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A model for probabilistic health impact assessment of exposure to food chemicals

Hilko van der Voet [a,b,*], Gerie W.A.M. van der Heijden [a,b], Peter M.J. Bos [c], Sieto Bosgra [c,d], Polly E. Boon [b], Stefan D. Muri [e], Beat J. Brüschweiler [e]

[a] Biometris, Wageningen University and Research Centre, P.O. Box 100, 6700 AC Wageningen, Netherlands
[b] RIKILT – Institute of Food Safety, Wageningen University and Research Centre, Netherlands
[c] National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands
[d] Institute for Risk Assessment Sciences (IRAS), Utrecht University, Netherlands
[e] Federal Office of Public Health (FOPH), Zürich, Switzerland

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ABSTRACT

A statistical model is presented extending the integrated probabilistic risk assessment (IPRA) model of van der Voet and Slob [van der Voet, H., Slob, W., 2007. Integration of probabilistic exposure assessment and probabilistic hazard characterisation. Risk Analysis, 27, 351–371]. The aim is to characterise the health impact due to one or more chemicals present in food causing one or more health effects. For chemicals with hardly any measurable safety problems we propose health impact characterisation by margins of exposure. In this probabilistic model not one margin of exposure is calculated, but rather a distribution of individual margins of exposure (IMoE) which allows quantifying the health impact for small parts of the population. A simple bar chart is proposed to represent the IMoE distribution and a lower bound (IMoEL) quantifies uncertainties in this distribution. It is described how IMoE distributions can be combined for dose-additive compounds and for different health effects. Health impact assessment critically depends on a subjective valuation of the health impact of a given health effect, and possibilities to implement this health impact valuation step are discussed. Examples show the possibilities of health impact characterisation and of integrating IMoE distributions. The paper also includes new proposals for modelling variable and uncertain factors describing food processing effects and intraspecies variation in sensitivity.

1. Introduction

A common problem of risk or risk–benefit analysis is the need to integrate conclusions based on relatively hard scientific data with more subjective information on what the risks or benefits really mean in terms of impact for humans. For example, in a typical scenario study it may be possible to quantify approximately the health effects of a changed behaviour (e.g. spraying less fungicide), both for the decreased health risk of the fungicide (e.g. less risk of neurotoxic effects) and the increased health risk due to natural mycotoxins (e.g. more risk of carcinogenic effects). However, the final risk assessment will have to consider how to balance these health effects. A proper risk assessment requires value judgment in interaction with risk management. Although different types of value exist and are important (e.g. health, environmental, economic, social and ethical values), attention in this paper is restricted to health values related to the presence or absence of chemicals in foods, i.e. the valuation of the absence of diseases or quantitative deviations from normal health.

Risk management is concerned with scenarios (Murray et al., 2003). The simplest scenario is to study the change in health impacts when one specific chemical is present rather than absent. Other scenarios may study the combined health impact of several chemicals, the replacement of chemical(s) A by chemical(s) B, or a change in the production system, so that there is less of chemical(s)

Abbreviations: ADI, acceptable daily intake; BMD, benchmark dose; BMDL, benchmark dose lower bound; CED, critical effect dose; ChE, cholinesterase; DALY, disability adjusted life years; Df, degrees of freedom; DW, disability weight; GM, geometric mean; GSD, geometric standard deviation; HIA, health impact assessment; HIC, health impact criterion; ICED, individual critical effect dose; IEXP, individual exposure; IMoE, individual margin of exposure; IMoEL, individual margin of exposure lower bound; IMoEp1, individual margin of exposure first percentile; IPRA, integrated probabilistic risk assessment; LI, low impact; MI, moderate impact; MoE, margin of exposure; PHIA, probabilistic health impact assessment; PoCE, probability of critical exposure; RPF, relative potency factor; SD, standard deviation; SI, severe impact; TEF, toxic equivalence factor; YLD, years lost due to disability; YLL, years of life lost; WHO, World Health Organization.

* Corresponding author. Address: Biometris, Wageningen University and Research Centre, P.O. Box 100, NL 6700 AC Wageningen, Netherlands. Tel.: +31 317 480811; fax: +31 317 483554.
E-mail address: hilko.vandervoet@wur.nl (H. van der Voet).

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A, but more of B. In this paper we only consider negative health impacts, including risk–benefit cases where the benefit is measured as a risk reduction.

We approach the problem of health impact assessment from a population standpoint. The main question to answer is: How many people are at risk in different degrees considering multiple hazards? For this, we first present a general outline of the integrated probabilistic risk assessment model (IPRA) developed earlier (van der Voet and Slob, 2007). We discuss several refinements of the IPRA model with respect to the modelling on processing, and interspecies and intraspecies factors. In a next step, we introduce the concept of probabilistic health impact assessment (PHIA) which allows extending the IPRA model to multiple compounds and effects. New features are the use of multiple levels of health impact, a submodel for cumulative effects of multiple dose-additive compounds, and a submodel to combine health impacts due to different toxicological effects. The algorithm is described in detail, and the method is illustrated by examples.

2. The IPRA model: one chemical and one health effect

Integrating exposure assessment and hazard characterisation into risk characterisation is an important step in risk assessment of exposure to food chemicals (Renwick et al., 2003). When appropriate data are available this may be performed by probabilistic modelling. The integrated probabilistic risk assessment (IPRA) model (van der Voet and Slob, 2007) has been developed to implement such an integrated assessment. Here, we only give a general description of IPRA. In Section 5 we will present some detailed proposals for a possibly more useful way of specifying some of the model inputs. These inputs are the processing factors describing changes in chemical concentrations due to food processing, and the interspecies and intraspecies extrapolation factors.

The basic structure of the IPRA model is shown in Fig. 1. All inputs to the model are shown in the boxes on the left side. The upper three input boxes refer to data underlying a probabilistic exposure assessment with respect to food consumption, chemical concentrations in food, and effects on chemical concentration by food processing. This is shown by the arrows converging on the box 'Distribution of Exposures'. 'Distribution' is added to stress the probabilistic nature of the model: a distribution of individual exposures is calculated for individual persons in the human population for which we have representative consumption data.

The fourth input box in Fig. 1 represents the data from animal studies which are used to fit an appropriate dose–response or dose-effect model (see e.g. Slob, 2002). The fifth box represents a chosen critical effect size (CES, Slob and Pieters, 1998) for the effect under consideration, e.g. a 10% decrease in organ weight that is applied to the fitted dose–response curve to establish the corresponding critical effect dose (CED) for animals. Subsequently this dose is divided by an appropriate interspecies factor (according to the input in box 6) to obtain the CED for the average human. Next, information on intra-human variability is added (box 7) to obtain the human individual CED (ICED).

In principle there can be hard scientific data on inter- and intraspecies variation, but in practice the information is often limited, and soft information is used, like the traditional assessment factors of 10. Van der Voet and Slob (2007) described how a probabilistic interpretation of such soft information can be made. An important element in this is that the intraspecies factor is used to estimate variability between individuals in the human population. In our model, interindividual variation is described by a statistical distribution. Whereas empirical data or expert judgment could indicate another distribution, we currently apply the lognormal distribution, which has been found to describe many susceptibility factors and equipotent doses reasonably well (Slob and Pieters, 1998; Hattis et al., 1999a,b; Dorne et al., 2002).

Usually probabilistic exposure assessment and probabilistic hazard characterisation are performed separately, and a direct comparison of single-value characterisations (e.g. the average exposure and the acceptable daily intake, ADI) is performed by risk managers. The main IPRA result, by combining the distribution of individual exposure (IEXP) and ICED levels, is a distribution of individual margins of exposure (IMoE = ICED/IEXP) in the population (see Fig. 2). It is important to remember that the traditional assessment factors to extrapolate from an average animal to a sensitive

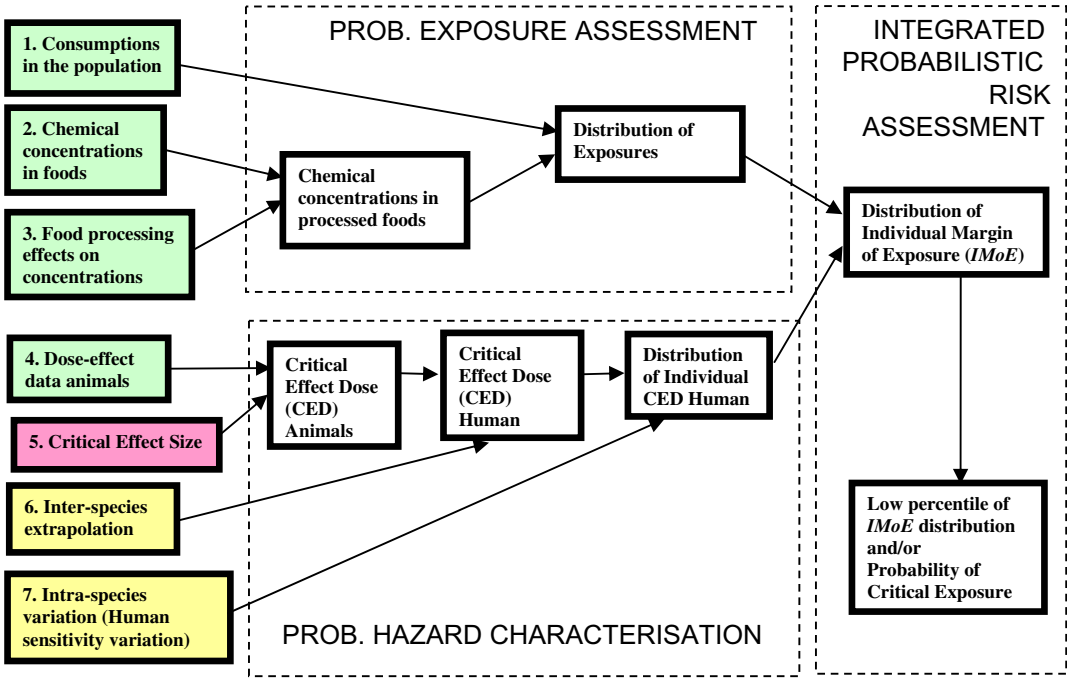

Fig. 1. Schematic representation of the IPRA model, necessary data, and output.