Uncertainties in food intake/exposure assessment

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Dr David Tennant
Food Chemical Risk Analysis
Food Intake Methodology TF
Introduction

- Dietary intake/exposure assessments are critical in determining whether risk management measures are required.
- Options available to risk managers range from an outright ban to simple guidance.
- A clear understanding of the exposure assessment is therefore needed to balance costs and benefits of risk mitigation measures.
- What opportunities are available for providing a clearer understanding of uncertainty?
Why uncertainty?

Uncertainties associated with dietary exposure assessment are unavoidable because we do not have perfect information about:

• The levels and frequency of occurrence of chemicals in food;
• The amounts consumed, by whom and how often;
• Relationships between these variables and those unidentified

We are unable to make measurements of people’s **real** exposures and so **models** based on the available data become a necessity.

“uncertainty **forces** decision makers to judge how probable it is that risks will be overestimated or underestimated for every member of the exposed population”*

* US National Institute for Health 1994
Assessment objectives

The exposure analyst must make choices:

- **Best estimate** – exposure that is representative of the majority of consumers?
- **Worst case** - the highest level that an individual could be exposed to?

Many exposure models involve compromises and conventions, such as use of upper percentile values to determine a ‘high level’ exposure - without really specifying what these mean.

What is a ‘conservative’ approach and how does this translate into uncertainty analysis? – Managing uncertainty through conservatism?

“For exposure assessors, uncertainty analysis increases **transparency** and, thereby, the **credibility** of the process. Consequently, reliance on worst-case assumptions can be reduced and decision support improved.”*

* WHO/IPCS, 20008
Separating variability and uncertainty

Figure 2: Diagrammatic comparison between three alternative probabilistic approaches for the same exposure assessment. In option 1, only variability is quantified. In option 2, both variability and uncertainty are propagated together. In option 3, variability and uncertainty are propagated separately. MC = Monte Carlo.

* WHO/IPCS, 20008
WHO/IPCS Guidelines on Characterising and Communicating Uncertainty*

Sources of uncertainty:

1. **Scenario** uncertainty - Uncertainty in specifying the exposure scenario

2. **Model** uncertainty: - uncertainty due to gaps in scientific knowledge

3. **Parameter** uncertainty - uncertainty associated with values for the factors that determine the exposure

Scenario uncertainty

‘Uncertainty in specifying the exposure scenario that is consistent with the scope and purpose of the assessment.’

- **Source** of the chemical
- **Route(s)** of exposure
- **Target** populations
- **Geographical** locations
- **Frequency/duration** of exposure
Model uncertainty

‘Uncertainty due to gaps in scientific knowledge that hamper an adequate capture of the correct causal relations between exposure factors.’

Model uncertainty is principally based upon:

- Modelling errors (i.e. non-consideration of parameters) and
- Relation (dependency) errors (i.e. drawing incorrect conclusions from correlations).

e.g. Over-simplification:

- Limiting number of food categories in assessment
- Use of average bodyweights for correction
Parameter uncertainty

‘Uncertainty involved in the specification of numerical values (be they point values or distributions of values) for the factors that determine the exposure.’

- measurement errors (random or systematic);
- sample uncertainty;
- data type (e.g. surrogate data, expert judgement, default data, modelling data, measurement data);
- extrapolation uncertainty; and
- uncertainty in the determination of the statistical distribution used to represent distributed parameter values.

Typically represented by uncertainties associated with food consumption survey data and data on the levels and distribution of chemicals in food.
Tiered approach to uncertainty analysis

Tier 0 (screening) uncertainty analysis
Tier 1 (qualitative) uncertainty analysis
Tier 2 (deterministic) uncertainty analysis
Tier 3 (probabilistic) uncertainty analysis

Corresponds to JECFA ‘tiered approach’ to exposure analysis
Quantifying and expressing uncertainty

The scale of level of uncertainty

<table>
<thead>
<tr>
<th>Determinism</th>
<th>Ignorance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.75</td>
</tr>
<tr>
<td>0.25</td>
<td>0.5</td>
</tr>
<tr>
<td>0.5</td>
<td>1</td>
</tr>
</tbody>
</table>

- Low level of uncertainty: Known outcomes & known distributions
- Medium level of uncertainty: Known outcomes & unknown distributions
- High level of uncertainty: Unknown outcomes & unknown distributions
EFSA Scientific Committee Guidance on Uncertainties in Dietary Exposure Assessment*

The term “sources of uncertainty” refers to components of exposure assessment that can contribute to overall uncertainty in the output. There are five main sources:

1. the **assessment objectives**,  
2. the exposure scenario(s),  
3. the exposure model,  
4. the model inputs, and the  
5. **performance** of the assessment.

For each source of uncertainty there can be several “types of uncertainty” such as:

- **ambiguity** (due to vagueness or imprecise description),
- measurement uncertainty, **sampling** uncertainty (due to limited sample sizes),
- **default value** uncertainty,
- **extrapolation** uncertainty,
- uncertainty about **model structure**, 
- uncertainty about **correlations or dependencies** between inputs,
- differences in **expert opinion**, 
- **excluded factors**, and
- **ignorance** (the possibility that unknown factors may influence exposure).

Uncertainty may also be introduced through **errors by the assessors**, e.g. during data entry, calculations, programming or reporting of results, or in failing to ensure conformance of the assessment with the specified objectives and exposure scenario.
## Qualitative analysis of uncertainties

<table>
<thead>
<tr>
<th>Source of uncertainty</th>
<th>Type of uncertainty</th>
<th>Description</th>
<th>Direction &amp; magnitude *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment objectives</td>
<td>Ambiguity/imprecise description</td>
<td>Duration of exposure</td>
<td>- -</td>
</tr>
<tr>
<td>Exposure scenario</td>
<td>Ambiguity/imprecise description Extrapolation</td>
<td>Age groups not defined Limited national data</td>
<td>++++</td>
</tr>
<tr>
<td>Exposure model</td>
<td>Correlations Excluded factors</td>
<td>Concurrent usage Other routes</td>
<td>++/- - -</td>
</tr>
<tr>
<td>Model inputs</td>
<td>Measurement Sampling</td>
<td>High lod Limited sample numbers</td>
<td>++ ++/- -</td>
</tr>
<tr>
<td>Performance</td>
<td>Ignorance</td>
<td>Disagreement on scope</td>
<td>++/- -</td>
</tr>
</tbody>
</table>

* Plus signs for an uncertainty indicate that it could have caused **small** (+), **medium** (++) or **large** (+++) over-estimation of exposure, minus signs that it could have caused **small** (-), **medium** (- -) or **large** (- - -) under-estimation of the exposure. Some uncertainties are evaluated as potentially causing either over- or under-estimation (e.g. ++/- -).
Qualitative analysis of uncertainties

Table 18: Qualitative evaluation of influence of uncertainties

<table>
<thead>
<tr>
<th>Sources of uncertainties</th>
<th>Direction a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consumption data: different methodologies / representativeness / under reporting / misreporting / no portion size standard</td>
<td>+/-</td>
</tr>
<tr>
<td>Extrapolation from food consumption survey of few days to estimate chronic exposure</td>
<td>+</td>
</tr>
<tr>
<td>Linkage between reported use levels and food items in the consumption database: uncertainties on which precise types of food the use levels refer.</td>
<td>+/-</td>
</tr>
<tr>
<td>Occurrence data: maximum reported use levels within a food category</td>
<td>+</td>
</tr>
<tr>
<td>Exposure model: uncertainty in possible national differences in use levels of food categories, data set not fully representative of foods on the EU market, exposure calculations based on the maximum reported use levels (no use of typical use levels when available)</td>
<td>+</td>
</tr>
</tbody>
</table>

a. +: uncertainty with potential to cause over-estimation of exposure;
-: uncertainty with potential to cause under-estimation of exposure.

As a whole, the total estimated uncertainty from all sources should generally lead to an overestimation of the calculated exposures (for aspartame and its related by-products: DKP, methanol, aspartic acid, phenylalanine), thus providing conservative estimates.
Quantitative analysis of uncertainties

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th>± 20%</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10x</td>
<td>10x</td>
<td>5x</td>
<td>2x</td>
<td>2x</td>
<td>5x</td>
<td>10x</td>
<td>&gt;10%</td>
<td></td>
</tr>
</tbody>
</table>

Underestimate **upper tail** exposures

Overestimate **upper tail** exposures

DRAFT Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs – Part: exposure assessment. EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF).

Quantitative analysis of uncertainties

| Scale used for evaluating the impact of uncertainties on estimates of total exposure to BPA |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| < x 1/10 | x 1/10 | x 1/5 | x 1/2 | ± 20% | 2x | 5x | 10x | >10% |
| Real value **lower** than estimate (over-estimation) | Real value **higher** than estimate (under-estimation) |
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WHO/IPCS - 10 guiding principles:

1) Uncertainty analysis should be an integral part of exposure assessment.
2) The level of detail should be based on a tiered approach consistent with the exposure assessment.
3) Sources of uncertainty and variability should be systematically identified and evaluated.
4) The presence or absence of dependencies between model inputs to be appropriately accounted for.
5) Data and/or, expert judgement should specify uncertainties for scenarios, models and model parameters.
6) Sensitivity analysis should be an integral component of the uncertainty analysis.
7) Uncertainty analyses should be documented in a transparent manner.
8) Uncertainty analysis should be subject to an evaluation process that may include peer review.
9) Exposure assessments should be iteratively refined to better characterise uncertainty and variability.
10) Communication of the results to stakeholders should reflect their different needs in a transparent and understandable manner.
Conclusions

• Are available approaches suited to the problem?
• Do they capture all of the necessary information in a realistic way?
• Do they help define the correct interpretation of the exposure assessment?
• Do they present information that is relevant and useful to risk managers?
• Do they add unnecessary detail or increase confusion?
• Do simple conservative models still have a role in communicating information about risks?
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Thank you!

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