoo</b>	0.01		
<b>DeoSpray</b>	0.235		0.0127
<b>Toothpaste</b>	0.1	0.05	
<b>Eau de Toilette</b>	0.8		0.00363

# Penetration Factor



# Anthropometric Data



Population Surveys

# Height and Weight Data

## US

2009-2014 NHANES Survey

Body weight and height data for 14,000 US Subjects



## EU

France INCA2

Poland Kilmek-Piotrowska *et al.*, 2015

Others NHANES data scaled based on EU country average weights and heights



# Surface Area Calculations

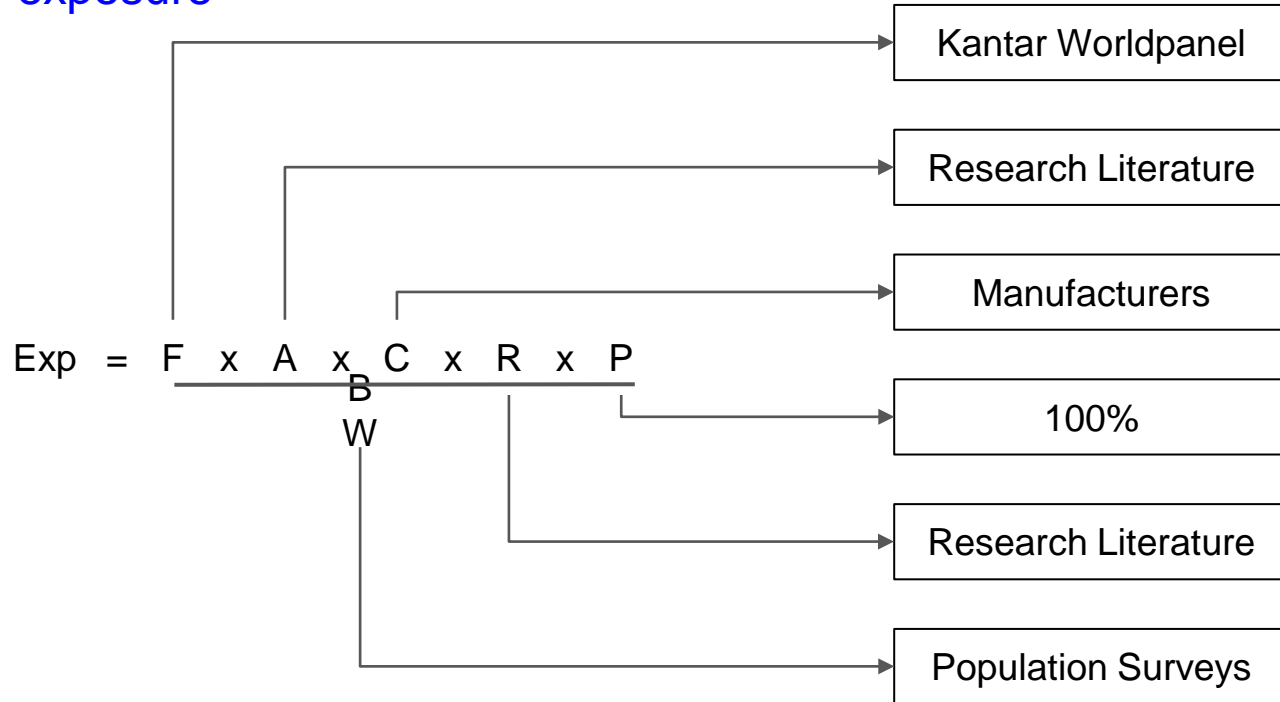


## Du Bois Formula

$$SA = a \times W^b \times H^c$$

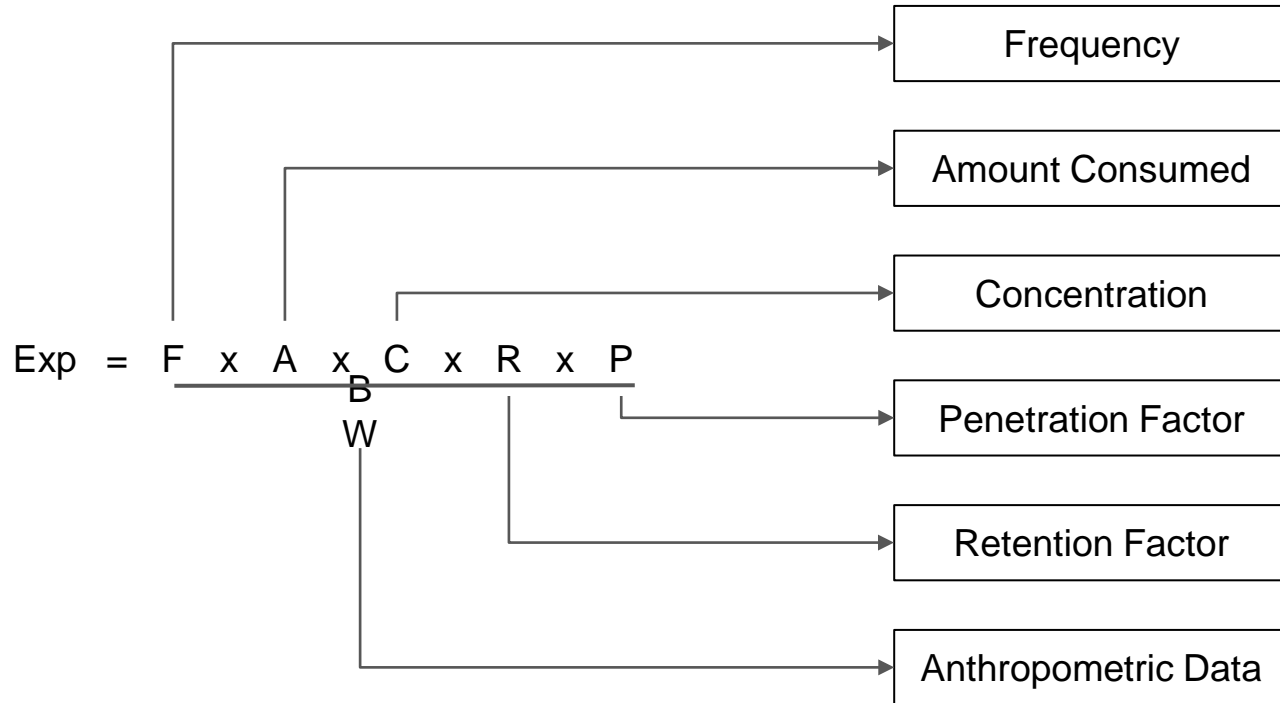
Head, trunk, arms, hands, legs  
and feet.

Multiple sources of data  
 Multiple conditions of use  
 Multiple routes of exposure

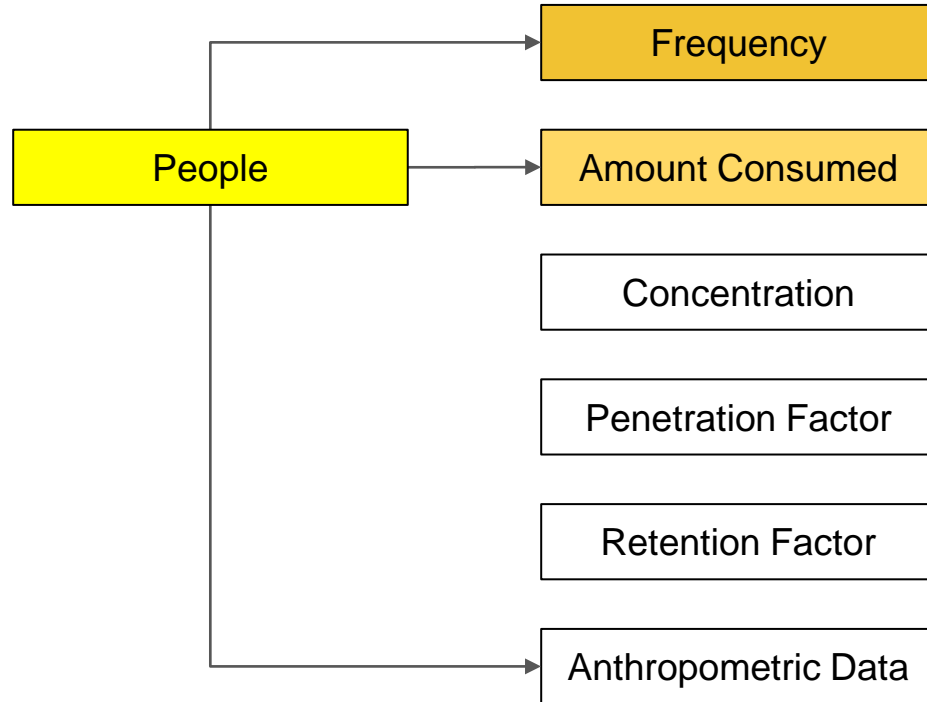




# How does the data get pulled together?



The problem is that the data comes from different people....



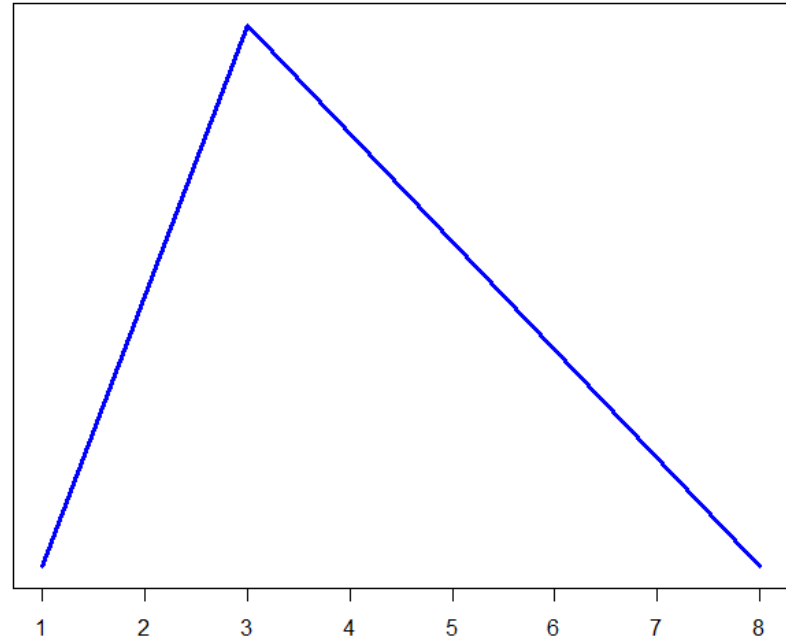
# Monte Carlo Simulation

Example - Triangular Distribution

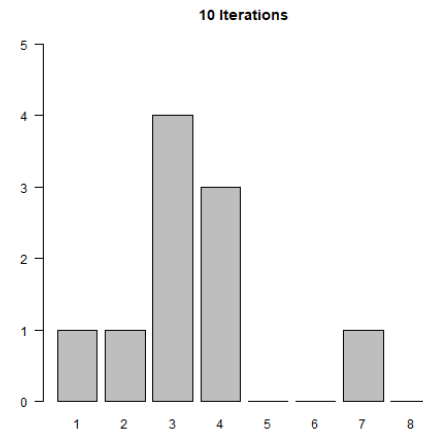
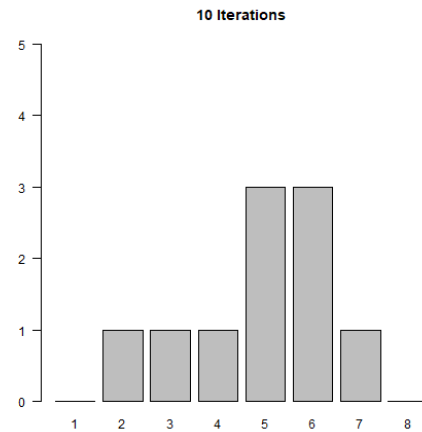
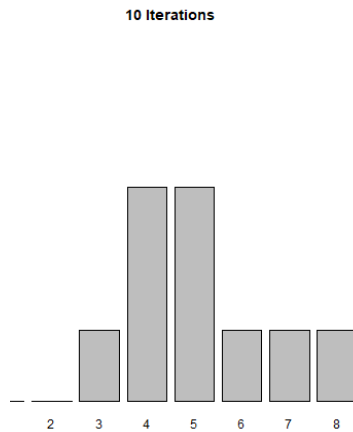
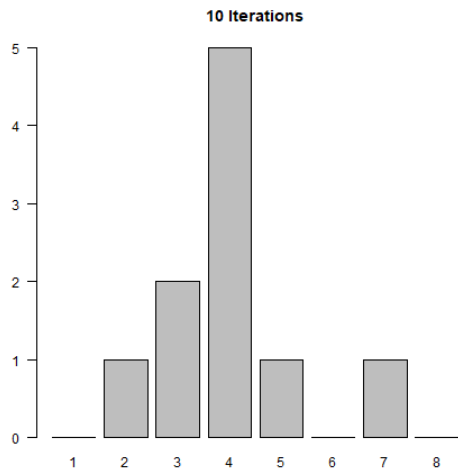
Lower limit: 1g

Upper limit: 8g

Mode: 3g

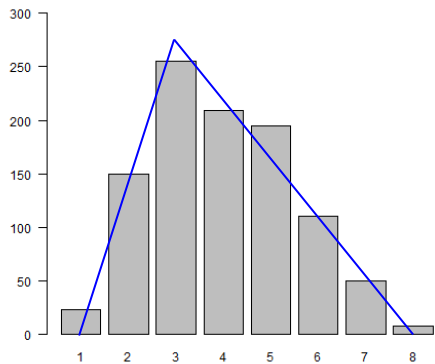


# Monte Carlo Simulation 10 Subjects

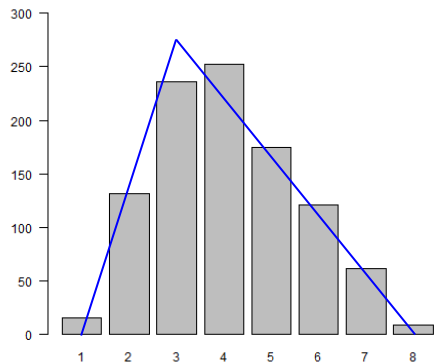


# Monte Carlo Simulation 1000 Subjects

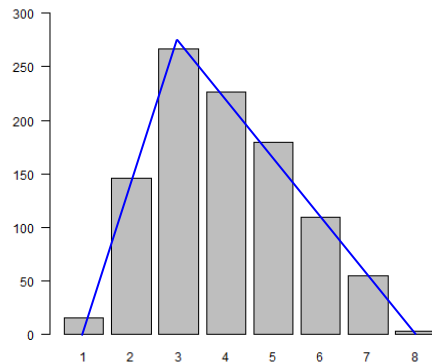
1000 Iterations



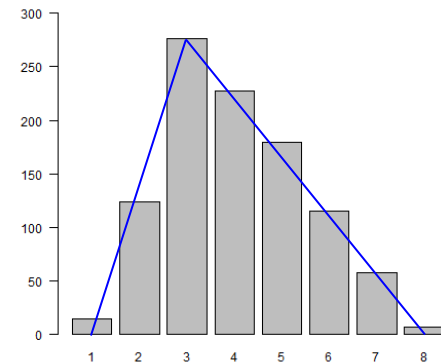
1000 Iterations



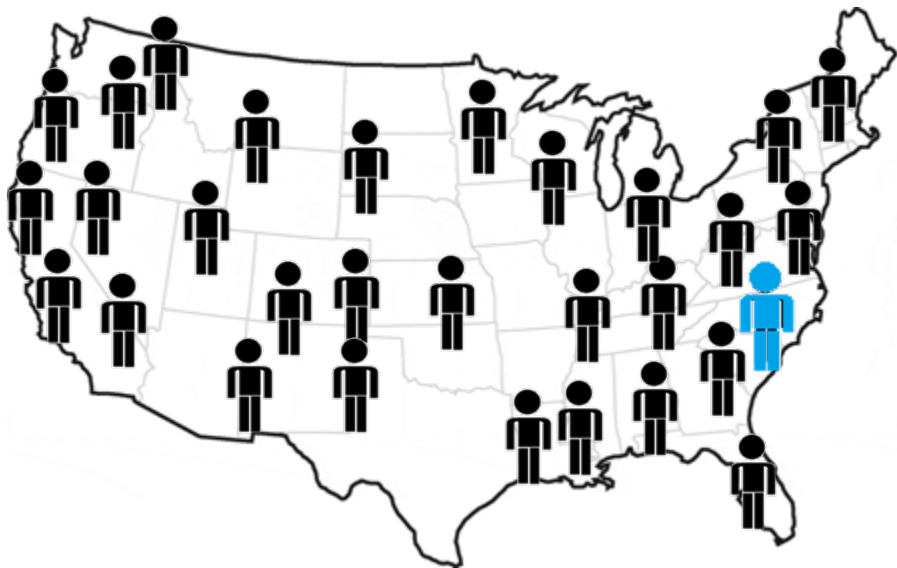
1000 Iterations



1000 Iterations



# Population Exposure Modelling



# Population Exposure Modelling



Age: 18-25



# Individual Exposure



Diary Day 1



FREQUENCY





# Individual Exposure



Diary Day 1



FREQUENCY



x1



x2



x2

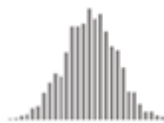


x9

AMOUNT



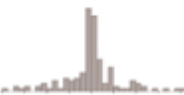
6 g



2.2 g



0.5 g

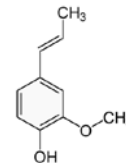


0.8 g

# Individual Exposure



Diary Day 1



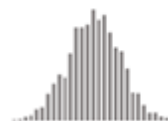
FREQUENCY



AMOUNT



6 g



2.2 g



0.5 g



0.8 g

SUBSTANCE CONCENTRATION

0.006 %

0.002 %

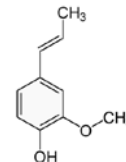
0.001 %

0.0005 %

# Individual Exposure



Diary Day 1



FREQUENCY

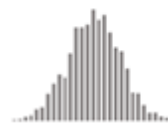
AMOUNT

SUBSTANCE CONCENTRATION



6 g

0.006 %



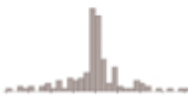
2.2 g

0.002 %



0.5 g

0.001 %



0.8 g

0.0005 %

Total aggregate exposure: 510 µg

# Individual Exposure



+



+



+



+



+







































=

510  $\mu$ g

# Individual Exposure



1	 +  +  +  +  +  = 510 µg
2	 +  +  +  +  = 480 µg
3	 +  +  +  +  +  = 601 µg
4	 +  +  +  = 590 µg
5	 +  +  +  +  +  = 380 µg
6	 +  +  +  +  = 420 µg
7	 +  +  +  = 360 µg

# Individual Exposure



1 + + + + + + = 510 µg

2 + + + + + = 480 µg

3 + + + + + + = 601 µg } Acute

4 + + + + = 590 µg





































5 + + + + + + = 380 µg

6 + + + + + = 420 µg

7 + + + + = 360 µg

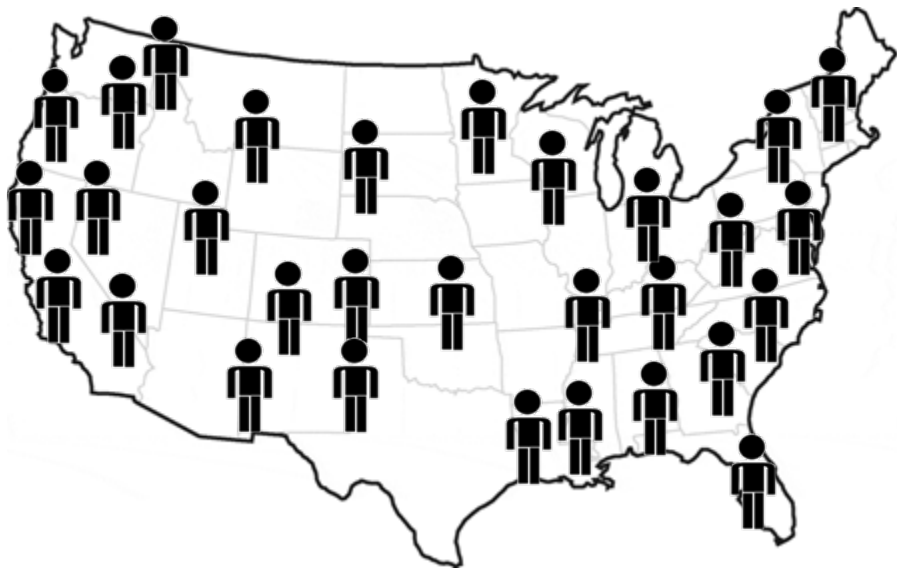
# Individual Exposure



1	 +  +  +  +  + 	= 510 µg
2	 +  +  +  + 	= 480 µg
3	 +  +  +  +  + 	= 601 µg
4	 +  +  + 	= 590 µg
5	 +  +  +  +  + 	= 380 µg
6	 +  +  +  + 	= 420 µg
7	 +  +  + 	= 360 µg

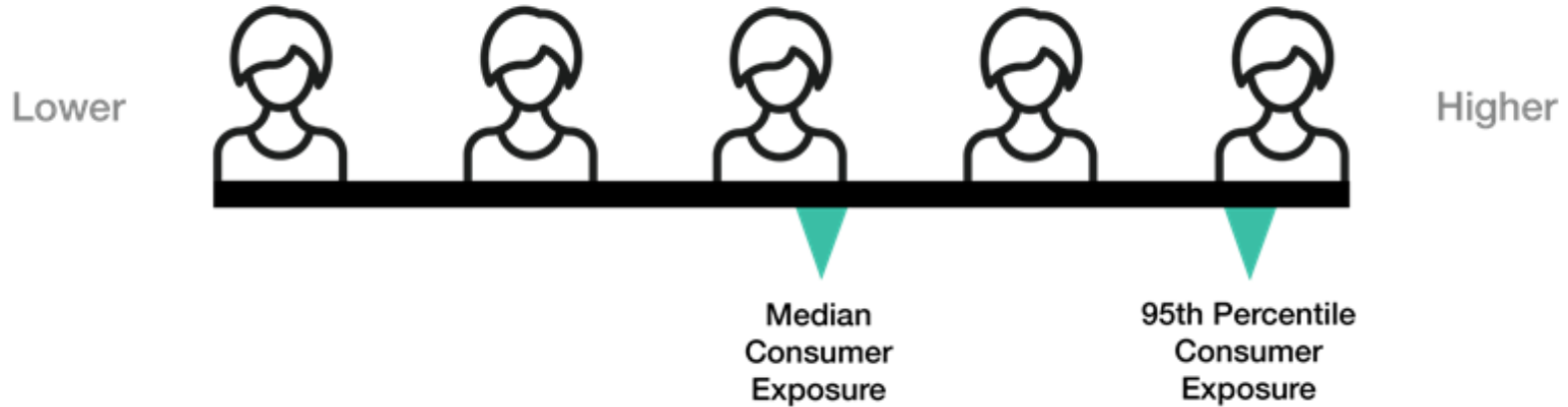
Daily  
Average

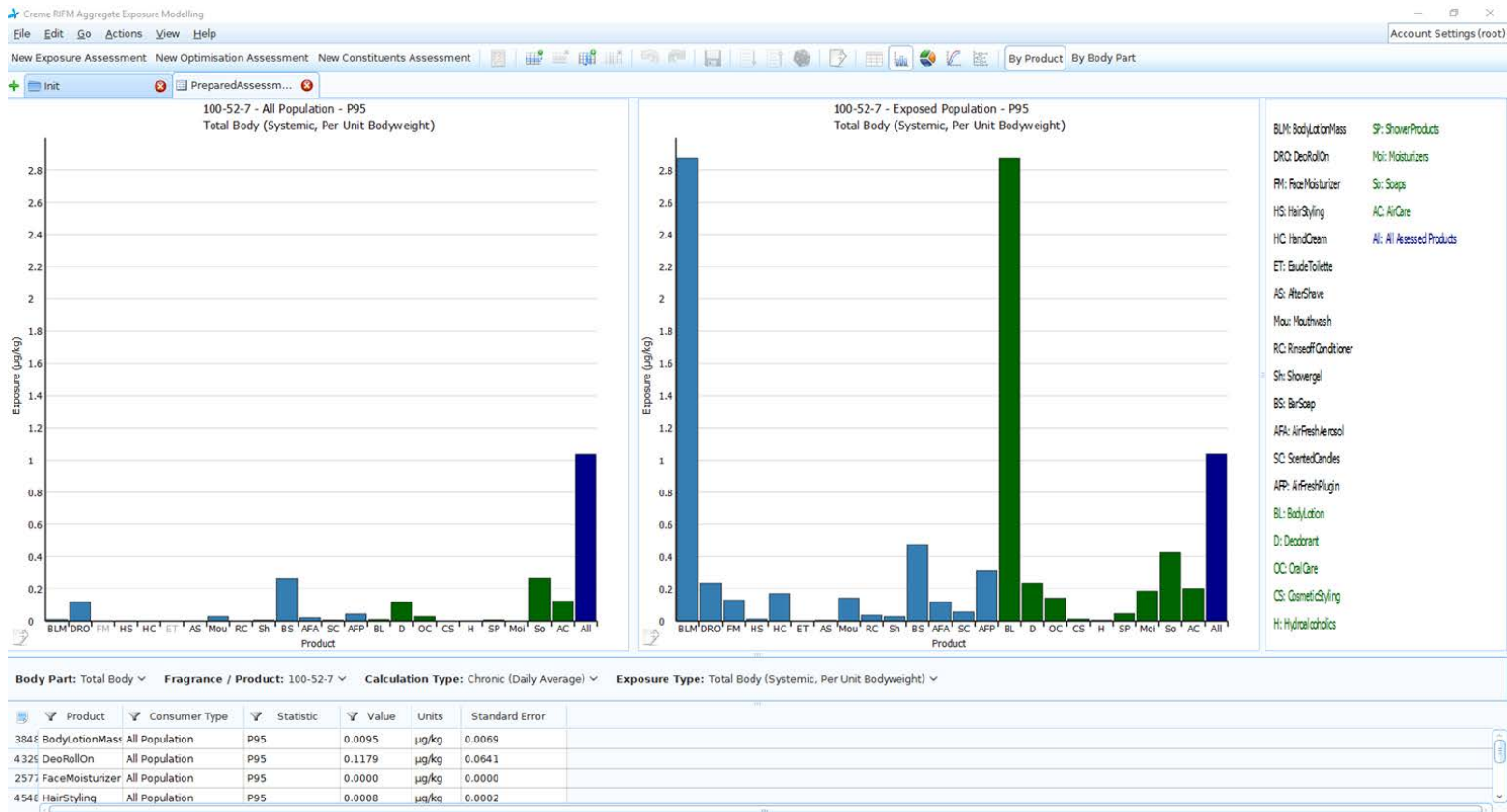
# Population Exposure





# Population Exposure





## How is the exposure model used?

- 1 RIFM **fragrance ingredient safety assessment**, ethyl 2-methyl-1,3-dioxolane-2-acetate, CAS Registry Number 6413-10-1.  
**Api AM**, et al. Food Chem Toxicol 2018 - Review. PMID 30287335  
Ethyl 2-methyl-1,3-dioxolane-2-acetate (CAS # 6413-10-1) was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental **safety**. ...Data from ethyl 2-methyl-1,3-dioxolane-2-acetate show that there are no **safety** concerns for skin sensitization under the current, declared levels of use. ...  
“ Cite  Share
  
- 2 RIFM **fragrance ingredient safety assessment**, 1,1-diethoxyheptane, CAS Registry Number 688-82-4.  
**Api AM**, et al. Food Chem Toxicol 2018 - Review. PMID 30300725  
The use of this material under current conditions is supported by existing information. 1,1-Diethoxyheptane was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental **safety**. ...  
“ Cite  Share
  
- 3 RIFM **fragrance ingredient safety assessment**  $\beta$ -Patchoulene, CAS Registry Number 514-51-2.  
**Api AM**, et al. Food Chem Toxicol 2018 - Review. PMID 29626575  
“ Cite  Share

## Many ways to consider exposure

**People:** Everyone or Consumers only

**Time:** Chronic or Acute

**Route:** Dermal, Inhalation, Ingestion, or Systemic

**Product:** Aftershave, Bar soap, Shampoo, etc.

**Grouping:** Product, Category, or All Products

**Site:** Palms, Wrists, Arms, Back, Stomach, etc.

**Statistic:** Minimum, Median, Mean, P90, P95, etc.

# Publications

Comiskey *et al.* (2015).

Novel database for exposure to fragrance ingredients in cosmetics and personal care products.

Regul Toxicol Pharmacol. **72(3)**:660-72.

doi: [10.1016/j.yrtph.2015.05.012](https://doi.org/10.1016/j.yrtph.2015.05.012)

Safford *et al.* (2015).

Use of an aggregate exposure model to estimate consumer exposure to fragrance ingredients in personal care and cosmetic products

Regul Toxicol Pharmacol **72(3)**:673-682.

doi: [10.1016/j.yrtph.2015.05.017](https://doi.org/10.1016/j.yrtph.2015.05.017)

Safford *et al.* (2017).

Application of the expanded Creme RIFM consumer exposure model to fragrance ingredients in cosmetic, personal care and air care products

Regul Toxicol Pharmacol. **86**:148-156.

doi: [10.1016/j.yrtph.2017.02.021](https://doi.org/10.1016/j.yrtph.2017.02.021)

Comiskey *et al.* (2017).

Integrating habits and practices data for soaps, cosmetics and air care products into an existing aggregate exposure model.

Regul Toxicol Pharmacol. **88**:144-156.

doi: [10.1016/j.yrtph.2017.05.017](https://doi.org/10.1016/j.yrtph.2017.05.017)

► Creme Global

# Thank You.

[clare.thorp@cremeglobal.com](mailto:clare.thorp@cremeglobal.com)

**Creme Global**

4th Floor, The Design Tower,

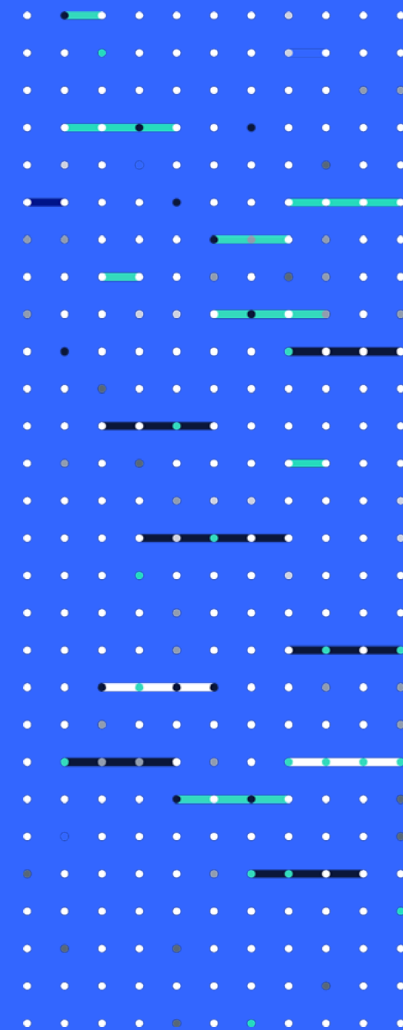
Trinity Technology & Enterprise Campus,

Grand Canal Quay, Dublin 2, Ireland, D02 P956

+353 (1) 677 0071

[info@cremeglobal.com](mailto:info@cremeglobal.com)

[www.cremeglobal.com](http://www.cremeglobal.com)



# Capabilities

Exposure Assessments

Optimisation Assessments

Highly configurable

Highly customisable

Data exploration