Symposium on ‘Nutritional aspects of food safety’

The use of food consumption data in assessments of exposure to food chemicals including the application of probabilistic modelling

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Emphasis on public health and consumer protection, in combination with globalisation of the food market, has created a strong demand for exposure assessments of food chemicals. The food chemicals for which exposure assessments are required include food additives, pesticide residues, environmental contaminants, mycotoxins, novel food ingredients, packaging-material migrants, flavouring substances and nutrients. A wide range of methodologies exists for estimating exposure to food chemicals, and the method chosen for a particular exposure assessment is influenced by the nature of the chemical, the purpose of the assessment and the resources available. Sources of food consumption data currently used in exposure assessments range from food balance sheets to detailed food consumption surveys of individuals and duplicate-diet studies. The fitness-for-purpose of the data must be evaluated in the context of data quality and relevance to the assessment objective. Methods to combine the food consumption data with chemical concentration data may be deterministic or probabilistic. Deterministic methods estimate intakes of food chemicals that may occur in a population, but probabilistic methods provide the advantage of estimating the probability with which different levels of intake will occur. Probabilistic analysis permits the exposure assessor to model the variability (true heterogeneity) and uncertainty (lack of knowledge) that may exist in the exposure variables, including food consumption data, and thus to examine the full distribution of possible resulting exposures. Challenges for probabilistic modelling include the selection of appropriate modes of inputting food consumption data into the models.

In the Western world food choice is a facet of everyday existence where judgements of risk appear to be a major concern. As pointed out by Walker (1995), ‘while voluntary risks from driving a car, drinking alcohol or even skiing or rock climbing are readily accepted (and frequently underestimated), risks associated with chemicals in food are commonly overestimated and considered totally unacceptable’. While the preoccupation of the public with toxic effects of contaminants and additives may be disproportionate to the health problems posed by these substances (Helsing & Verster, 1995), these concerns genuinely exist and must be taken into account by those in charge of ensuring the safety of the food supply. The European Union (2000) White Paper on Food Safety lays the foundations for a food policy, with food safety and consumer health at its core. The greater drive to protect consumer health, coupled with globalisation of the food supply, is leading to an increased demand for assessments of exposure to food chemicals and improvements in the methods used to carry out these assessments. Efforts to improve exposure assessments have brought together experts from the disciplines of toxicology, analytical chemistry, nutrition and mathematics. The role of nutritionists lies primarily in provision of expertise in the collection and analysis of food consumption data. Extending the use of food consumption surveys from the assessment of nutrient intake to food chemical intake has provided, and is continuing to provide, many intellectual and practical challenges for those who manage national food consumption databases.

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Exposure assessments for food chemicals

A variety of chemicals may enter our food supply, by means of intentional or unintentional addition, at different stages of the food chain. These chemicals include food additives, pesticide residues, environmental contaminants, mycotoxins, novel food ingredients, packaging-material migrants, flavouring substances and micronutrients. Monitoring exposure to these chemicals has become an integral part of ensuring the safety of the food supply. Results of exposure assessments are used to make judgements about risks to human health and to assess compliance with legislation. They may also provide a means of revealing sources of contamination and assessing the effectiveness of current strategies for minimizing the risk from chemical contaminants in the food supply.

Many methods exist for carrying out exposure assessments (e.g. duplicate-diet studies, theoretical daily intakes, biomarkers; Nutriscan, 1992; European Commission, 1998; Tennant, 1995). The choice of method for carrying out an exposure assessment will be influenced by the purpose of the exposure assessment, in addition to the nature of the chemical and the resources available. The purpose of some assessments is to establish the possibility or probability of a particular level of intake being exceeded (Wagstaffe, 1996; European Commission, 1998), whereas other assessments are carried out to determine baseline levels of exposure or to monitor trends within the population (Fisher, 1987; Galal-Gorchev, 1993). There is a general consensus that the most sensible approach to the assessment of exposure to food chemicals is that of a decision-tree or priority-based approach (Nutriscan, 1992, 1994; Pentillä, 1995; Renwick, 1996; Gibney & Lambe, 1996; European Commission, 1998), which should consider in tandem both the likely exposure to the food chemical and the risks which unacceptably-high exposures would pose. The decision-tree approach proceeds from the level of least exactitude (i.e. most conservative) to the level of most exactitude, only if the less-exact levels do not rule out the possibility of concern. Thus, although it may be possible to obtain extremely detailed exposure assessments, even at sub-cellular level (i.e. biomarkers of effect), such approaches are rarely used when simpler less-costly alternatives indicate that the exposure levels do not pose a significant risk to public health. The most commonly used approach is that of modelling dietary exposure by combining estimates of food consumption with estimates of chemical concentration.

Sources of food consumption data used in exposure assessment

As in the case of nutrient intake assessments, the sources of food consumption data used in exposure assessment range from food balance sheets to detailed food consumption surveys of individuals and duplicate-diet studies. Many of the international assessments of exposure to contaminants carried out by the WHO Joint Expert Committee on Food Additives are based on FAO food balance sheets (World Health Organization, 1998). Such data are used because of the absence of food consumption data at national level for many countries. The food balance sheet data are currently clustered to represent five regions, the Far East, Middle East, Africa, Latin America and European-type countries, and work is underway to refine the data to thirteen cluster consumption diets, to be more representative of the various consumption patterns of countries. Household survey data may be used to provide estimates of mean total population intakes of foods. In the UK, the National Food Survey is used to provide consumption data for the national total diet study. Although certainly more refined than food balance sheets, household survey data have a number of limitations for exposure assessments, including lack of data on the percentage consumers of foods, possible overestimation of intake due to waste and underestimation of intake for foods consumed outside the home. Efforts have been made to consider how data from household surveys may be made more useful for exposure assessments (Lambe et al. 1998). The most commonly used and appropriate source of food consumption data for exposure assessments is food consumption surveys of individuals. Such surveys may be conducted using 24 h recalls, diet histories, food records or food-frequency questionnaires. The use of these methods in exposure assessments has been considered by Löwik (1996). Each of these methods has advantages and disadvantages, but given the cost of collecting food consumption data for a nationally-representative sample of subjects, the emphasis for exposure assessors will most often be placed on determining which type of food consumption survey would be most appropriate for the assessment. The extent of flexibility for manipulation of food consumption data, in terms of defining food categories and expressing results, will vary from one database to another, depending on the survey methodology and also the food coding scheme that was used.

Fitness-for-purpose

For any input variable in an exposure assessment it is important to assess the quantity and relevance of the available information about that input. Data may be abundant or scarce, representative or non-representative. When evaluating food consumption data for exposure assessments, factors that should be considered include the time frame represented by the food consumption survey, the population groups to which the data refer, the food groups for which the data are available and the overall amount and quality of the data.

Chronic v. acute exposure

Chronic-toxicity studies usually form the basis of the acceptable or tolerable intakes with which exposure estimates are compared for the purpose of characterizing risk (Walker, 1998; Hermann & Younes, 1999). Ideally, an exposure assessment for a chemical, and thus the food consumption data underpinning it, should reflect the time frame of the safety statement for that chemical (Löwik, 1996; Chambolle, 1999; Löwik et al. 1999). Obviously, the measurement of
food consumption over a lifetime is implausible. A short survey duration, however, will lead to an overestimate of the prevalence of low and high intakes (Beaton, 1982; Sempos et al. 1991) due to the high level of within-individual variation that exists in food intake. This variation is of particular relevance for food chemical exposure assessments where the parameters of interest are at the extremes of the exposure distribution rather than at the centre. A number of methods have been proposed for extrapolating from short-term to longer-term intakes of foods and nutrients based on repeated short-term measurements (Slob, 1991; Wallace et al. 1994; Nusser et al. 1996). Price et al. (1996) propose an alternative strategy for modelling exposure which characterizes long-term exposures as a series of individual exposure events (microexposure event analysis).

For certain chemicals, acute toxicological end points must be considered. Since the acute reference dose should not be exceeded during the acute effect period, usually a single meal or day, the food consumption data should ideally be based on a single eating occasion or consumption over a single day (Rees & Day, 2000). Thus, modelling of acute intakes should employ databases of food consumption that are formatted to present information for each food, for each meal, for each day, for each subject in the survey. Obviously, as a prerequisite, the survey methodology must have been designed originally to record this level of detail for each eating occasion.

**Population groups**

Exposure assessments may be required for the total population or for specific subgroups of the population that have been deemed to be at higher risk than the general population. The additional risk may be the result of physiological or pathological factors and/or the composition of ingested foods (Verger et al. 1999). Groups considered by experts to be ‘at risk’ on the basis of previous knowledge of dietary habits (e.g. diabetics and weight-reducers for sweeteners) may not be well represented in national food-consumption surveys, and it may be more appropriate to conduct ad hoc surveys to obtain consumption data for these groups. Children have a higher intake of food and fluid on a per kg body weight basis, and therefore may also be considered as an at risk group.

There is some debate about whether the distributions of food chemicals should reflect the distribution for the total population or for consumers only. The Joint FAO/WHO Expert Consultation (World Health Organization, 1995) state that detailed food consumption data for the average and median consumer as well as for different population groups are important for assessing exposure. This view is shared by many committees and experts responsible for evaluating the intakes of food chemicals, and has become an accepted norm for many exposure assessments where the purpose is seen as evaluating the risk for those who are highly exposed (European Commission, 1998). Löwik et al. (1999) point out, however, that the total population or subgroups such as children should be used for estimating exposure if quantification of the risk as a prevalence is required.

**Food groups**

Ideally, the food consumption data included in exposure assessments should mirror the foods on which the food chemical concentration data are based. In many instances this ideal approach provides a real challenge for food consumption database managers, especially if the food consumption data has been collected only for the purpose of estimating nutrient intakes (Gibney & Lambe, 1996; Langlais, 1996; European Commission, 1997). This problem arises because the foods are usually coded using coding schemes that differentiate on the basis of nutrient composition of the foods (e.g. Holland et al. 1988). When estimating food chemical exposure these food codes, or the food groups into which they have been aggregated, have to be matched with descriptions of the foods in which the food chemicals are permitted or for which chemical concentration data are available. For food-additive exposure estimates, food consumption data are usually required for the food categories specified in the food additive directives. These directives, however, were designed for setting conditions of use for manufacturers, and therefore foods are described in terms of their state at manufacture. These descriptions do not always correspond to the descriptions of foods as eaten. For example, categories in the directives include ‘liquid egg (white, yolk or whole egg)’, ‘fat emulsions’, ‘decorations and coatings’. Also, there may be ambiguity about what foods are included in certain categories, and this factor will obviously influence the estimate of intake (European Commission, 1997). Chemical food surveillance for pesticide residues and contaminants may also provide chemical concentration data for food categories that are difficult to match with estimates of food consumption. The chemical analyses may have been conducted for the purpose of assessing compliance with regulations, and therefore it is the raw products that are sampled. For many foods the raw product does not correspond to the food ‘as eaten’, e.g. wheat is not eaten as wheat but as bread, bakery wares, breakfast cereals etc. In several countries databases have been developed to convert foods as eaten back to raw agricultural commodities. These databases contain information obtained from industry and from recipes. For example, in Ireland information was obtained from industry on the quantity of apples that would be used to make 1 litre cider, the quantity of milk that would be used to make 1 litre ice-cream, etc. While some foods are consumed in their raw state, e.g. apples and tomatoes, they may also enter the food chain and be incorporated into many different foods or recipes, e.g. apple pies, cider, tomato purée, soup, etc. Use of recipe databases as adjuncts to food consumption databases can help to ensure that foods consumed as ingredients of other foods or composite dishes are not neglected in exposure assessments.

**Data quality and quantity**

The quality of the food consumption data is relevant for exposure assessments in the same way as it is for nutrient assessments, and will be influenced by measurement errors, including under-reporting. Measurement errors in dietary...
surveys include errors in reporting of food intake, estimation of portion size, food coding and data entry. These errors have been discussed in detail by Bingham (1987). Underreporting of intake is a common feature of dietary surveys (Livingstone et al. 1990). It may exist as a consequence of deliberate or unintentional omission of foods or under-estimation of the portion size by the respondent (Becker et al. 1999). Levels of under-reporting are routinely calculated in dietary surveys, by dividing the reported energy intake of the subjects by their BMR, in order to assess the quality of the data. The implication of under-reporting for the assessment of food chemical exposure is an issue that has been raised by Gibney (1999). If high levels of under-reporting exist in a survey, then it is conceivable that food chemical exposure estimates based on the food consumption data will be underestimated. This underestimation will only happen, however, if the foods being under-reported are those foods in which the food chemicals are likely to be present. This possibility will obviously differ between food additives, pesticide residues and other contaminants which may all be found in quite different types of foods. It is most unlikely that all foods are under-reported equally, but, as yet, it is not possible to determine which foods may be under-reported more than others (Gibney, 1999) and whether the pattern of foods being under-reported differs between groups within the population. Preliminary analysis by Gilsenan et al. (2001) has suggested that inclusion of under-reporters may not significantly influence upper percentile estimates of food additives. This finding may be related to the number and type of foods in which the additives are present. It is also possible that individuals may over-report certain food items (e.g. fruit or vegetables) and thus lead to overestimates of exposure to chemicals found on these foods.

The quantity as well as the quality of the data is also an important consideration. In food consumption databases there may be very few data for a particular food in cases where (1) the food is only eaten by a small proportion of the population that is not well represented in the survey (e.g. teenagers, vegetarians, dieters, inhabitants of a particular geographic area), (2) the food is seasonal (e.g. certain berries, Christmas pudding), (3) the food is a ‘luxury’ food (e.g. caviar, champagne, oysters), (4) the food is used as an ingredient in other foods and therefore does not appear as a separate food item in the database. For some foods there may be a complete absence of data. Since food consumption surveys are still carried out primarily to assess nutrient intakes, food considered to be non-nutritive (e.g. tap water, diet soft drinks) may not be recorded. Also, not all surveys collect information on dietary supplement use. In exposure assessments results are usually required to reflect the exposure at the upper tail of the distribution. By their nature, the tails of the distribution will contain the least amount of data. Unless the sample size of a survey is very large, there will be very few data points at the tails of the distribution, and therefore there will be large uncertainties associated with estimates based on the tails. A brief discussion on dealing with limited data is presented later (see p. 16).

Approaches to modelling food consumption in exposure assessments

Assessments of exposure to food chemicals usually require some extent of modelling because, with the exception of duplicate diet surveys, the food consumption and chemical concentration data are not related to the same individuals within a population. While food consumption data are usually drawn from national food consumption surveys, the chemical concentration data may have been obtained from manufacturers, public analysts laboratories or field trials. Unlike for nutrients, no tables of food composition exist for chemicals such as additives, pesticides or contaminants. There may be a high extent of variability in the concentrations of these chemicals in the same types of foods, e.g. in the additive content between brands of the same type of food. The assessor must make a decision about how to combine the food consumption data with the chemical concentration data to create a representation of the real-life situation. In its broadest sense the model to represent dietary exposure can be considered as consumption \(\times\) concentration = dietary exposure. There are, however, a number of different models for combining or integrating the consumption data with the concentration data, and a number of factors that influence the choice of model for any given exposure assessment. Three approaches to modelling can be considered: (1) point estimates; (2) simple distributions; (3) probabilistic models.

Point estimates

The point-estimate approach multiplies a fixed value for consumption of a food (usually the mean population value) by a fixed value for chemical concentration in that food (usually the mean concentration or maximum permitted level) and then sums the intake from all foods. Point estimates are commonly used as a first step in assessing exposure because they are relatively simple and inexpensive to carry out. Examples of point estimates of dietary exposure include the theoretical maximum daily intake for food additives (Food and Agriculture Organization/World Health Organization, 1989), and the theoretical added maximum daily intake for flavouring substances (Cadby, 1996). Inherent in the point-estimate approach are the assumptions that all individuals consume the specified food(s) at the same level, that the food chemical is always present in the food(s) and that it is always present at an average or high level. This approach, therefore, does not provide an insight into the range of possible exposures that may occur within a population, or the main factors influencing the results of the assessment.

Simple distributions

Simple distributions employ distributions of food intake but use a fixed value for the concentration variables. The results are more informative than point estimates because they take account of the variability that exists in food consumption patterns. Nonetheless, they retain conservative assumptions related to the presence and concentration of the chemical,
and therefore can only be considered to give an upper bound estimate of exposure. Examples of this approach are tier 1 of the (US) Environmental Protection Agency (1996) Office of Pesticide Programs tiered approach to acute dietary exposure assessment, and the step 2 approach described in the European Commission (1997) SCOOP Task 4.1 report.

### Probabilistic models

In contrast to the deterministic estimates of exposure which use a single estimate of each variable, probabilistic models take account of every possible value that each variable can take and weight each possible scenario by the probability of its occurrence (Vose, 1996). This approach ensures that any variability (true heterogeneity) and/or uncertainty (lack of knowledge) in variables, including food consumption, are reflected in the model output. The structure of a probabilistic model may be similar to a deterministic model, with all the multiplications, additions, etc. that link the variables together, except that each uncertain variable is represented by a distribution function instead of a single value. Two primary advantages of probabilistic modelling are that (1) it permits the exposure assessor to consider the whole distribution of exposure, from minimum to maximum, with all modes and percentiles, and (2) it includes a comprehensive analysis of the sensitivities of the resulting exposures with respect to uncertainties in variables. The results of sensitivity analyses permit the risk managers to consider the relative merits of different strategies for reducing exposure in cases where levels of exposure are deemed to be unacceptably high.

To illustrate the application of probabilistic modelling, we can consider the model used by Lambe et al. (2001) for the estimation of exposure to intentionally-added flavouring substances. A point-estimate approach, entitled the theoretical added maximum daily intake, is currently used in Europe to estimate the intake of flavouring substances. This method assumes fixed values for the daily intake of flavoured food (160 g/d) and flavoured drinks (324 g/d). It then assumes that the full amount of flavoured food and beverages will contain the particular flavouring substance of interest at the upper usage limit, as specified by the Council of Europe (Cadby, 1996). The exposure estimate generated is a possible intake for a worst case scenario, but the estimate provides no information about the likelihood of this intake occurring. An examination of the Irish national food ingredient database (Department of Clinical Medicine, 1999) revealed that not all brands of food within flavourable-food groups contained flavourings. Information from the flavouring industry also revealed that, even if a flavouring was present in a brand, it did not necessarily contain the flavouring substance of interest. If it did contain the flavouring substance, then the flavouring substance was more likely to be used at a concentration at the lower end of the distribution of concentrations than at the upper end. Lambe et al. (2001) developed a probabilistic model to take account of the uncertainty and variability associated with each of these variables (Fig. 1). The food consumption data and chemical concentration data were modelled as histograms, and chance of encountering a flavouring in a brand and a flavouring substance in a flavouring were modelled with discrete distributions. The authors found that for the twelve flavouring substances examined, the theoretical added maximum daily intake estimates were very conservative relative to the modelled intakes.

### Food consumption data in probabilistic models

Food consumption data can be entered in probabilistic models using full electronic food consumption databases or indicative data. The choice of data input method will depend largely on the computer resources available. If sufficient computing power is available, use of full electronic databases is usually considered preferable as it maintains data at the level of individual subjects and eliminates the need for building in correlations between intakes of multiple foods. It also provides greater flexibility for designing models to combine the consumption data with the concentration data. There may be limitations to the use of this approach in cases where there are very few intake values for a food. Also, a potential disadvantage is that the minimum and maximum of the observed food consumption data will be the minimum and maximum entered in the model. These values may not reflect the population minimum and maximum. The alternative to using the full electronic database is to use indicative food intake distributions. These distributions may be empirical or parametric. Empirical distributions represent a mathematical description of their shape, whereas parametric distributions are based on a mathematical function whose shape and range is determined by one or more distribution parameters (Vose, 2000). Empirical distributions include histograms and cumulative distribution functions. Parametric distributions include Lognormal, Normal, Beta, Weibull, Gamma and many more. Vose (2000) proposes that parametric distributions rather than empirical distributions should be used only in the following situations: (1) when the underlying mathematics for the distribution is known; (2) when the distribution to be fitted to the data is well known to closely fit this type of variable; (3) when the modeller simply wishes to find the best-fitting theoretical distribution for his/her data without any previous knowledge of what it is.

**Fig. 1.** Elements of a probabilistic model of exposure to intentionally-added flavouring substances. (From Lambe et al. 2001.)
Finley & Paustenbach (1994) state that one of the main barriers to the adoption of probabilistic modelling is a lack of consensus on the proper distributions to use for key variables. A central part of any probabilistic exposure assessment to food chemicals is the selection of probabilistic distributions for the uncertain input variables, one of which is food consumption. Determining appropriate models and distributions to represent food consumption data in probabilistic assessments has become one of the main challenges for nutritionists and food consumption database managers involved in exposure assessments. As part of an EU Fifth Framework-funded project entitled Development, validation and application of stochastic modelling of human exposure to food chemicals and nutrients (www.iefs.org/montecarlo), the Institute of European Food Studies have undertaken numeric experiments using the commercially-available software BestFit Probability Distribution Fitting for Windows (Palisade Corporation, Ivybridge, Devon) to assess the goodness-of-fit of distributions for a variety of foods as reported in the North/South Ireland Food Consumption Survey (Irish Universities Nutrition Alliance, 2001). Thirty-five foods, with varying percentage consumers, were included in the analysis, and the results are presented in Table 1. No parametric distributions were accepted for intake data referring to total population intakes due to the peak of zeros for non-consumers. Total population intakes should be modelled using either a histogram of total population intakes or as a two-stage model, with a discrete distribution to describe the probability of being a consumer or a non-consumer, and then an empirical or suitable parametric distribution to describe the intakes among consumers only. For intakes among consumers only, the Lognormal and Pearson VI distributions were the distributions most commonly ranked in the top three according to the Anderson Darling goodness-of-fit statistic (Cullen & Frey, 1999). The work of this project is continuing to look at the implications of using different distributions and models to describe food intake in probabilistic models of exposure, and to consider issues such as truncation of distributions, correlations between foods and the influence of under-reporting. Also related to food consumption is the influence of including factors such as brand loyalty and market share in probabilistic models of exposure to food chemicals. Ascertaining the influences of these factors will be critical for the development of valid models that will generate realistic estimates of exposure but that will not have the potential to underestimate true intakes.

In cases where food consumption data are limited or absent, a decision must be made about whether to collect new data or to use assumptions, predictive models or expert judgement. The approach taken should depend on the extent of the uncertainty introduced by the lack of data and the sensitivity of the final model output to this uncertainty. If a sensitivity analysis shows that the level of intake of a particular food is unlikely to have a significant effect on the exposure assessment of a chemical, even at the extremes, then a point estimate or assumption might be used to describe the intake of that food. It would be a waste of resources to collect new data or elicit expert judgement. It is very important that modelling is not seen as a means of compensating for poor quality or inappropriate data. In cases of limited data the advantage of the probabilistic approach lies not in stretching data beyond their limits, but rather in facilitating the estimation of the uncertainty introduced by the limited data. Techniques such as bootstrapping can be used to estimate CI for the mean or other statistics calculated from a sample (Cullen & Frey, 1999).

Future directions

The future direction of food consumption data in exposure assessments has been considered in detail as part of the EU Fifth Framework-funded project Food Safety in Europe (www.ilsi.org/europe/fosie). The results of these deliberations will be available as a supplement to Food and Chemical Toxicology towards the end of this year. There may be advances in the collection of food consumption data using bar codes. This approach would provide data at brand level, and thus remove much of the uncertainty about the presence or absence of food additives in foods. However, more detail at brand level for foods with bar codes may have to be weighed up against less detail about foods eaten out of the home. Current methodologies for collecting food consumption data may not record certain details of food preparation, e.g. washing of fruit, that may be significant for estimating exposure to pesticide residues. Knowledge of the proportion of raw agricultural commodities imported from different climatic regions of the world may be necessary for estimating exposure to mycotoxins.

The use of sensitivity analysis as part of probabilistic modelling of food chemical exposure will be an essential element in effectively directing the allocation of future resources and data collection for the purpose of improving estimates. The relative importance of each variable in the model will be considered with respect to how significant it is for the exposure estimates. It will be interesting to see how improving the level of detail of food consumption ranks compared with, for example, provision of detailed chemical concentration data or information about market share or brand loyalty. Whatever the outcome, nutritionists will
undoubtedly continue to play a valuable role in carrying out and interpreting assessments of exposure to food chemicals in the future.

References


