Project overview DRESS
DeRmal Exposure aSSessment Strategies

B9: Characterising the nature of dermal exposure from consumer products and articles
Background

Estimating **realistic** dermal consumer exposure via modelling is difficult due to:

– Lack of appropriate models featuring realistic exposure estimates from the use of consumer products and articles

– Conservatism of tier 1 models and lack of data on parameters for dermal exposure, for instance

  • Defaults
  • Databases on dermal transfer factors (thickness films,...)
  • Use patterns
  • Parameter variability
Objectives DRESS project

• Identification of key consumer products and articles for which demonstration of safe use is most challenging
• Identification of those dermal exposure determinants that benefit the most from data generation, including:
  – Habits and practices of consumers
  – Transfer factors (migration rates, thickness of contact films, ... )
  – External dermal exposure
• Identification of the main knowledge gaps in these exposure determinants and ways to fill them
• Perform experiments to fill these data gaps
• Integrate the information collected and data generated in a refined dermal exposure strategy
• Demonstrate this refined strategy in case studies
DERMAL exposure

- Fingertips
- Direct

- Hands
- Occasional
- Unavoidable

- Deposition on surfaces
- Indirect

- Body
- Frequent
- Intended

- Feet
- Unavoidable
Inventory

From mapping of processes (conceptual framework)

Developing model equations & data parameterization

* Existing dermal exposure models (consumers & workers)
* Literature search:
  - Foundations exposure parameters
  - Available exposure data

Focus on selected group of articles & products
Data collection

Focus on articles, refinements compared to ECETOC TRA model
- Consumer survey
- Experimental work
  - Migration \(\rightarrow\) release from articles
  - Transfer \(\rightarrow\) surface wipes

Migration: Release (rate) of a substance from an article; substances diffused from the matrix of the article to bioavailable amounts in the contact volume layer; movement of substance from within the matrix into outer boundary

Transfer: The mass rate of substance transferred from surface (i.e. after migration) to skin
Consumer Survey

• Online questionnaires, participants recruited from IPSOS panel

• Textiles, PVC flooring and paper articles, covering in total about 20 specific articles.

• The questionnaire included dedicated questions about penetration of the articles in their everyday life, frequency and duration of contact with specific articles, use context and habits.

• Completed by 9000 individuals (> 18 years) from 6 EU countries (Czech Republic, Germany, Spain, Poland, Sweden, UK).
Migration experiments

Initial concentration - $C_0$ (µg/cm³)

Surface concentration at $t \sim 0$ (µg/cm²)

Diffusion coefficient (m²/s)
Transfer experiments

Black dots: dry cotton wipes
Grey dots: wipes with artificial sweat
White dots: wipes with methanol
Approach Guidance

- Focus on articles
- ECETOC TRA as starting point
- Harmonized way for deriving defaults
- Taking into account all available information
  - Evaluation dermal exposure processes
  - Evaluation available models
  - Experimental data on migration and transfer
    - Migration: PVC flooring, printed paper, textiles
    - Transfer: PVC flooring, printed paper
  - Use patterns based on internet survey
    - PVC flooring, printed paper, textiles
## Parameters ECETOC TRA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change defaults</th>
<th>Clear definition</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product ingredient (PI)</td>
<td>+</td>
<td>+</td>
<td>Assumed to be available</td>
</tr>
<tr>
<td>Skin contact area (CA)</td>
<td>+</td>
<td>+</td>
<td>Variable and uncertain, difficult to estimate</td>
</tr>
<tr>
<td>Frequency of use (FQ)</td>
<td>+ *</td>
<td>+/-</td>
<td></td>
</tr>
<tr>
<td>Thickness of layer (TL)</td>
<td>(-) **</td>
<td>-</td>
<td>Variable and uncertain, difficult to estimate</td>
</tr>
<tr>
<td>Density (D)</td>
<td>(-) **</td>
<td>+</td>
<td>Assumed to be available</td>
</tr>
<tr>
<td>Transfer factor (TF)</td>
<td>+ *</td>
<td>+/-</td>
<td>Variable and uncertain, difficult to estimate</td>
</tr>
<tr>
<td>Body weight (BW)</td>
<td>(-) **</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

* For new subcategories  
** When using equation instead of tool
### Other relevant parameters

#### Refined exposure modelling

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Related to</th>
</tr>
</thead>
<tbody>
<tr>
<td>Released substance / transferable amount</td>
<td>Amount that can be transferred during exposure event</td>
<td>TL</td>
</tr>
<tr>
<td>Day of use</td>
<td>Day in which there is contact with the product / article (handling, unavoidable skin contact)</td>
<td>FQ</td>
</tr>
<tr>
<td>Exposure event</td>
<td>One more or less continuous period of handling / contact with the material; more than 1 event / day</td>
<td>FQ</td>
</tr>
<tr>
<td>Contact</td>
<td>Actual contact of bare skin with article without any material/air in between (opportunity transfer)</td>
<td>FQ, TF</td>
</tr>
<tr>
<td>Number of contacts</td>
<td>Number of times separate period of contact between skin and article (per event or day of use)</td>
<td>FQ, TF</td>
</tr>
<tr>
<td>Duration of exposure</td>
<td>Duration of exposure (short vs prolonged); released substance considered duration-depended</td>
<td>TL</td>
</tr>
<tr>
<td>Surface area article in contact with skin</td>
<td>Surface area of article that comes into contact with skin during an exposure event / day of exposure</td>
<td>CA</td>
</tr>
</tbody>
</table>

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## Parameters ECETOC TRA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Default</th>
<th>New general default(s)</th>
<th>Article-specific defaults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product ingredient (PI)</td>
<td>Per category 0.1 – 0.5</td>
<td>No Assumed available</td>
<td>Assumed available</td>
</tr>
<tr>
<td>Skin contact area (CA)</td>
<td>Per category</td>
<td>Yes - Gender specific - For body parts not in TRA</td>
<td>Assumption to be made by exposure assessor</td>
</tr>
<tr>
<td>Frequency of use (FQ)</td>
<td>1/day</td>
<td>Yes: &lt;1 for articles with non-daily use</td>
<td>Yes (based on time activity patterns)</td>
</tr>
<tr>
<td>Thickness of layer (TL)</td>
<td>0.01 / 0.001 cm</td>
<td>No</td>
<td>No; other approaches</td>
</tr>
<tr>
<td>Density (D)</td>
<td>1 (g/cm³)</td>
<td>No Assumed available</td>
<td>Yes Assumed available</td>
</tr>
<tr>
<td>Transfer factor (TF)</td>
<td>1 (100%)</td>
<td>No</td>
<td>Yes, indicative</td>
</tr>
<tr>
<td>Body weight (BW)</td>
<td>10 / 60</td>
<td>10 / 65 (gender / age)</td>
<td>NA</td>
</tr>
</tbody>
</table>
Alternatives – Additional parameters

• ECETOC TRA: Probably focused on articles with one long duration event; need additional approach for articles with typically short, frequent contacts

• Interaction between number of contacts ($n_c$), duration of exposure ($t$) and surface area of article in contact with skin (SA)
  – Number of contacts per event can be high
  – Non-linear increase of exposure with increase of duration (↓ transfer)
    • Max. loading of skin
    • Limited migration
  – Assumption $CA = SA$ not always conservative

• $t = t_c \times n_c$

• $SA = SA_c \times n_c$
  – $SA = SA_{new} \times SA_c \times n_c$
  – $SA_{new}$: between 1 (all contacts with new surface) and ~0 ($1/n_c$; all with same surface)
1. Constant contact situations

- $t_{exposure} = t_{contact}$, e.g. clothing, bed linen
- $t_c$ and CA considered most important
- CA as proxy for SA
  - small number of contacts, all with same surface
- $DE = (PI \times TL \times D \times CA \times TF \times DF \times 1000) / BW$
  - $DF = \text{duration factor, 0-1}$
    - $1 =$ reasonable worst case (e.g. 18 hr. for clothing)
    - 8 instead of 18 hr. $\rightarrow 8/18 = 0.44$
2. Many short duration contact situations

- $t_{\text{exposure}} >> t_{\text{contact}}$, e.g. children playing, reading newspaper
- Surface area article in contact with skin proxy for ‘intensity of exposure’
- $DE = \frac{\pi \times TL \times D \times TF \times SA \times 1000}{BW}$
Alternatives – Additional parameters

• Washing / cleaning of articles by consumers (W)
  – Occurs regular for some articles groups
    • E.g. clothing, kitchen, floors
  – Influences transferrable amount: ↓
    • W between 0 and 1
  – Although relevant, no defaults for W could be derived (article-substance specific information if available) on dermal exposure of consumers
  – \( (DE = (PI \times TL \times D \times CA \times TF \times W \times 1000) / BW) \)
Alternatives - Release

• TRA: \[ DE = \left( \frac{PI \times TL \times D \times CA \times TF \times 1000}{BW} \right) \]

  = release (per unit surface of article during exposure event ‘ASRA’)

• Refinements of ‘release’ estimates by refining PI, D & TL?
  
  PI & D: yes
  TL: ??

• PI and D do not have an independent role in the DE release
• Refinements in PI & D possible, but always in combination with ‘TL’
• Uncertain about validity of TL defaults

→ Alternative approaches to avoid uncertainly about TL
→ Release

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Alternatives - Release

- Tiered approach amount of substance released from article during exposure event
Tier 1: Diffusion based model

Based on physical concept of molecules moving within a matrix

Concept of diffusion modelling, applied in fields of

- Migration of substances from food packaging to food
- Emissions from building materials to indoor air
- Paper of Delmaar et al. 2013 (Regul. Pharm. Tox.): ‘Alternative screening tool for dermal exposure to substances in articles (consumer exposure)’
- Complete diffusion equation → simplified diffusion based model

\[
\frac{dA}{dt} = S \times D_{diff} \times \left. \frac{\partial C}{\partial x} \right|_{\text{surface}} \quad A_s(t) = C_0 \times \sqrt{2 \times D_{diff} \times t}
\]

Diffusion coefficient

- Experimentally determined (from extraction curves in methanol) OR
- Estimates from \( MW \), matrix specific coefficients \( A_p \) and \( T \) (Holmgren et al. (2012):

\[
D_{diff} = \exp \left( A_p - 0.1351(Mw)^{2/3} + 0.003Mw - \frac{10450}{T} \right)
\]
Alternatives - Release

**Tier 2: Artificial sweat extractions**

- Empirical method; combining both aspects of diffusion and solubility in (artificial) sweat
- Experimental data need; no modelling approaches to estimate available, besides some rule of thumbs for textiles

<table>
<thead>
<tr>
<th>Substance category</th>
<th>Migration rate *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dye</td>
<td>0.5 %</td>
</tr>
<tr>
<td>Hydrophilic textile auxiliary</td>
<td>2 %</td>
</tr>
<tr>
<td>Hydrophobic textile auxiliary</td>
<td>0.1 %</td>
</tr>
</tbody>
</table>

*Migration rate is defined by Krätze and Platzek (2004) as the ratio of artificial sweat extractable amounts to the initial content of substance in the textile, at a fixed time t (60 min.).

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Dermal exposure assessment strategy

**TRA based approach**

**OPTION 1:** TRA equation + TRA defaults

**OPTION 2:** TRA equation + specific values instead of defaults
(+ population variability)

**OPTION ‘Additional’ (1*,2*,3*):** Additional parameters:
- number of contacts
- article surface area
- duration factor
- skin contact factor
- washing/cleaning factors

**Alternative approach**

**OPTION 3:** alternative approach for 'release from article' instead of TRA concept 'thickness of layer'

3A: mass balance
3B: diffusion model
3C: leachable amount

*additional factors might be used in combination with either the TRA-based approach or the alternative approach for assessing release from article*
Case study – Textile DMF in polyester T-shirt

OPTION 1: default TRA

OPTION 2: TRA & specific values

OPTION 2*: TRA & specific values - washing reduction

OPTION 3A*: mass balance & specific values

OPTION 3B*: diffusion based model & specific values

OPTION 3C*: sweat extractable amount & specific values

Systemic exposure (mg DMF/kg bw/day)

adult men
child two years old
Case study – Printed paper
DB 360 in home printed paper
Case study – PVC flooring
DEHP in PVC flooring
Remaining gaps

Estimating release from articles

• Moving from assumption (‘TL’) towards chemical-physical based models
• Diffusion based modelling → high (unrealistic) estimates → ignoring other limiting factors: solubility, saturation (absence of removal)
  • Towards model combining diffusion with solubility and removal?
  • Integrated approach external exposure and internal dose?
  • Experimental testing (parallel: experimental testing is the standard for generating realistic emissions from building materials to indoor air)

Transfer factors

• Moving from defaults towards experimental testing based on real articles → 1000-fold reduction (NB: differentiation between release and transfer)
• Lack of generic rules to estimate TF → Consensus on design experiments
• Experiments log Kow → not enough support do derive rules for TF (below 1)

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Remaining gaps

Use habits and practices

• Use data of **products** $\rightarrow$ dose
• Use data of **articles** $\rightarrow$ no linear relationship with dose (dose is also affected by CA, SA, release)
• Online questionnaires related to frequency, duration, way of handling articles $\rightarrow$ useful for derivation of defaults for some parameters (frequency) and relevance additional factors (washing before 1st use), also relevant for deriving an exposure scenario
• For other behavioural factors: observational studies needed instead of online questionnaires, e.g.
  – Number of contacts PVC flooring
  – Surface area of contacted PVC flooring
Available information


Any questions?

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