An Integrated Framework for Probabilistic Cumulative Risk Assessment of Chemicals in Food

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Introduction

In the EU Integrated Project SAFE FOODS, we have developed an integrated framework that addresses the most important aspects of food risk assessment: the toxic effects of chemicals in relation to their exposure, the health impact of the effects, variability in the population and uncertainty.

Variability is accounted for by predicting the effect size for a large number of individuals, each with its unique exposure (food consumption, chemical concentrations, food processing habits, body weight) and sensitivity towards the chemicals.

A distribution of these effect sizes expected in the population gives a general picture of the health impact of a chemical. The fraction of the population exceeding a specific critical effect size can then be interpreted as a probability of a critical exposure (PoCE).

Uncertainty in these calculations is assessed by repeating them many times, each time randomly drawing values from uncertainty distributions for all uncertain parameters.

Here, we propose an extension of this probabilistic framework in order to deal with possible exposure to combinations of "common mechanism" chemicals. We have incorporated the relative potency factor (RPF) approach to predict the cumulative effects.

A stepwise illustration of the framework for probabilistic cumulative risk assessment is shown on the right.

Relative potency factors

In the RPF approach, doses of all chemicals are expressed as equally effective doses of one of them: the *index* chemical. The effect of the combination equals that of the sum of equivalents of the index chemical.

This approach requires (i) chemicals with the same target/effect; (ii) parallel dose-response curves; (iii) no interactions between chemicals.

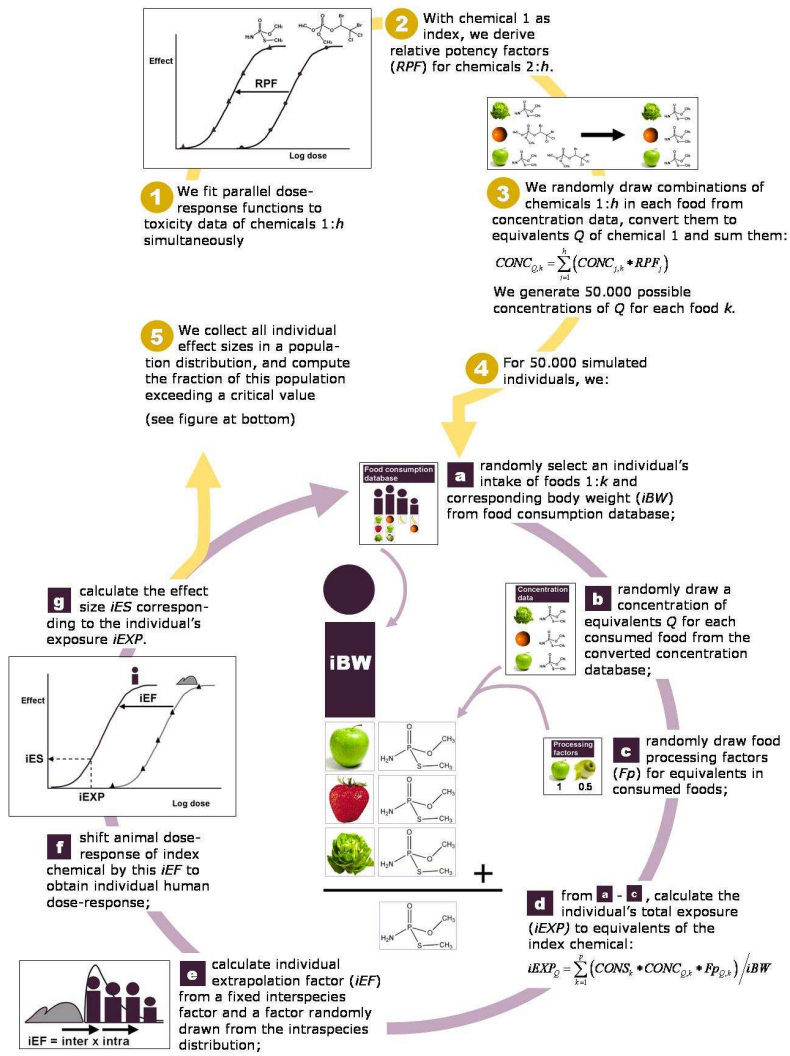
Once the concentrations are converted to equivalents of the index and summed, no distinction can be made between the chemicals. By performing this step before the Monte Carlo simulations (step 4), we implicitly assume that each processing factor and an individual's intra-species factor are equal for all chemicals.

In the uncertainty analysis, the uncertainty in RPFs is accounted for by a bootstrap: refitting the dose-response models to new datasets randomly generated from the best fit model. In each iteration, the RPFs are newly calculated, and the concentration table newly transformed.

Concluding remarks

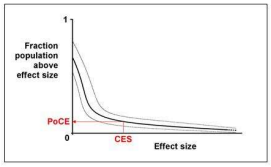
1. With a few simplifying assumptions, the framework now deals with possible exposure to combinations of chemicals in a fully integrated probabilistic way;
2. It can be used to assess the cumulative risk of any class of chemicals that meets the requirements of the RPF approach.

Cumulative model framework:



Uncertainty in these calculations is evaluated by repeating steps 1 - 5 many (10.000) times. In each iteration, values are randomly drawn from uncertainty distributions for all uncertain parameters (instead of their best estimates).

A possible presentation of the outcome is shown in the graph to the right, showing for each effect size the fraction of the population exceeding that effect size (solid curve, confidence bands in dotted curves). For any specific critical effect size (CES), the fraction above that value can be interpreted as the probability of a critical exposure (PoCE).



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