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

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Creme Global
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

Associations
Data Science Challenges

- **Gathering Data**
  - Collect the Data

- **Understanding**
  - Structuring, Validating and Sharing

- **Insight**
  - Analysing and Visualising the Data

- **Foresight**
  - Developing Predictive Models
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.

♭ Creme Global
What Are the Data needs?

Exp = F x A x C x R x P

- Frequency
- Amount Consumed
- Concentration
- Penetration Factor
- Retention Factor
- Anthropometric Data
Deterministic Method
Percentile Exposure

- Toothpaste
- Deodorant
- Body Lotion
- Soap
- Aggregate
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

Exp = F x A x C x R x P

Kantar Worldpanel

- Frequency
- Amount Consumed
- Concentration
- Penetration Factor
- Retention Factor
- Anthropometric Data
Kantar - Online Consumption Diaries

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

Body
- Decolleteage
- Outer Chest
- Stomach
- Back
- Shoulders
- Arms
- Shoulders
- Back of Hands
- Fingers
- Intimate Parts
- Legs
- Feet
Amounts Used

\[ \text{Exp} = F \times A \times C \times R \times P \]

- Kantar Worldpanel
- Research Literature

- Frequency
- Amount Consumed
- Concentration
- Penetration Factor
- Retention Factor
- Anthropometric Data
Amounts Used

Europe  → COLIPA (Hall et al., 2007; 2011)
       → Ficheux et al., 2016

USA    → CTFA (Loretz et al., 2005; 2006; 2008)

Hydroalcoholics → Tozer et al., 2004
Concentration of the fragrance chemical in the final product

\[ \text{Exp} = F \times A \times \frac{B}{W} \times C \times R \times P \]
Fragrance Concentration

Fragrance Manufacturers

Consumer Product Companies
Retention Factor

\[ \text{Exp} = F \times A \times C \times R \times P \]

- Kantar Worldpanel
- Research Literature
- Manufacturers
- Research Literature

Sub-branches:
- Frequency
- Amount Consumed
- Concentration
- Penetration Factor
- Retention Factor
- Anthropometric Data
### Retention Factors (Examples)

<table>
<thead>
<tr>
<th></th>
<th>Dermal</th>
<th>Ingestion</th>
<th>Inhalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Lotion</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shampoo</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeoSpray</td>
<td>0.235</td>
<td>0.0127</td>
<td></td>
</tr>
<tr>
<td>Toothpaste</td>
<td>0.1</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Eau de Toilette</td>
<td>0.8</td>
<td></td>
<td>0.00363</td>
</tr>
</tbody>
</table>
Penetration Factor

\[ \text{Exp} = F \times A \times B \times C \times R \times P \]

- Kantar Worldpanel
- Research Literature
- Manufacturers
- X %
- Research Literature
Anthropometric Data

Exp = F x A x C x R x P

- Kantar Worldpanel
- Research Literature
- Manufacturers
- 100%
- Research Literature
- Population Surveys

- Frequency
- Amount Consumed
- Concentration
- Penetration Factor
- Retention Factor
- Anthropometric Data

BW or SA
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

Exp = F x A x C x R x P

Kantar Worldpanel
Research Literature
Manufacturers
100%
Research Literature
Population Surveys
How does the data get pulled together?

Exp = F x A x B x C x R x P

- Frequency
- Amount Consumed
- Concentration
- Penetration Factor
- Retention Factor
- Anthropometric Data
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
Population Exposure Modelling
Population Exposure Modelling

Age: 18-25
Individual Exposure

1 Diary Day 1

- Frequency
  - x1
  - x2
  - x2
  - x9
Individual Exposure

Diary Day 1

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>x1</td>
<td>6 g</td>
</tr>
<tr>
<td>x2</td>
<td>2.2 g</td>
</tr>
<tr>
<td>x2</td>
<td>0.5 g</td>
</tr>
<tr>
<td>x9</td>
<td>0.8 g</td>
</tr>
</tbody>
</table>
Individual Exposure

1 Diary Day 1

<table>
<thead>
<tr>
<th>FREQENCY</th>
<th>AMOUNT</th>
<th>SUBSTANCE CONCENTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>x1</td>
<td>6 g</td>
<td>0.006 %</td>
</tr>
<tr>
<td>x2</td>
<td>2.2 g</td>
<td>0.002 %</td>
</tr>
<tr>
<td>x2</td>
<td>0.5 g</td>
<td>0.001 %</td>
</tr>
<tr>
<td>x9</td>
<td>0.8 g</td>
<td>0.0005 %</td>
</tr>
</tbody>
</table>
Individual Exposure

Diary Day 1

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<tr>
<td>x9</td>
<td>0.8 g</td>
<td>0.0005 %</td>
</tr>
</tbody>
</table>

Total aggregate exposure: 510 μg
Individual Exposure

1 + + + + + = 510 µg
Individual Exposure

<table>
<thead>
<tr>
<th>Day</th>
<th>Products</th>
<th>Total Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1+1+1+1+1+1</td>
<td>510 µg</td>
</tr>
<tr>
<td>2</td>
<td>1+1+1+1+1+1</td>
<td>480 µg</td>
</tr>
<tr>
<td>3</td>
<td>1+1+1+1+1+1</td>
<td>601 µg</td>
</tr>
<tr>
<td>4</td>
<td>1+1+1+1+1+1</td>
<td>590 µg</td>
</tr>
<tr>
<td>5</td>
<td>1+1+1+1+1+1</td>
<td>380 µg</td>
</tr>
<tr>
<td>6</td>
<td>1+1+1+1+1+1</td>
<td>420 µg</td>
</tr>
<tr>
<td>7</td>
<td>1+1+1+1+1+1</td>
<td>360 µg</td>
</tr>
</tbody>
</table>
## Individual Exposure

<table>
<thead>
<tr>
<th>Day</th>
<th>Exposure</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1+2+3+4+5+6+7</td>
<td>510 µg</td>
</tr>
<tr>
<td>2</td>
<td>1+2+3+4+5+6+7</td>
<td>480 µg</td>
</tr>
<tr>
<td>3</td>
<td>1+2+3+4+5+6+7</td>
<td>601 µg</td>
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<td>4</td>
<td>1+2+3+4+5+6+7</td>
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<tr>
<td>7</td>
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<td>360 µg</td>
</tr>
</tbody>
</table>

**Acute**
Individual Exposure

<table>
<thead>
<tr>
<th>Day</th>
<th>Exposures</th>
<th>Total Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 + 2 + 3 + 4 + 5 + 6 + 7</td>
<td>510 μg</td>
</tr>
<tr>
<td>2</td>
<td>1 + 2 + 3 + 4 + 5 + 6 + 7</td>
<td>480 μg</td>
</tr>
<tr>
<td>3</td>
<td>1 + 2 + 3 + 4 + 5 + 6 + 7</td>
<td>601 μg</td>
</tr>
<tr>
<td>4</td>
<td>1 + 2 + 3 + 4 + 5 + 6 + 7</td>
<td>590 μg</td>
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<td>380 μg</td>
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<td>420 μg</td>
</tr>
<tr>
<td>7</td>
<td>1 + 2 + 3 + 4 + 5 + 6 + 7</td>
<td>360 μg</td>
</tr>
</tbody>
</table>

Daily Average: 480 μg
Population Exposure
Population Exposure

Lower  Median Consumer Exposure  95th Percentile Consumer Exposure  Higher
Software
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.
   
   
   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.
   
   
   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 β-Patchoulene, CAS Registry Number 514-51-2.
   
   
   “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. (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
Thank You.

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Capabilities

Exposure Assessments
Optimisation Assessments

Highly configurable
Highly customisable
Data exploration