Approaches for Prioritizing and Evaluating Trace Contaminants

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Challenges in Using Risk Assessment for the Management of Chemical Contaminants in Foods

Occurrence
- Increasing analytical sensitivity leads to detection of more and more chemicals at very low levels
- Occurrence data available in raw materials and/or finished products
- Incidental vs recurring contamination (acute vs chronic exposure)

Exposure
- Sources of exposure can be varied (different dietary sources & non-dietary sources)
- Exposed population (infants, adults)

Regulation
- Regulatory limits do not exist for all chemical contaminants in all foods or raw materials
- Global vs local legislation (inconsistencies)
- Health Based Guidance Values (ADI, TDI) may have been established, refer to human exposure (need to be translated into levels in food/ raw materials)

Need to be managed to protect the consumer
Objective

To define a global, harmonised and consistent strategy to manage chemical contaminants in raw materials that is scientifically sound and defendable

- Global
- Raw materials
- Scientific

Output:

Tool for the prioritisation of chemicals to be managed in raw materials, entailing the use of decision trees

- Severity
- Risk (likelihood to cause harm)
Concept: General Risk Assessment Paradigm

1. Hazard identification
   - Toxic effect (severity)
   - Decision tree
   - Grading: α, β, γ, δ

2. Hazard characterisation
   - Safe levels of exposure (HBGVs)
   - ‘Surrogate’ HBGVs
   - Safety-based guidance values (SBGV)

3. Exposure assessment
   - Occurrence in raw materials
   - Raw material categorisation
   - Dietary intake

4. Risk characterisation
   - Risk (likelihood to cause harm)
   - Decision tree
   - Grading: N, L, M, H
Severity

Criteria for setting the severity (decision tree)

- Chronic exposure (not acute), oral route (not inhalation or injection)
- Carcinogenicity, reproductive and developmental toxicity
- Structural changes/ functional damage in critical organs or systems
- Mutagenicity/ absence of a threshold
- Reversibility
- Evidence in humans/ plausibility for human effect

➢ Categorisation into $\alpha$, $\beta$, $\gamma$, $\delta$ (most severe - least severe)
Decision Tree for Severity

Is the substance \textbf{carcinogenic} or toxic for the reproduction or the development? NO

Is there evidence for mutagenicity or absence of threshold? NO

Is there evidence for Human health effect or a strong \textbf{plausibility} for a Human health impact based on the mode of action? NO

\textbf{Category} $\alpha$

Is the substance \textbf{neurotoxic}, \textbf{immunotoxic}, or damaging the functional structure of a vital \textbf{organ} or blood or bones? NO

Is the adverse effect \textbf{permanent}? NO

Is there evidence for Human health effect or a strong \textbf{plausibility} for a Human health impact based on the mode of action? NO

\textbf{Category} $\beta$

\textbf{(1)} for substances with ratio LOAEL/NOAEL $\leq$ 3 or substances with toxicity data of low quality, e.g. missing chronic studies

\textbf{(2)} for substances with good toxicological database that suggests the severity is overestimated

Is the substance leading to diarrhea, decrease in food intake or in body weight or any other \textbf{mild transient} physiological effect? NO

\textbf{Category} $\gamma$

\textbf{Category} $\delta$
Health Based Guidance Values

HBGV

- Established by competent authorities (JECFA, EFSA…)
- Most comprehensive, global, recent

Surrogate HBGV (sHBGV)

- In absence of HBGV
- Depending on type of effect (threshold or not)

**Issue:** how to translate HBGV into safe levels in raw materials?

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**Table: No HBGV available (no ADI or TDI)**

<table>
<thead>
<tr>
<th>Non-threshold effect</th>
<th>Threshold effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>POD¹, e.g. BMDL₁₀, TD₅₀</td>
<td>NOAEL, LOAEL, in silico tox</td>
</tr>
<tr>
<td>Margin of exposure (MOE)²</td>
<td>Uncertainty / extrapolation factors²</td>
</tr>
<tr>
<td></td>
<td>- Inter-, intra-species</td>
</tr>
<tr>
<td></td>
<td>- Subchronic to chronic</td>
</tr>
<tr>
<td></td>
<td>- Route to route</td>
</tr>
<tr>
<td></td>
<td>- LOAEL to NOAEL</td>
</tr>
<tr>
<td></td>
<td>- ...</td>
</tr>
</tbody>
</table>

POD/MOE → POD/UFs

Surrogate HBGV

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¹ POD, point of departure
² Appropriate margin of exposure (MOE) or uncertainty factor (UF) associated with low concern for human exposure
Exposure

Occurrence data
- Nestlé database (6’000’000 analytical data for RM, almost 3’000 compounds)
- Defined ‘cleaning’ process (e.g. treatment of left censored data, \( n \))

Food intake
- GEMS/Food cluster diets (WHO, 2012)
- Global average diet: weighted average across clusters

Raw material categorisation
- Definition of main and subcategories based on GEMS and FoodEx2* categories
- Mapping of all Nestlé raw materials to subcategories

Exposure
- Deterministic, using median occurrence values
- Based on intakes of the \textit{main} category, using 60 kg body weight

*(EFSA, 2015)
RM Categorisation

- Alignment with GEMS/Food Cluster diets
- Global food intake scenario (weighted average across all cluster diets)

<table>
<thead>
<tr>
<th>groups</th>
<th>intake (g)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Grains</td>
<td>353</td>
<td>Wheat</td>
<td>Rye</td>
<td>Oats</td>
<td>Corn</td>
<td>Rice</td>
<td>Barley</td>
<td>Others</td>
</tr>
<tr>
<td>2 Seeds and roots</td>
<td>193</td>
<td>Nuts</td>
<td>Leguminous seeds</td>
<td>Oilseeds</td>
<td>Starchy roots</td>
<td>Rice</td>
<td>Barley</td>
<td>Others</td>
</tr>
<tr>
<td>3 Vegetables</td>
<td>265</td>
<td>Brassica vegetables</td>
<td>Fruiting vegetables</td>
<td>Leafy, stalk and stem vegetables</td>
<td>Bulb and root vegetables</td>
<td>Legume vegetables</td>
<td>Other vegetables</td>
<td>Other vegetables</td>
</tr>
<tr>
<td>4 Fruit</td>
<td>197</td>
<td>Berries and other small fruits</td>
<td>Citrus fruits</td>
<td>Pome fruits</td>
<td>Stone fruits</td>
<td>Tropical and subtropical fruits</td>
<td>Other fruits</td>
<td>Heat processed fruits</td>
</tr>
<tr>
<td>5 Dairy</td>
<td>151</td>
<td>Milk (raw, processed and powder)</td>
<td>Whey &amp; other milk derivates</td>
<td>Cheese</td>
<td>Yoghurt</td>
<td>Butter Milk</td>
<td>Cocoa &amp; Malt beverages</td>
<td>Lactose</td>
</tr>
<tr>
<td>6 Proteins</td>
<td>159</td>
<td>Mammals</td>
<td>Eggs &amp; Eggs derivates</td>
<td>Poultry</td>
<td>Fish &amp; Sea food</td>
<td>Vegetable proteins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Sweets</td>
<td>72</td>
<td>Sugars, candies</td>
<td>Cocoa &amp; its non-liquid derivate</td>
<td>Chocolate and chocolate equivalent</td>
<td>Honey</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Fats</td>
<td>38</td>
<td>Vegetable fats &amp; Oils</td>
<td>Terrestrial animal fats (incl. poultry fats)</td>
<td>Marine animal fats</td>
<td>Milk fat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 Miscellaneous</td>
<td>35</td>
<td>Seasonings (spices, herbs, &amp; condiments)</td>
<td>Sauces, savories &amp; vinegar</td>
<td>Miscellaneous agents for food processing</td>
<td>Additives, flavorings, sweeteners &amp; coloring agents</td>
<td>Vitamins and minerals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 Beverages</td>
<td>2000</td>
<td>Water</td>
<td>Fruit &amp; vegetable juices</td>
<td>Coffee</td>
<td>Tea</td>
<td>Coffee substitutes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Issue: Translation of HBGV into Safe Levels in Raw Materials

Quota concept

- Allocate fractions of the TDI/ADI to food categories and beverages
- Additional margin was reserved for other sources of exposure (environmental) or process formation (if applicable) and uncertainties on sources
- Default setting:
  - Consider equal contamination in all raw materials across categories → exposure contribution is determined by the relative food intake.
- Quota concept:
  - Allocation of fractions of the TDI to the different RM (main) categories, based on available knowledge on occurrence (or absence) in different RM categories
  - Safety Based Guidance Values (SBGV)
Safety Based Guidance Value (SBGV)

Definition:

The **SBGV** refers to the level of a given chemical in a specific food raw material (expressed in mg/kg of raw material) consumed in the context of an average global diet, that can be ingested (orally) on a daily basis over a lifetime without an appreciable health risk.
Risk (likelihood to cause harm)

Decision tree

- Used to set the level of risk
- Categories: negligible (N), low (L), medium (M), high (H)

Based on

- Level of exhaustion of HBGV (<50%, >50%, >100%)
- Frequency of exceeding the SBGV (cut-off 25%) → ‘occurrence flag’
- Numerical median concentration value (>2x SBGV)
- Significant exposure contribution to HBGV (>10% of HBGV)
### Decision Tree for Risk

1. **Is total average exposure to the compound ≥ 50% of the HBGV?**
   - **YES**
   - **NO**

2. **Is total average exposure to the compound ≥ 100% of the HBGV?**
   - **YES**
   - **NO**

3. **Is the sub-category flagged for ≥ 25% prevalence above the SBGV?**
   - **YES**
   - **NO**

4. **Is the median concentration in the flagged sub-category ≥ 2-fold above the SBGV?**
   - **YES**
   - **NO**

5. **1 - Negligible risk**

6. **2 - Low risk**

7. **3 - Medium risk**

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(1) Health Based Guidance Value (ADI, TDI, ‘surrogate’ HBGV)
(2) Safety Based Guidance Value
## Risk Assessment Tool

### Consumption

<table>
<thead>
<tr>
<th>Group</th>
<th>Quota</th>
<th>Safety Based Guidance Value ([\text{mg/kg}])</th>
<th>Exposure</th>
<th>Health Based Guidance Value ([\text{mg/kg bw/day}])</th>
</tr>
</thead>
<tbody>
<tr>
<td>MARGIN</td>
<td>10.0%</td>
<td>10.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beverages</td>
<td>2.0%</td>
<td>20.0%</td>
<td>1.714288</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>0.04%</td>
<td>5.0%</td>
<td>24.49179</td>
<td></td>
</tr>
<tr>
<td>All-Food</td>
<td>1.44%</td>
<td>65.0%</td>
<td>7.03125</td>
<td></td>
</tr>
<tr>
<td>Grains</td>
<td>0.35%</td>
<td>27.0%</td>
<td>6.523808</td>
<td>2.6%</td>
</tr>
<tr>
<td>Seeds and roots</td>
<td>0.04%</td>
<td>3.7%</td>
<td>7.03125</td>
<td>0.5%</td>
</tr>
<tr>
<td>Vegetables</td>
<td>0.42%</td>
<td>29.4%</td>
<td>7.03125</td>
<td>8.6%</td>
</tr>
<tr>
<td>Fruit</td>
<td>0.20%</td>
<td>13.8%</td>
<td>7.03125</td>
<td>1.5%</td>
</tr>
<tr>
<td>Dairy</td>
<td>0.35%</td>
<td>10.5%</td>
<td>7.48140</td>
<td>0.0%</td>
</tr>
<tr>
<td>Proteins</td>
<td>0.16%</td>
<td>11.1%</td>
<td>7.03125</td>
<td>5.4%</td>
</tr>
<tr>
<td>Sweets</td>
<td>0.07%</td>
<td>5.0%</td>
<td>7.03125</td>
<td>0.2%</td>
</tr>
<tr>
<td>Fats</td>
<td>0.04%</td>
<td>0.5%</td>
<td>1.466165</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

### RESULTS

<table>
<thead>
<tr>
<th>Health Based Guidance Value</th>
<th>Consumption ([\text{Kg/day/capita}])</th>
<th>Exposure</th>
<th>Groups contribution to exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammals</td>
<td>1.75</td>
<td>2.00000</td>
<td>0.03200</td>
</tr>
<tr>
<td>Eggs &amp; Eggs derivatives</td>
<td>90</td>
<td>0.00000</td>
<td>9.00000</td>
</tr>
<tr>
<td>Fish &amp; Seafood</td>
<td>521</td>
<td>5.40000</td>
<td>0.84480</td>
</tr>
<tr>
<td>Vegetable proteins</td>
<td>767</td>
<td>19.00000</td>
<td>19.00000</td>
</tr>
</tbody>
</table>

### Analytical data

- Distribution of contaminant in the group
- Groups contribution to exposure

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Significance Matrix

Combination of Severity x Risk (from decision trees)

Triggers consideration in:
- HACCP studies
- Surveillance/ monitoring programs
- RM purchasing specifications
Case study: Cadmium

Background
• Heavy metal naturally present in the environment
• Human activities lead to release into the environment

Severity
• Category 3 (high)
  ▪ Nephrotoxic, endocrine-disrupting, and non-genotoxic carcinogenic properties (threshold effect)

Risk
• Foodstuffs are major sources of exposure, large analytical database (little uncertainty)
• HBGV: TWI = 2.5 µg/kg body weight/week (EFSA, 2011)
• Total exposure is close to the TWI (consistent with literature)
  ➢ Significant hazard in cocoa, chocolate and some of their derivates
Conclusions

Prioritisation based on the principles of food chemical risk assessment

- Results are consistent with published information (exposure, risks)
- The outcome of the matrix can be used as an input to management of chemical contaminants (justification for monitoring, mitigation, investigation, HACCP studies, setting of specifications…)
- Flexibility
  - Applicable to more specific dietary scenarios (regional diets, local populations or customer defined diets)
  - Chemicals can be grouped according to a common mode of action or existence of a group TDI, using equivalence factors (e.g. chlorate/perchlorate)
  - Limited applicability to process related contaminants (if occurring in RMs)
  - Currently out of scope: small children, ‘pure’ process contaminants, allergens, packaging materials
Publication

Re-submitted

‘A new global scientific tool for the assessment and prioritization of chemical hazards in food raw materials’

Authors

Thomas Stroheker, Gabriele Scholz and Paolo Mazzatorta
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Project team

Nestle Research Center
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• Thomas Stroheker
• Gabriele Scholz
• Benoît Schilter

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• Pascal Volery
• Richard Stadler

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