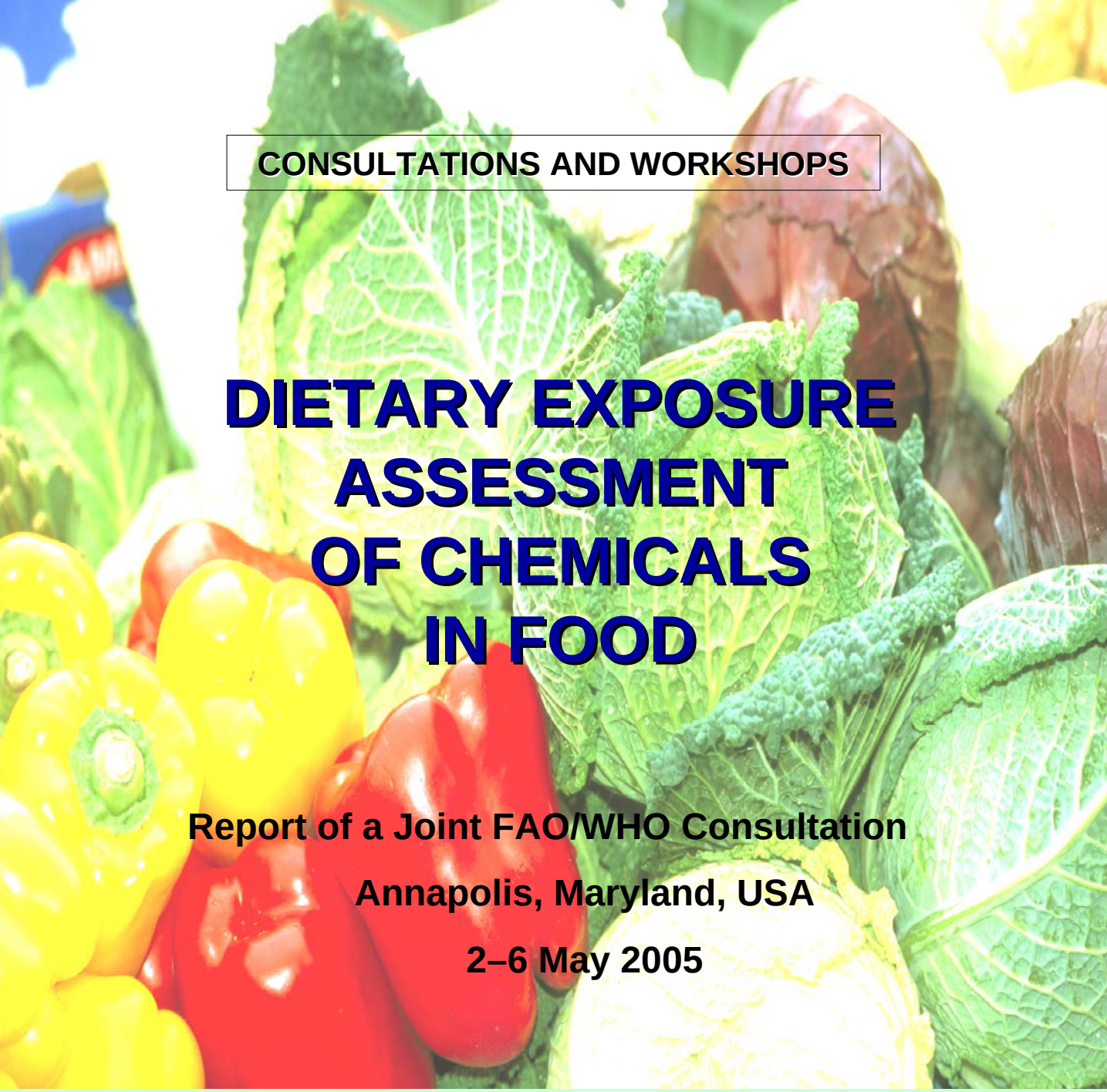

CONSULTATIONS AND WORKSHOPS

DIETARY EXPOSURE ASSESSMENT OF CHEMICALS IN FOOD

Report of a Joint FAO/WHO Consultation

Annapolis, Maryland, USA

2–6 May 2005

World Health Organization

Food and Agriculture Organization of the United Nations

Issued by the World Health Organization in collaboration with the Food and Agriculture Organization of the United Nations

CONSULTATIONS AND WORKSHOPS

DIETARY EXPOSURE ASSESSMENT OF CHEMICALS IN FOOD

Report of a Joint FAO/WHO Consultation
Annapolis, Maryland, USA
2–6 May 2005

Issued by the World Health Organization in collaboration with
the Food and Agriculture Organization of the United Nations

WHO Library Cataloguing-in-Publication Data

Consultations and workshops : dietary exposure assessment of chemicals in food : report of a joint FAO/WHO consultation, Annapolis, Maryland, USA, 2-6 May 2005.

1.Food contamination - analysis. 2.Eating. 3.Diet - standards. 4.Body burden. 5.Risk assessment - methods. I.World Health Organization. II.Food and Agriculture Organization of the United Nations.

ISBN 978 92 4 159747 0 (NLM classification: WA 701)

CONTENTS

EXECUTIVE SUMMARY

An international Expert Consultation on Dietary Exposure[1] Assessment of Chemicals[2] in Food was held in Annapolis, Maryland, USA, from 2 to 6 May 2005. The list of participants is given in Annex 3. The purpose of the expert consultation was to update and expand the report of the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Consultation on Food Consumption and Exposure Assessment of Chemicals (WHO, 1997a), which was held in Geneva, Switzerland, in 1997.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) have served as scientific advisory bodies to FAO and WHO, the Codex Alimentarius Commission, member countries, and other interested parties since the early 1960s. JECFA and JMPR have regularly held meetings at which general principles have been developed and updated; however, these general principles have not been consolidated in a guidance document. In light of this, and to take account of advances in the science of risk assessment, FAO and WHO have initiated a joint Project to Update and Consolidate Principles and Methods for the Risk Assessment of Chemicals in Food. This expert consultation is one of a series of workshops being held in the context of this project.

The aim of this consultation was to provide guidance to WHO and FAO and their expert advisory bodies, the Codex Alimentarius Commission, national governments, and the risk analysis community at large on how to perform and interpret dietary exposure assessments at the international, regional, national and local levels.

The consultation considered wide issues related to dietary exposure assessments of chemicals in food from data sources to how to present.. The consultation recommended that national authorities who wish to estimate national dietary exposures perform their own dietary exposure assessment by using international toxicological reference value(JECFA and JMPR) but national food consumption and concentration data. And exposure assessments should cover critical groups that are either more vulnerable or are expected to be more exposed.

According the specific purpose, different data sources, assumptions, methodologies can be used. But in the final step, the data sources, assumptions, exposure assessment on critical group should be noted.

The consultation recommended the stepwise approach. Screening method was considered as a first step. If estimated dietary exposure does not exceed its relevant toxicological reference value, then the level of exposure will be acceptable because the screening method overestimate exposure. If the existence of a safety concern cannot be ruled out on the screening-level, more accurate assessments of dietary exposure may be needed which should be designed in a such a way that potential high dietary exposure to a specific chemical is not underestimated. The methodologies should take into consideration non-average individuals, and in particular those foods containing the highest concentration of the chemical of interest, or who have a low or infrequent consumption of foods with very high food chemical concentrations.

The consultation noted that total diet studies are useful tools for assessing mean chronic dietary exposures to chemical hazards and identifying priorities. And the consultation recommended that the 13 Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme (GEMS/Food) Consumption Cluster Diets should

[1] The term “dietary exposure” is used synonymously with the term “dietary intake”, depending upon existing regulatory frameworks or other related considerations.

[2] In this report, “chemicals” includes food additives, contaminants, pesticides, veterinary drugs, and nutrients.

replace the currently used GEMS/Food 5 Regional Diets as the tool for international chronic dietary assessments.

The consultation noted that, in principle, the determination of potential exposure is the same across all food chemicals, including veterinary drugs. However, the consultation recognized that the specific application of these procedures to different food chemicals may differ.

The consultation recommended that all countries, including developing countries, should conduct food consumption surveys on a periodic basis, preferably based on individual dietary records. As the design of food consumption surveys could have a critical impact on the results of any dietary exposure assessment, harmonization of study design should be achieved to the extent possible. Surveys should include drinking-water, beverages, and food supplements.

The consultation noted that exposures to some chemicals through routes other than consumption may occur (aggregate exposure) and that exposures to chemicals or drugs sharing the same mechanism of action (toxicity) may also be encountered (cumulative exposure). The issue of aggregate exposure to food chemicals from multiple sources is under review, with a focus on the use of probabilistic approaches. The methodology for the cumulative dietary exposure to chemicals with a common mechanism of action could be considered for use at the international level, regardless of the development of probabilistic methods.

1. INTRODUCTION

As the Swiss physician Paracelsus stated in the 16th century, "all substances are poisons; there is none which is not a poison. Therefore, the right dose differentiates a poison and a remedy" (Winter & Francis, 1997). This fundamental relationship between a chemical's inherent toxicity and the exposure of the population to that chemical forms the foundation for modern risk assessment of potentially hazardous chemicals. Consequently, exposure assessment is essential for quantifying risk and, ultimately, for determining whether a substance poses an unacceptable risk to public health.

The role of dietary exposure assessments has grown significantly in light of the World Trade Organization's "Agreement on the Application of Sanitary and Phytosanitary Measures". Paragraph 16 of this agreement requires that sanitary and phytosanitary measures be based on sound scientific risk assessment. The agreement also states that sanitary measures that are consistent with standards, guidelines, and recommendations of the Codex Alimentarius Commission are considered to comply with the requirements of the agreement. This reference to the Codex Alimentarius Commission is based on the underlying risk assessments that support Codex risk management decisions.

Risk analysis for food chemicals is made up of three components: risk assessment, risk management, and risk communication (WHO, 1995a). Risk assessment at the international level provides the scientific basis for the establishment of Codex standards, guidelines, and other recommendations and includes dietary exposure assessments as an essential component. This ensures that safety requirements for food are protective of public health, consistent among countries, and appropriate for use in international trade.

The Codex Alimentarius Commission Procedural Manual (Codex Alimentarius Commission, 2006) defines exposure assessment as "the qualitative and/or quantitative evaluation of the likely intake of biological, chemical, and physical agents via food as well as exposures from other sources if relevant". The present document deals with dietary exposure assessment of chemicals, including nutrients, present in food. However, some of the principles and approaches described here can have application to biological agents in food as well.

Dietary exposure assessments combine food consumption data with data on the concentration of chemicals in food. The resulting dietary exposure estimate is then compared with the relevant toxicological or nutritional reference value for the food chemical of concern. Assessments may be undertaken for acute (short-term) or chronic (long-term) exposures, where acute exposure covers a period of 24 h (reference) and long-term exposure covers average daily exposure over the entire lifetime. Dietary exposure assessments of nutrients use default assumptions that tend to underestimate exposure, whereas dietary exposure assessments of potentially toxic food chemicals use default assumptions that tend to overestimate exposure. For some nutrients, two assessments may be necessary because of the specific need to look at both nutrient adequacy and the potential to exceed upper safety levels.

The general equation for both acute and chronic dietary exposure would be expressed as follows:

$$\text{Dietary exposure} = \frac{\Sigma\ (\text{Food chemical concentration} \times \text{Food consumption})}{\text{Body weight}}$$

where the units typically are milligrams per kilogram body weight, for example, for dietary exposure, milligrams per kilogram for food chemical concentration, kilograms for food consumption, and kilograms for body weight.

The use of standard terminology is recommended to ensure consistent application and understanding. It is recommended that "consumption" refer to the amount of food consumed and "dietary exposure" to the amount of chemical ingested via food. In this document, the term "food" also includes beverages, drinking-water, and food supplements.

1.1 General considerations

The following points are basic general principles and considerations when undertaking dietary exposure assessments:

- The objective of the dietary exposure assessment must be clearly identified before the appropriate food consumption data and data on chemical concentrations in food are selected. For example, pre- and post-regulation[1] dietary exposure assessments are undertaken for different purposes and may have different data sources and default assumptions.

- As stated in the 1995 Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) consultation on the application of risk analysis to food standard issues (WHO, 1995a), the Codex Alimentarius Commission should ensure harmonized approaches to the risk assessment of food chemicals. In the present report, harmonization is understood to result in equivalence, which does not necessarily mean that all dietary exposure assessment procedures across food chemicals need to be the same. Rather, such procedures should aim at providing equivalent levels of consumer protection.

- Exposure assessments should cover the general population, as well as critical groups that are vulnerable or are expected to have exposures that are significantly different from those of the general population (e.g. infants, children, pregnant women, or the elderly).

- Irrespective of the severity of the toxicological end-point, the type of chemical in food, possible population subgroups of concern, or reasons for performing the dietary exposure assessment, the most appropriate data and methodology among those available should be used.

- International dietary exposure assessments should provide exposure estimates that are equal to or greater than (lower than in the case of nutrient deficiency) the best available estimates carried out at the national level. If the estimated international dietary exposure to a chemical does not exceed its relevant toxicological reference value (or is not below the nutritional reference value), then the level of exposure should be acceptable at the national level because the international dietary exposure assessment was developed not to underestimate exposure. This applies to both acute and chronic exposure assessments.

- If international dietary exposure assessments exceed a toxicological reference value, then national authorities should be asked to submit their national exposure estimates through the Codex Alimentarius Commission or its technical committees, or directly

[1] Pre-regulation means before the approval for use, and post-regulation means after the approval for use.

to the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) or the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

- It is recommended that national authorities that wish to estimate national dietary exposures perform their own dietary exposure assessments using international nutritional and toxicological reference values but national food consumption and chemical concentration data. It is suggested that national and regional authorities provide their data on food consumption and chemical concentrations in food, as well as the results of their dietary exposure assessments, to the Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme (GEMS/Food), JECFA, and JMPR.

1.2 Dietary exposure assessment methods

The following are general considerations and principles pertaining to the methodology used in dietary exposure assessments:

- In principle, international dietary exposure assessments need to be performed for all identified chemical hazards present in the diet. Similar methods are appropriate for contaminants, pesticide residues, veterinary drug residues, nutrients, food additives (including flavourings), processing aids, and other chemicals in foods.

- A stepwise approach is recommended, in which screening methods can be applied to identify, among the large number of chemicals, those of no safety concern using minimal resources in the shortest possible time. No refined exposure assessment is needed for these substances.

- Screening methods, if used, need to overestimate the exposure of "high consumers" (e.g. those loyal to a specific brand of processed food that contains a high concentration of the chemical of concern) using conservative assumptions in terms of food consumption and chemical concentrations in food (section 3.4.1). This will avoid situations where the exposure estimated using the screening methods erroneously indicates that no safety concern exists (i.e. exposure is under the toxicological reference value) and that no further refined dietary exposure assessment is necessary.

- In order to effectively screen chemical substances and establish risk assessment priorities, the screening procedure should not use unsustainable diets to estimate consumption. Rather, physiological limits of consumption should be taken into account.

- Further steps to allow the refinement of the dietary exposure assessment should be designed in such a way that potential high dietary exposures to a specific chemical are not underestimated. The methodologies should take into consideration non-average individuals or high consumers.

1.3 Presentation of results of dietary exposure assessments

The following general considerations apply to the presentation of the results of dietary exposure assessments:

- The methodology applied should be clearly stated and reproducible. Information about the model and data sources used, assumptions, limitations, and uncertainties should also be documented (section 3.3).

- The assumptions concerning chemical concentrations in food and food consumption patterns upon which the dietary exposure estimates are based need to be transparent (sections 2.1 and 2.2).

- The percentiles (e.g. 95th or 97.5th) used to represent the highly exposed consumers should be clearly stated and their derivation described (section 2.2.3).

2. DATA SOURCES

The data required for assessing dietary exposure are determined by the objective of the assessment. Dietary exposure can be assessed for a chemical before the chemical has been approved for use (pre-regulation) or after the chemical has potentially been in the food supply for years (post-regulation), or for a chemical that is present naturally or as an unavoidable contaminant in foods. In the first case, chemical concentration data are available or estimated from the food manufacturer/producer. In the other cases, additional chemical concentration data could be obtained from food in the marketplace. For each assessment, the suitability of the available data should be assessed (e.g. some market data may not be sufficient for acute exposure assessments, as monitoring of food in the market usually uses composite samples).

2.1 Data on chemical concentrations in food

In dietary exposure assessments, it is as important to obtain accurate information on the levels of chemicals in food as it is to obtain accurate information on food consumption. The selection of the sampling, analysis, and reporting procedures is critical for obtaining consistent and comparable data on chemical concentrations in food (WHO, 1985; Petersen et al., 1994). The selection of data based on consistent procedures is particularly important at the international level, where data from several countries may be compared or combined. Possible sources of data on chemical concentrations in food are summarized in Table 1.

Table 1 Sources of data on chemical concentrations in food

Chemical	Pre-regulation dietary exposure assessments	Post-regulation dietary exposure assessments[a]
Food additives	Proposed MLs	Reported manufacturers' use levels
	Proposed manufacturers' use levels	Food industry surveys
		Monitoring and surveillance data
		TDSs
Contaminants, including natural toxicants	Proposed MLs	Monitoring and surveillance data
		TDSs
		GEMS/Food databases on chemical concentrations and dietary intake
Pesticide and veterinary drug residues	Proposed MRLs	Monitoring and surveillance data
	HR	TDSs
	STMR levels	GEMS/Food database on chemical concentrations and dietary intake
Nutrients	Proposed MLs for fortification	Food composition data
		INFOODS
		Monitoring and surveillance data
		TDSs

GEMS/Food, Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme; HR, highest residue level from trial; INFOODS, International Network of Food Data Systems; ML, maximum level; MRL, maximum residue limit; STMR, supervised trial median residue; TDS, total diet studies

[a] In addition to all pre-regulation data sources.

Appropriate data sources and levels of food chemicals to use in dietary exposure assessments at an international level may be determined by the relevant Codex Alimentarius Commission committee based on the advice of JECFA or JMPR.

2.1.1 Use of maximum levels or maximum residue limits in dietary exposure assessments (pre-regulation)

The first objective or purpose of Codex standards, as international food standards, is "Protecting the health of the consumers and ensuring fair practices in the food trade" (Codex Alimentarius Commission, 2001).

It is important to understand the method of derivation of Codex maximum levels (MLs) or maximum residue limits (MRLs) for various food chemicals when considering the potential uncertainties in the data if they are to be used in dietary exposure assessments. In the case of pesticide residues, MRLs are proposed by JMPR based on field trial studies performed under good agricultural practice (GAP), then considered and established by the Codex Committee on Pesticide Residues (CCPR). For veterinary drugs, the MRLs are derived by JECFA from controlled metabolism and distribution studies performed under good veterinary practice, then considered and established by the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF).

In the case of pesticide and veterinary drug residues and food additives, MRLs (MLs in the case of food additives) are usually based on good practice considerations; if these levels result in exposures below the reference safe levels (i.e. ADIs), the uses are considerable acceptable. However, when MRLs based on good practice are higher than those levels predicted to ensure consumer safety, either for chronic or acute dietary exposure in the pre-regulation phase, the refinement of dietary exposure estimates with more accurate data should first be undertaken before a final decision on the MRL is taken. In all cases, MRLs should be set to ensure consumer safety.

In the case of chemical contaminants, MLs are established by the Codex Committee on Food Additives and Contaminants (CCFAC),[1] with advice from JECFA, to be compatible with tolerable intake levels and are based on the lowest level of contamination that can be reasonably achieved without removing the food from the food supply. For a contaminant that has a chronic toxic effect and a lognormal distribution, the setting of an ML for that chemical in the food in which it occurs often has little impact on the mean exposure of the population. If a reduction in exposure is desired, a significant proportion of the food would have to be removed from the market in order to shift the mean value. In addition, in cases where the mean exposure to a chemical is well below the toxicological reference value, establishing an ML in the food is unlikely to have any impact in terms of public health.

2.1.2 Use of other data sources for dietary exposure assessments (pre- and post-regulation)

MLs and MRLs are convenient values to use to assess dietary exposure for pre-regulation purposes, but it is recognized that a person would not always consume foods containing chemicals at their corresponding MLs. Analytical data on the concentrations of chemicals in food are needed to more accurately estimate the levels likely to be found in the diet as consumed.

The internationally recommended MLs or MRLs for food chemicals can be replaced by national surveillance or monitoring data or data from national or regional supervised trials (pesticides, veterinary drugs). For acute exposure assessments, it should be recognized that although aggregated monitoring data may provide a reliable estimate of mean residue level, such data do not provide reliable estimates of maximum residue levels in single units. When using data from national governments as well as other sources in international exposure assessments, it is important, wherever possible, to have detailed information regarding the

[1] In 2007, CCFAC split into two committees: the Codex Committee on Food Additives (CCFA) and the Codex Committee on Contaminants in Foods (CCCF).

data source, survey type/design, sampling procedures, sample preparation, analytical methodology, limit of detection (LOD) and/or limit of quantification (LOQ), and quality assurance procedures.

Correction factors can be applied to these data to take into account edible portions and effects of storage, processing, or cooking practices on chemical concentrations in food. When modelling dietary exposure to pesticide residues, the proportions of crop or food commodity treated or produced domestically and imported may be used for refining residue levels in some cases. However, there is no international consensus on using this type of information in the context of MRL setting. In addition, certain foods are widely blended across many individual units (e.g. orange juice), and in these cases it may be appropriate to estimate concentrations in blended commodities by using the arithmetic mean of the concentrations in the individual or composite samples. However, some of these factors are country or region specific and may be appropriate to use only when undertaking national dietary exposure assessments.

2.1.3 Approaches for obtaining data on chemical concentrations in food

2.1.3.1 Supervised trials (pesticide and veterinary drug residues only)

Traditionally, the primary source of pre-regulation residue data in foods has been supervised trial data that must be submitted in support of the registration of a pesticide or veterinary drug. The trials are usually performed by a manufacturer or other parties, in which a worst-case usage scenario (with respect to application rates, number of applications, pre-harvest or withdrawal intervals, etc.) is simulated. They are designed to determine maximum residues that may be present in food and feed of animal or plant origin at the earliest point at which these food commodities could enter commerce. These data are used to establish legally enforceable residue limits. They data often overestimate the residues that are likely to occur in food as actually consumed, because they reflect the maximum application rate and shortest pre-harvest interval. Therefore, these data should not be the first choice when assessing actual dietary exposure. However, for assessing the safety for consumers of a commodity containing residue at the level of the MRL, these data are the first choice. Supervised trial data do not account for residue degradation that sometimes occurs during the interval from the farm to the market to the home or subsequent residue losses when food is processed and prepared for consumption.

2.1.3.2 Monitoring and surveillance data for chemicals in food

Data that reflect chemical concentrations in food are often available from monitoring and surveillance programmes in which food samples are obtained closer to the dinner table in the chain of commerce. These data generally provide a better characterization of the concentration of chemicals in foods as purchased by consumers (European Union, 2004; USDA, 2004; USFDA, 2004b).

There are two types of monitoring and surveillance data: targeted and random. Often targeted data are collected for enforcement purposes in response to specific problems and should be used with caution in dietary exposure assessments, as they may not be representative of all the food available for sale. Truly representative residue data are scarce, and the source of residue data used in the dietary exposure assessments should always be carefully described and evaluated.

For post-regulation chronic dietary exposure assessments of pesticide and veterinary drug residues, monitoring and surveillance data are preferred over supervised trial residue data to assess long-term exposure because they more closely simulate what is consumed. The samples are usually collected on a random basis close to the point of consumption, at terminal

markets and large chain store distribution centres immediately prior to distribution to supermarkets and grocery stores. Such sampling therefore accounts for residue degradation during transit and storage and also provides data on residues resulting from post-harvest applications of fungicides and growth regulators used as preservatives during food delivery. However, for acute dietary exposure assessments, the fact that only a small proportion of any commodity entering the food-chain is monitored means that there are significant limitations in using monitoring data.

2.1.3.3 Processing studies to refine concentration data for use in dietary exposure estimates

Processing factors can be routinely incorporated into dietary exposure assessments to make the results more reflective of actual exposures. Specifically, processing of agricultural commodities can increase or decrease chemical concentrations or alter the nature of chemicals in foods. Processing studies are usually regarded as being specific for the food, the active substance, or the process. In cases where processing studies are not available, standard mass balance assumptions based on general information of the effects of some processing operations, such as drying of grapes to make raisins, may sometimes be used (USEPA, 1996).

2.1.3.4 Total diet studies

Conducting a total diet study (TDS) is considered to be one of the most cost-effective means of ensuring that people are generally not exposed to unsafe levels of toxic chemicals in food. While the TDS approach can be applied to nutrients and even food additives, TDSs are usually used to assess exposure to pesticide residues and contaminants. The advantages of the TDS approach are as follows:

- They focus on chemicals in the diet rather than individual foods.
- They provide more accurate estimates of human exposure, as the levels are measured in foods as consumed (e.g. peeled or cooked).
- They provide an assessment of background exposures not obtainable from regulatory monitoring.

For developing countries, the TDS approach offers one of the best means for setting priorities to enable risk managers to focus their limited resources on those chemicals, both contaminants (in excess) and nutrients (in deficiency), that pose the greatest risks to public health. A TDS can also be used to assess the adequacy and acceptability of food standards, such as those developed by the Codex Alimentarius Commission.

Concentration data from TDSs differ from data obtained from other chemical surveillance or monitoring programmes because concentrations of chemicals are measured in foods after they have been prepared as for normal consumption. Concentration data in a TDS are not based on historical composition data, and processing factors for raw food commodities (WHO, 1997a) do not need to be applied, because estimated dietary exposures are based on the edible portions of the food (e.g. bananas are peeled and the skin discarded along with any associated chemical residues). A TDS also incorporates the impact of cooking on less stable chemicals and on the formation of new ones.

Analytical methods used in a TDS should be capable of measuring concentrations of chemicals in foods at appropriate levels. Typically, methods with LODs/LOQs 10–1000 times lower than those needed for enforcement purposes are used for TDSs.

The broad scope of a TDS (survey of foods across the total diet, many analytes) and the level of accuracy achieved in measuring chemical concentrations (foods prepared as consumed, methods with low LODs/LOQs) may necessitate significant compositing of

samples in a TDS if resources are limited. Compositing may be either on an individual food basis or into food groups. Such compositing will not prevent the estimation of total exposure but will limit the ability to identify the specific source of the food chemical. Because of resource considerations, TDSs usually have quite a small number of mean concentration data (1–8) for each individual food or food group, in contrast to those data usually generated through surveillance or monitoring of individual food commodities (30–50).

2.1.4 Sampling

2.1.4.1 Sample collection

When undertaking programmes to generate data on chemical concentrations in food, the sampling procedure selected and how it is carried out are critical to the validity of the results obtained. Different sampling plans and methods are required, depending on the objectives of the studies.

The following questions should be answered when the sampling plan is designed (WHO, 1985; Kroes et al., 2002; Vannoort cited in WHO, 2002a:

- Is the food list representative of those foods normally consumed by the population or the specific age/sex groups to be investigated?
- Are foods of very low consumption but of potential concern regarding chemical content included?
- How many sampling sites are involved, and are they representative?
- Should the sampling be representative of food processing enterprise or of homemade foodstuffs?
- Does sampling account for regional differences in soil content, climates, pest vectors, and GAP, as well as those foods extensively distributed on a national basis, including imported foods? Are seasonal differences also considered?
- Are the main brands/cultivars covered for each food?
- Is sample size sufficient to cope with localized analytes such as aflatoxins?
- Have standard operating procedures been established to standardize sampling?

For example, for a chronic dietary exposure assessment, data based on random composite samples for selected food items may be used. Food items may be taken from different regions, locations, and seasons from different brands, varieties, and even food types (e.g. milks and milk products) in order to be nationally representative.

For an acute exposure assessment, additional information is required on residues in sample increments or individual crop units. If such detailed data are not available, concentrations in single samples can also be derived from composite samples taken from a lot by applying a variability factor to take into account the differences in chemical concentrations in sample increments or unit crops.

2.1.4.2 Sample preparation and processing

Sample preparation includes actions taken to prepare the analytical sample from the laboratory (bulk) sample: for example, reducing the size of the large bulk sample by subsampling and removing foreign materials or parts of the sample material that are not analysed (e.g. stones, withered leaves, stone of fruits, bones of meat). For generating data to be used in dietary exposure assessment, the chemical concentrations in the edible portion of the commodities are of interest; for enforcement, the portion of the commodity specified in the relevant regulation should be prepared for analysis. The sample preparation may include, for instance, washing, peeling, and cooking, so that foods are prepared as for normal

consumption (i.e. table ready). In such a case, the cooking of foods needs to be based on one or more recipes or methods for each food item, in order to account for variations in food preparation habits.

Sample preparation might also involve compositing of food samples taken from different regions, brands, and even food types (e.g. milks and milk products) before homogenization and analysis. Such preparation will provide an estimate closer to the true average.

Sample processing includes physical operations performed to prepare a well mixed or homogeneous matrix to form the analytical sample, from which the test portions for the analysis are taken. Some labile and volatile compounds may be lost during these processes, so special handling, including cryogenic processing, may be required. Special care should also be taken to ensure that the size of the test portion is representative and sufficient for the accurate and reproducible determination of the average chemical/residue content of the analytical sample (Codex Alimentarius Commission, 2003).

2.1.4.3 Specific design approaches for generating concentration data

A good study design is the most important element of any exposure study (WHO, 2000). There are two main approaches to analysing foods when generating analytical data from surveys, including TDSs, and both can impact significantly, but differently, on the estimated dietary exposures. These two approaches, analysis of food group composites and analysis of individual foods (either as single samples or as composites), are described below.

a) Food group composite approach

In this approach, samples of similar foods (e.g. milk, cheese, butter, cream) are prepared and then combined to form a composite for a food group (e.g. dairy products). The basis for the relative proportions of foods contributing to the food group composite needs to be defined, but the proportions are generally based on food consumption data for an average consumer in the population.

The advantage of the food group composite approach primarily relates to the ability to determine the approximate dietary exposure to chemicals by analysis of a relatively small number of samples. By analysis of perhaps 10–20 representative food group composites that are carefully prepared to represent the national, socioeconomic, regional, or ethnic dietary habits of a population, an approximation of chemical dietary exposure can be obtained.

The main disadvantage of the food group composite approach is that it restricts the calculation of chemical exposures to only that segment of the population upon which the proportional contribution of foods was based. If, for example, it was based on an adult male diet, this can only roughly approximate an adolescent or child or adult female diet, as types of foods and proportions of each consumed may differ substantially between age/sex groups.

The food group composite approach is often used when undertaking a TDS. As an example, the United Kingdom TDS has 20 food group composites (Ysart et al., 1999; Food Standards Agency, 2004). Separate groups have been established for foods consumed in large quantities (e.g. staples such as bread, milk, and potatoes), and also for food groups that may make a significant contribution to dietary exposure because they are known to be susceptible to contamination (e.g. offal and fish). This combined approach can facilitate the identification of sources of exposure while conserving resources.

b) Individual food approach

In this approach, each food is prepared and analysed separately. Often multiple samples of the same food purchased across the country are composited so as to get as representative a

sample across the diet as possible. Each individual food composite may, depending on available resources, be composited in a targeted manner across brands or retail outlets or even cities/regions or seasons for that food.

The major advantages of the individual food approach over the food group composite approach for analyses are the ability to estimate the contribution of individual foods to exposures as well as the greater flexibility in calculating dietary exposures for various segments of the population, provided appropriate food consumption information is available (WHO, 1985). The major disadvantage of the individual foods approach is the larger number of samples that need to be analysed in order to represent all foods consumed by the population. If the individual foods are also composited, then the principal disadvantage, which also applies to food group composites, is the so-called "dilution effect" inherent in the use of composites. For example, the concentration of one food in the composite may well be significantly in excess of the LOD/LOQ, but diluted to below the LOD/LOQ by other foods in the composite, such that the overall composite has a "not detected" (ND) result. This dilution effect can lead to significant under- or overestimation of dietary exposures, depending on the protocol used for assigning values to the samples with "ND/not quantified (NQ)" results (see section 2.1.5.2). In addition, unusual sources of elevated levels could be masked in the composite.

Some countries that use the individual food approach in their TDSs, with the associated number of individual foods specified, are Canada (135 foods; Dabeka et al., 2003), Czech Republic (220 foods; Ruprich in WHO, 2005a), France (338 foods; Leblanc et al., 2005), Ireland (107 foods; Tlustos in WHO, 2005a), New Zealand (121 foods; Vannoort, 2003, 2004a, 2004b, 2004c), and the United States of America (USA) (286 foods; USFDA, 2004a). Australia has tended to use a more limited range of individual foods (70 foods; FSANZ, 2003), but this has occasionally presented problems for dietary exposure estimates (e.g. when lead was detected in honey and honey was mapped to represent sugar-containing products, including highly consumed soft drinks that were not likely to contain lead) (FSANZ, 2001).

2.1.5 Analysis

There are a number of important differences in analytical methodology depending on whether the samples are analysed to provide data for dietary exposure assessment (e.g. TDSs) or for enforcement of MRLs or MLs. For instance, some veterinary drug residue metabolites that are of toxicological concern and are important for dietary exposure assessment are not analysed in monitoring programmes for enforcement purposes, if they are not part of the relevant residue definition of the pesticide. Method sensitivity can also differ. Generally, for accurate exposure assessments, the LOD/LOQ should be as low as technically possible, since most foods will not contain detectable residues and the value assigned to those samples will affect the estimated exposures. Most TDSs utilize very sensitive methods. Typically, monitoring or surveillance programmes use less sensitive methods since the purpose is to confirm that the residues are below the legal limits. In any case, residue data generated for enforcement purposes can be used for exposure assessment provided the appropriate assumptions for samples below the LOD/LOQ are applied.

2.1.5.1 Quality assurance

Obtaining best estimates for dietary exposure assessment is critically dependent on the quality of the chemical concentration data. Best estimates should be obtained using validated methods that are fit for the purpose of the assessment and that have comprehensive quality assurance/quality control programmes. The latter include employing properly trained

personnel familiar with the specific objectives of the tasks performed, regular testing of the performance parameters of the analytical methods by applying reference materials, where available and applicable, and testing the bias/accuracy, reproducibility, and sensitivity of the procedures. Participation in proficiency tests provides objective means to verify the capability of the laboratory and comparability of the results obtained in different laboratories. The established quality system and capability of the laboratory should be demonstrated by appropriate accreditation. Relevant detailed information can be obtained from a number of sources (Keith et al., 1983; NRC, 1993; Hughes in WHO, 2002a; Kroes et al., 2002; Sack in WHO, 2002a; Vannoort in WHO, 2002b; Codex Alimentarius Commission, 2003; International Accreditation New Zealand, 2004).

2.1.5.2 Handling non-detected or non-quantified results

The protocol for assigning concentration values to ND or NQ results is critical to the dietary exposure estimate. Concentrations should err on the side of nutritional or toxicological caution, while remaining scientifically defensible. This issue has been extensively considered (NRC, 1993; GEMS/Food-Euro, 1994, 1995; USEPA, 2000; Vannoort et al., 2000; Egan et al., 2002; Kroes et al., 2002; Renwick et al., 2003).

Unless there is reason to assume that a food contains no concentration of a chemical of interest (e.g. foods for which a pesticide is not registered for use, or foods that undergo extensive processing during which a chemical is likely to be completely removed), one has to assume that samples without detectable (or quantifiable) concentrations may contain chemicals below the LODs or LOQs. The risk assessor must decide what value to assign for those samples. One common, albeit arbitrary, option is to assign a value of one half the LOD or LOQ to these samples. If the number of samples with non-quantifiable (or non-detectable) residues is large, such replacement would distort the calculated mean and chemical variability values.

Another option is to use lower- or upper-bound values (e.g. zero and the LOD). In general, for chemicals likely to be present in the food (e.g. naturally occurring contaminants, nutrients, and mycotoxins), both lower and upper bounds should be estimated for mean chemical concentration data. The lower bound is obtained by assigning a zero value to those samples in which the chemical was ND or NQ and using these values to estimate exposure. An upper-bound exposure is estimated by assigning the LOD to all samples with ND results and the LOQ to all samples with less than the LOQ but more than the LOD. In some cases, the LOD may equal the LOQ.

The impact of these assumptions should be presented along with the risk assessment. Some guidance has been provided. For example, GEMS/Food-Euro (1995) has suggested that if fewer than 60% of results are less than the LOD or LOQ, then a reasonable estimate of the mean can probably be obtained by setting all ND and NQ results to LOD/2 or LOQ/2, respectively. Some experts have suggested that if more than 10–15% of the samples are below the LODs, additional considerations should be undertaken (e.g. see Helsel, 1990). In general, when data sets have a large number of samples that are less than the LOD or LOQ, it may be advisable to perform sensitivity analyses by first assigning all ND/NQ results to zero, setting these values to the full LOD or LOQ, and then evaluating how the exposure estimates change.

Table 2 illustrates the fact that the assignment of different values to ND results may have a significant impact on estimated dietary exposures, the effect being greater for less sensitive analytical methods with higher LODs. Alternatively, more sophisticated methods, such as maximum likelihood estimation or regression on order statistics, can be used to evaluate the impact of the values assigned to ND/NQ results. For chemicals unlikely to be

present unless specifically added (i.e. pesticide and veterinary drug residues, additives), using a lower-bound mean concentration only is generally the norm.

Table 2 Cadmium dietary exposure: effect of treatment of non-detect results

% of foods analysed with ND results	LOD (µg/kg)	ND protocol	Dietary exposure (µg/kg body weight per week) for a young male (19–24 years)
90	<33	ND = 0	1.5
	<33	ND = LOD/2	6.8
	<33	ND = LOD	12.0
10	<0.33	ND = 0	2.8
	<0.33	ND = LOD/2	2.8
	<0.33	ND = LOD	2.8

LOD, limit of detection; ND, not detected

In field trial residue data, the occurrence of samples in which no pesticide residue was detected requires a decision about how to include a precise quantitative value into the residue data file if it is to be used for probabilistic analysis. Unlike non-treated crops, it can be assumed that there is a finite residue present, but that it is merely below the LOD. The United States Environmental Protection Agency (USEPA) has chosen to use a value of LOD/2 or LOQ/2 as a reasonable means to address such findings. This is clearly distinguished from consideration of non-treated crops (above), in which the pesticide residue is properly assigned as "zero". For estimation of the variability factor from individual data points for acute dietary exposure assessments based on the JMPR approach (section 3.6.2, Annex 4), the chemical concentration can be taken as zero in samples with non-detectable chemicals. In all cases, as the chemical concentration value assigned to ND or NQ results in the data set for food chemicals may significantly influence the result of the dietary exposure assessment, the treatment of these results should be clearly stated.

2.1.6 Deriving data on chemical concentrations in food for use in estimating dietary exposures

The choice of concentration data to use in a dietary exposure estimate depends on the purpose of the modelling exercise. For a probabilistic approach, all available concentration data are used. For a deterministic or point estimate approach, a statistic such as the mean or median may be used. The approach taken and underlying reasoning should be clearly stated in the dietary exposure assessment.

For contaminants, the mean concentration in food derived from monitoring or surveillance data is often used in dietary exposure estimates. However, depending upon the anticipated profiles of contaminants or the sampling design, in some situations a median or geometric mean may be the most appropriate measure of the concentration. For the TDS and nutrients, the mean is generally used, since there are usually insufficient concentration data to justify use of the median, especially for the individual food composite approach, where often only a few results for each food may be available. For food chemicals that are intentionally added to foods, the mean concentration is often used to reflect the expected concentration in food over time and may be derived from manufacturers' use data (food additives, flavourings) or monitoring or surveillance data (food additives, flavourings, pesticide residues, veterinary drug residues). The high or median residue levels from supervised trials (highest residue level from trial [HR], supervised trials median residue [STMR]) or the MRL may be used for pesticide and veterinary drug residues, depending on the dietary exposure scenario.

2.1.7 Uncertainty in data on chemical concentrations in food

The use of maximum chemical concentrations in food in dietary exposure estimates substantially overestimates the amount of the chemical present in the food, and these data therefore have the greatest uncertainty. Data from direct measurement after use of or treatment with pesticides or veterinary drugs (e.g. field trial residue data) or manufacturers' use data for food additives have less associated uncertainty. While these data provide a more accurate estimate than maximum levels of the chemical in or on the food commodity as it enters the food distribution system, they do not reflect the impact of storage, transportation, and preparation of the food. Still more accurate information on chemical concentrations in food is available from national monitoring and surveillance data. The most accurate data are obtained from the measurement of chemical levels in foods as consumed. While this approach would provide the least uncertainty, it is typically the most resource intensive.

Uncertainties in data on chemical concentrations in food can be reduced by improving the quality of the data available. Data quality is defined to include the suitability of the sampling plan in order to obtain representative samples of food, appropriateness of sample handling procedures, selection and validation of the analytical methodology, use of analytical quality control programmes, and the number of samples determined based on statistical characteristics of each data set. Early identification of the foods contributing most to the estimated dietary exposures can assist in directing resources to including the most important foods in the sampling plan.

Indicators of data quality need to be clearly defined and provided to users of the data. This information should be sufficiently complete to allow critical decisions to be made concerning the appropriateness of available data for the specific use.

2.1.7.1 Errors in analytical measurements

In most measurements, we can distinguish among three types of errors:

- *Gross errors* refer to unintentional/unpredictable errors while generating the analytical result. Errors of this type invalidate the measurement. It is not possible or desirable to statistically evaluate and include the gross errors in the estimation of uncertainty. Laboratory quality assurance procedures should minimize gross errors, and they need no further discussion in this document.

- *Random errors* are present in all measurements and cause replicate results to fall on either side of the mean value. The random error of a measurement cannot be compensated for, but increasing the number of observations and training of the analyst may reduce the effects.

- *Systematic errors* occur in most experiments, but their effects are quite different from those of random errors. The sum of all the systematic errors in an experiment is referred to as the *bias*. Since they do not sum to zero over a large number of measurements, individual systematic errors cannot be detected directly by replicate analyses. The problem with systematic errors is that they may go undetected unless appropriate precautions are taken. For example, systematic errors in an analysis can be identified only if the analytical technique is applied to a reference material, the sample is analysed by another analyst or, preferably, in another laboratory, or the sample is reanalysed by another analytical method. However, only if the reference material matches identically in terms of analyte, matrix, and concentration does it meet the ideal conditions for determining the bias of the method. The bias of a method

may also be investigated by recovery studies. However, recovery studies assess only the effects of analysis and do not necessarily apply to naturally incurred samples or components of the bias that may be introduced prior to the analytical step. In pesticide residue analysis, results are not normally corrected for the recovery, but they should be corrected if the average recovery is significantly different from 100%. If the result has been corrected for recovery, the uncertainty associated with recovery should be incorporated in the uncertainty estimation of the measurement.

Some examples of sources of errors are illustrated in Tables 3, 4, and 5. It should be noted that not all sources mentioned have to be evaluated in the uncertainty estimation. Some sources are already incorporated in the overall uncertainty, whereas others are negligible and may be disregarded. However, it is important to recognize and assess all sources before elimination. Further information may be obtained from published documents (Eurachem, 1999; FAO, 2002a).

Table 3 Sources of error in sampling and field/external operations

	Sources of systematic error	Sources of random error
Sampling	Selection of sampling position	Large variation of food chemical concentration in food/on treated crops
		Number of primary samples taken (sample size)
	Incorrect labelling	Gross errors
	Contamination of sample	Gross errors
Shipping and storage	Decomposition of analytes	

Table 4 Sources of error in preparation of test portions

	Sources of systematic error	Sources of random error
Sample preparation	The portion of sample to be analysed (analytical sample) may be incorrectly selected	The analytical sample is in contact with and contaminated by other portions of the sample
		Rinsing, brushing is performed to various extent, stalks and stones may be differentially removed
		Is food for analysis raw or cooked, and if so, how is it cooked?
Sample processing	Decomposition of analyte during sample processing, cross-contamination of the samples	Non-homogeneity of the analyte in single units of the analytical sample
		Non-homogeneity of the analyte in the ground/chopped analytical sample
		Variation of temperature during the homogenization process
		Texture (maturity) of foods or plant materials affecting the efficiency of the homogenization process

Table 5 Sources of error in analysis

	Sources of systematic error	Sources of random error
Extraction/ cleanup	Incomplete recovery of analyte	Variation in the composition (e.g. water, fat, and sugar content) of sample materials taken from a commodity
	Interference of co-extracted materials (load of the adsorbent)	Temperature and composition of sample/solvent matrix
Quantitative determination	Interference of co-extracted compounds	Variation of nominal volume of devices within the permitted tolerance intervals
	Incorrect purity of analytical standard	Precision and linearity of balances
	Biased weight/volume measurements	Incomplete and variable derivatization reactions
	Operator bias in reading analogue instruments, equipment	Changing of laboratory environmental conditions during analysis

	Sources of systematic error	Sources of random error
	Determination of substances that do not originate from the sample (e.g. contamination from the packing material)	Varying injection, chromatographic, and detection conditions (matrix effect, system inertness, detector response, signal to noise variation, etc.)
	Determination of substance differing from the residue definition	Operator effects (lack of attention)
	Biased calibration	Calibration

2.1.7.2 Procedures for estimating measurement uncertainty

Whereas there are a number of options available to laboratories for the estimation of measurement uncertainty, there are two preferred procedures, described commonly as the "bottom up" approach and the "top down" approach. The bottom up or component-by-component approach breaks down all the analytical operations into primary activities. These are then combined or grouped into common activities, and an estimate is made of the contribution of these activities to the combined uncertainty value of the measurement process.

The top down approach is based on method validation and long-term precision data derived from laboratory control samples, proficiency testing results, published literature data, or interlaboratory collaborative trials. Uncertainty estimates based on interlaboratory studies may also take into account the between-laboratory variability of the data and provide a reliable estimate of the method performance and the uncertainty associated with its application. It is important to acknowledge, however, that collaborative studies are designed to evaluate the performance of a specific method and participating laboratories. They normally do not evaluate imprecision due to sample preparation or processing, as the samples generally tend to be highly homogenized.

2.1.8 Available databases on chemical concentrations in food

2.1.8.1 Food composition data for nutrients

Guidelines on the interchange of food composition data have been proposed since 1992 and have been expanded or updated since (FAO, 2005a, 2005b, 2005c, 2005d).

Food composition databases contain information on the nutrient content of various foods and beverages. They are based on chemical analysis of nutrients in foods, which are complemented with calculated and imputed values. Most food composition databases are compiled at a national level, whereas some exist at a regional level. Most national databases report nutrient values that are not readily comparable at an international level owing to differences in foods from different countries (e.g. variety, soil, processing, and fortification), but also because of artificial differences as a result of component identification, food description and nomenclature, analytical methods, mode of expression, and units used (Deharveng et al., 1999). International efforts are under way to harmonize these issues under INFOODS (http://www.fao.org/infoods/index_en.stm), an international network that serves as a general resource for organizations interested in food composition data on a worldwide basis, or at the European level under the European Food Information Resource Network, or EuroFIR (http://www.EuroFir.net), in order to be able to generate and compile high-quality nutrient values that are more comparable among countries.

Generally, the interchange of nutrient compositions of foods on the basis of food names alone is not sufficient for these data to be used and evaluated, as the nutrient content depends on various factors, such as the method of analysis. Standardized nomenclature for foods and food components will facilitate international use of the data. Some work has already been completed, including standardized nomenclature (FAO, 2005b), component

identification (Klensin et al., 1989; FAO, 2005c), and interchange formats and procedures (Klensin, 1992; FAO, 2005d).

Increasingly, in many nations, voluntary fortification of a wide array of foods creates an almost insurmountable challenge to managers of food composition databases. To portray the nutrient content in foods accurately, composition databases should be updated frequently and be specific enough to accommodate many different formulations of the same foods. To improve the accuracy of estimates of nutrient intake, food consumption assessments should include the collection of sufficient information for processed foods to ensure that food composition data match the foods consumed.

2.1.8.2 GEMS/Food database

One of the activities of GEMS/Food is the maintenance of databases of information collected by contributing institutions on contaminant and pesticide residue levels in foods and estimated dietary intakes of contaminants from total diet and duplicate diet studies based on internationally recommended procedures (WHO, 1979, 1985, 1997a, 1997b).

GEMS/Food international databases include individual and aggregated data on contaminants and pesticide residues in foods. GEMS/Food has also provided information to assist in understanding the terminology used and in submitting data (European Union, 2004; WHO, 2005b). GEMS/Food has also developed core, intermediate, and comprehensive lists of priority contaminant/commodity combinations that should be considered for monitoring for public health reasons. These lists are periodically updated (see Annex V of WHO, 2002a).

In addition to protocols for electronic data submission, WHO has also developed a computer system to allow the direct entry of data into the GEMS/Food database as well as the retrieval of data and creation of reports from the database. The system, Operating Program for Analytical Laboratories for data on individual and aggregate contaminant levels in foods (OPAL I), is available on request (foodsafety@who.int). OPAL II, for dietary intakes of contaminants from total diet and duplicate diet studies, is also available. These computer programs are available in both English and French, and efforts will be made to develop versions in other languages.

The GEMS/Food database is accessible through the Internet at the WHO Summary Information on Global Health Trends (SIGHT) web site (http://sight.who.int). In this regard, data deemed confidential by the data submitter will not be made public without the expressed permission of the data submitter. In these cases, WHO SIGHT will display only the name of the country, the contaminant, and the number of records.

Examples of national data on chemical concentrations in food that can be accessed on the Internet are those of Australia (FSANZ, 2003), New Zealand (Vannoort, 2003, 2004a, 2004b, 2004c), the United States (USDA, 2004; USFDA, 2004a, 2004b), and Europe (European Union, 2004).

2.2 Food consumption data

Food consumption data reflect what either individuals or groups consume in terms of solid foods, beverages, including drinking-water, and supplements. Food consumption can be estimated through food consumption surveys (FCSs) at an individual or household level or approximated through food production statistics. FCSs include records/diaries, food frequency questionnaires (FFQ), dietary recall, and TDSs. The quality of the FCS data depends on the survey design, the methodology and tools used, the motivation and memory of the respondents, and the statistical treatment and presentation (foods as purchased versus foods as consumed) of the data. Food production statistics, by definition, represent foods available for consumption for the whole population, typically in the raw form as produced.

2.2.1 Food consumption data requirements

Ideally, food consumption data used at the international level should take into account the differences in food consumption patterns in different regions. To the extent possible, food consumption data used in dietary exposure assessments should include information on factors that may influence food consumption patterns or the dietary exposure (whether increasing or decreasing the risk). Such factors include demographic characteristics of the population sampled (age, sex, ethnicity, socioeconomic group), body weight, geographic region, day of the week on which the data are collected, and season. Consideration of food consumption patterns for sensitive subpopulations (e.g. young children, women of childbearing age, the elderly) and for individuals at the extreme ends of the distributions is also important. Given that the design of food consumption studies can have a critical impact on the results of any dietary exposure assessment, harmonization of study design should be achieved to the extent possible. All FCSs should include data on the consumption of drinking-water, other beverages, and food supplements.

Ideally, all countries, including developing countries, should conduct FCSs on a periodic basis, preferably with individual dietary records.

Individual record data will generally provide the most precise estimates of food consumption. Broad surveys, covering the food consumption patterns of the whole population, may not necessarily be needed if the food chemical of interest is consumed by only a subset of the population. If resources are limited, small-scale studies are appropriate and may cover specific foods or target population subgroups (e.g. children, nursing women, ethnic minorities, vegetarians). This approach can improve the precision of estimates of dietary exposure for specific population subgroups or food chemicals.

2.2.2 Approaches for food consumption data collection

Food consumption data can be collected using population-based methods, household-based methods, or individual-based methods.

2.2.2.1 Population-based methods

Food supply data at the national level, such as food balance sheets (FBSs) or food disappearance data, provide gross annual estimates of the national availability of food commodities. These data may also be used to calculate the average per capita availability of energy and macronutrients and exposure to chemicals (e.g. pesticides, contaminants). Because consumption is expressed in terms of raw and semi-processed commodities, these data are not generally useful for estimating dietary exposure to food additives. The major limitation of national food supply data is that they reflect food availability rather than food consumption. Losses due to cooking or processing, spoilage, and other sources of waste and additions from subsistence practices cannot easily be assessed. According to WHO, FBS consumption estimates tend to be about 15% higher than the consumption estimates derived from household surveys or national dietary surveys. These data do not include water consumption. Where water consumption data are not available, a default water consumption value of 2 litres per adult may be used as per the WHO Guidelines for Drinking-water Quality (WHO, 2004b).

Despite these limitations, FBS data are useful for tracking trends in the food supply, determining the availability of foods that are potentially important sources of nutrients or chemicals, and monitoring food groups targeted for control. Food supply data are not useful for either evaluating individual nutritional intake or food chemical dietary exposure or identifying subgroups of the population at risk.

2.2.2.2 Household-based methods

Information regarding food availability or consumption at the household level may be collected by a variety of methods. These methods include data on foodstuffs purchased by a household, follow-up of consumed foods, or changes in food stocks. Such data are useful for comparing food availability among different communities, geographic areas, and socioeconomic groups and for tracking dietary changes in the total population and within population subgroups. However, these data do not provide information on the distribution of food consumption among individual members of the household.

2.2.2.3 Individual-based methods

Data collected by individual-based methods provide detailed information on food consumption patterns; however, they may be prone to bias. For instance, several studies (Madden et al., 1976; Carter et al., 1981; Karvetti & Knuts, 1985) have found that nutrient intakes derived from 24-h recalls (see below) tend to underestimate true intakes of some macronutrients for some subjects. Regression analyses between recall and actual intakes exhibited the "flat-slope syndrome", whereby individuals tend to overestimate food amounts when consumption is low and underestimate food amounts when consumption is high. In some cases, individuals may overestimate consumption of foods perceived as "good foods" and underestimate consumption of foods perceived as "bad foods".

a) Food record survey

The food record, also called the food diary, requires that the subject (or observer) report all foods consumed during a specified period (usually seven days or less). These surveys generally collect information not only about the types of food consumed but also about the source of the foods (e.g. store bought, home cooked) and the time of day at which and place where foods are consumed. Amounts of each food item consumed may or may not be recorded, depending on the study objectives. If nutrient intakes or food chemical exposures are to be calculated, the amounts consumed should be measured as accurately as possible. Amounts may be determined by weighing or measuring volume.

b) Twenty-four-hour recall survey

The 24-h dietary recall consists of a listing of foods and beverages (including drinking-water and sometimes dietary supplements) consumed the previous day or during the 24 h prior to the recall interview. These surveys generally collect information not only about the types and amounts of food consumed, but also about the source of the foods (e.g. store bought, home cooked) and the time of day at which and place where the foods are consumed. Foods and drinks are recalled from memory with the aid of an interviewer who has been trained in methods for soliciting dietary information. The interview is usually conducted in person, but may be conducted by telephone or via the Internet. In some situations, the recall is self-administered by the subject, but this approach results in less reliable data. Researchers have developed multi-pass methods that guide the respondent through the 24-h reference period several times, providing opportunity for the respondent to remember food details and additional foods (Slimani et al., 1999; Raper et al., 2004).

c) Food frequency questionnaire

The FFQ, sometimes referred to as a "list-based diet history", consists of a structured listing of individual foods or food groups. For each item on the food list, the respondent is asked to estimate the number of times the food is usually consumed per day, week, month, or year.

The number or types of food items may vary, as well as the number and types of frequency categories. FFQs may be unquantified, semi-quantified, or completely quantified. The unquantified questionnaire does not specify serving sizes, whereas the semi-quantified tool provides a typical serving size. A completely quantified FFQ allows the respondent to indicate any amount of food typically consumed. Some FFQs include questions regarding the usual food preparation methods, trimming of meats, use of dietary supplements, and identification of the most common brand of certain types of foods consumed.

The validity of dietary patterns assessed with FFQs depends on the representativeness of the foods listed in the questionnaire. While some (Rimm et al., 1992; Green et al., 1998; Thompson et al., 2000; Brunner et al., 2001) have concluded that FFQs produce valid data for dietary exposure assessments, others (Kroke et al., 1999; Schaefer et al., 2000) have found that FFQs do not produce reliable estimates of intake of some macronutrients.

FFQs are commonly used to rank individuals by consumption of selected foods or nutrients. Although FFQs are not designed to be used to measure absolute dietary exposure, the method may be more accurate than other methods for use in estimating average dietary exposure to those chemicals having large day-to-day variability and for which there are relatively few significant food sources. Brief FFQs may focus on one or several specific nutrients or food chemicals and include a limited number of food items. In addition, FFQs can be used in the identification of absolute non-consumers of certain foods, or people who have never consumed the food within the specified period.

d) Diet history survey

The meal-based diet history is designed to assess usual individual food consumption. It consists of a detailed listing of the types of foods and beverages commonly consumed at each eating occasion over a defined time period, which is often a “typical week”. A trained interviewer probes for the respondent’s customary pattern of food consumption on each day of the typical week. The reference time frame is often over the past month or the past several months or may reflect seasonal differences if the reference time frame is the past year.

e) Food habit questionnaire

The food habit questionnaire may be designed to collect either general or specific types of information, such as food perceptions and beliefs, food likes and dislikes, methods of preparing foods, use of dietary supplements, and social settings surrounding eating occasions. These types of information are frequently included along with the other four methods, but may also be used as the sole basis for data collection. These approaches are commonly used in rapid assessment procedures. The questionnaire may be open-ended or structured and self- or interviewer-administered and may include any number of questions, depending on the information desired.

2.2.2.4 Combined methods

Methods for the collection of food consumption data may be combined to improve accuracy and facilitate the validation of the dietary data. They may also be combined for practical reasons. For example, the food record has been combined with the 24-h recall. The FFQ that focused on selected nutrients has been used in addition to the 24-h recall. The 24-h recall is frequently used to help establish the typical meal plan. This information can be used for getting better information from the diet history method. The FFQ may also be used as a cross-check for the other three types of methods.

The European Food Consumption Survey Method (EFCOSUM) project recommended a method for harmonizing food consumption data between countries as follows: at least two

24-h recalls should be performed for each subject on non-consecutive days, in combination with a questionnaire on habitual consumption of infrequently consumed foods to get insight into the proportion of non-consumers (Brussard et al., 2002). The collection of repeated non-consecutive recalls allows for the estimation of usual intake by a modelling technique that separates intra- and interindividual intake (see section 2.2.4).

2.2.3 Data reporting and use

2.2.3.1 Mapping

Food consumption data should be available in a format that allows matching the consumption data with the chemical concentration data used in the dietary exposure assessment. For example, for raw agricultural commodities and some semi-processed commodities (e.g. polished rice and flour), the GEMS/Food format (section 7.2.1.8 of the GEMS/Food Instructions for the Electronic Submission of Data on Chemicals in Food; http://www.who.int/foodsafety/publications/chem/gems_instructions/en/index.html) uses the Codex Classification System for Food and Feeds. This system was established by the CCPR to specify foods for which pesticide MRLs are applicable. The system includes the common name of the food in English, French, and Spanish as well as the Latin name or names. This coding is also used by CCFAC for identifying foods subject to MLs for contaminants. The system is being revised and expanded to include more foods, including processed foods. In the case of acrylamide, which occurs only in processed foods, additional fields have been included to more accurately describe the analysed food. These fields include four fields for ingredients (in order of predominance), the Codex code for processed foods, the method of heating, and the processing method (FAO/WHO Acrylamide in Food Network: http://www.acrylamide-food.org/).

Foods may be consumed as such or as an ingredient as part of a recipe or food mixture. For example, ground beef may be consumed as a single food item or can be consumed as a component of a beef casserole. When modelling food consumption, it is important to know whether the consumption estimate includes all sources of the food. Recipes can be broken down into their ingredients, which can then be mapped to the corresponding individual food and added to the total consumption of that food from all sources (e.g. it is important to know whether "apples" includes the apples in a baked apple pie and apple juice and whether "potatoes" includes fried potatoes as in french fries or potato chips/crisps; if potatoes and french fries are considered separate foods, then this should be stated). The recipe and mapping approach needs to be documented.

The use of standard recipes and the attribution of the ingredients to individual foods introduce some uncertainty into the consumption data (e.g. assuming 70% of bread is flour, on average). The error would be significantly higher if the contribution of mixed foods were omitted. Using standardized recipes will result in reduced variability and underestimates the amount of individual foods or food ingredients consumed for high-percentile consumers. Another potential source of error lies in the decisions taken in mapping foods from FCSs to foods with concentration data, because in many cases the food and the food description do not always correspond exactly (Slimani et al., 2000).

2.2.3.2 Data format/modelling

a) Population food consumption data

Data collected using population-based methods are generally compiled and reported for raw or semi-processed agricultural commodities, and they represent the total amount of a commodity available for domestic consumption per year. The amount may be for the entire population or at the per capita level. A daily consumption amount may be estimated by

dividing the total annual amount by 365. It is not possible to estimate the consumption amount per eating occasion or only for consumers of the foods from these data alone.

b) Individual food consumption surveys

Data from individual consumption surveys are often not publicly available in raw format (i.e. at the individual respondent level), and risk assessors have to rely on published summary statistics. When the raw data are available, they can be used to estimate dietary exposures from multiple foods, dietary exposures for specific population subgroups, or distributions of food consumption, rather than just mean consumption.

When only summary data are available, it is important to know and document—in addition to the data requirements listed in section 2.2.1—the commodity, the type of commodity (e.g. raw, juice, juice concentrate), how the statistics are aggregated, whether the statistics refer to typical or high-end consumers, how a typical consumer is defined (e.g. median or mean food consumption or dietary exposure level), whether the data refer to consumers only or to the total population (all survey respondents, per capita estimates), and whether they represent daily consumption, consumption per eating occasion or per meal, or averages across survey days (in the case of multi-day surveys). When comparing food consumption data among countries or surveys, even if the same methods are used, one should use due caution, given that results may not be readily comparable because of differences in study design, tools, statistical analysis, and reporting of results (Slimani et al., 2000; Brussard et al., 2002).

c) Market share corrections

Food consumption data can also be corrected for market share of processed foods or percentage of treated crops. This approach is used mainly where the food chemical has been deliberately added to the food. The maximum or mean concentration of a chemical is assigned only to the proportion of the market in which the additive is used or the proportion of the crop in which a pesticide is used, and not to the consumption data for the whole food category. This technique may refine the estimate of mean dietary exposure, but it does not refine the dietary exposure estimate for the most exposed segment of the population (i.e. consumers who are loyal to the food products containing the additive or the pesticide), as it may underestimate their actual dietary exposure. When assessing dietary exposure to additives or flavourings, market share data should be used to consider brand loyalty where feasible. For pesticides, correction for the percentage of crop treated could be taken into account when setting MRLs; in post-regulation situations, however, consideration should be taken, at a national level, of the possibility that a segment of the population may systematically consume foods derived from treated crops only.

2.2.3.3 Food portion sizes

a) Unit weights

Unit weights represent weights of typical commodity unit (e.g. a single apple or a single banana) and are used in the calculation of acute dietary exposure estimates (international estimates of short-term intake, or IESTI, which are assessed for pesticides when JMPR has established an acute reference dose, or ARfD). JMPR routinely uses the IESTI in assessing potential risk of harm from short-term exposures; further details on this methodology are provided in section 3.6.2. Unit weights may also be used to convert reports of food consumption by single units in a food frequency or 24-h recall survey to gram weights. Estimates of mean/median unit weights of raw agricultural commodities and the per cent edible portion (e.g. one orange and the percentage of orange pulp) were provided by France,

Japan, Sweden, the United Kingdom, and the United States and were subsequently compiled by GEMS/Food; they are available at http://www.who.int/foodsafety/chem/acute_data/en/.

b) Standard portion sizes

In a large number of food surveys, standard portion sizes are used to assess the consumption of foods and beverages. That is, a standard weight will be assigned to a banana, a cookie, or a glass of soft drink. These portions can be more or less detailed (with, for example, differing weights for different glass types). However, standard portion sizes do not usually describe the full variability in the weights of portions as consumed in the population. Their use can lead to an overestimate of low portions and to an underestimate of high portions and thus corresponding over- or underestimates of dietary exposure. They are a very useful and pragmatic tool, but the uncertainty that they introduce in food consumption data must be kept in mind—specifically, the impact on the estimate of high levels of dietary exposure to food chemicals and low levels of intake for nutrients.

c) Large portion sizes

Large portion (LP) values have been used for a variety of risk assessments in Europe and by JMPR. For these purposes, the LP values have been based on the 97.5th percentile of food consumption derived from records of individual consumer days (i.e. survey days on which the foods of interest were consumed). For use in an acute dietary exposure assessment for pesticide residues (section 3.6.2), the LP value should be matched to the raw Codex commodity to which the residue data relate. In the case of commodities that are eaten predominantly fresh, as for fruit and vegetables, the LP value should be derived for the raw commodity. When a high proportion of the commodity, such as cereal grains, is consumed in a processed form, the LP value should relate to the processed commodity (e.g. bread, flour), providing matching residue concentration data are also available for the processed food.

Upper- and lower-percentile food consumption amounts should be defined based on individual consumer days. For surveys collecting multiple days of consumption data per person, the individual consumer days are assumed to be independent observations in the derivation of upper and lower percentiles, as follows:

- If the survey includes multiple days per participant, only the valid consumer days in which consumption of the food of interest occurs should be used.
- If a survey participant has multiple valid consumer days, these consumer days should be considered as independent observations, and not averaged.
- The number of consumer days on which the percentile is based should be explicitly stated.

In estimating acute dietary exposures from chemical residues in a single commodity or food, it is appropriate to use food consumption data for only those people who consume the single food (“consumers only”). Estimations of acute dietary exposures from chemical residues in multiple commodities or foods should be conducted for both consumers only and all respondents in the survey (total survey population).

LP (97.5th percentile) consumption values as well as body weights and ages are compiled by GEMS/Food and are available at http://www.who.int/foodsafety/chem/acute_data/en/. These data were provided by Australia, France, the Netherlands, Japan, South Africa, the United Kingdom, and the United States, along with body weights of the general population and children aged six and under.

Ideally, the food consumption values in the GEMS/Food LP database should be based on the 97.5th percentile of individual consumer days from national survey results from many countries. This database should be expanded to include data from additional countries to better represent all member countries. When data are provided, additional information is desirable that fully describes the underlying data and assumptions that were made in preparing the estimates of the LP values. Countries with data on the 97.5th level of consumption should provide these data to GEMS/Food.

d) Estimating high-percentile food consumption values

If individual records are not available, the risk assessor can estimate a high-percentile food consumption rate by multiplying a central estimate by an inflation factor. If the approximate shape of the distribution for a particular parameter is known, better high-percentile estimates can be developed.

2.2.4 Usual food consumption patterns

For a probabilistic exposure assessment, the readily available distributions of food consumption data are not representative of true long-term consumption (e.g. consumption data are collected over a period of few days and often used to represent the food consumption during a lifetime). It is difficult, from a methodological point of view, to obtain representative data from single subjects to represent the lifetime exposure of consumers. Nevertheless, food consumption data on a national or group level can be used to model lifetime consumption. As an approximation of lifetime consumption of a specific food, it could be acceptable to use the overall average adult food consumption for that food.

Approaches that have been used to estimate long-term consumption have included methods combining food frequency data with consumption amount information (e.g. IEFS, 1998; Tran et al., 2004) and statistical models that use the correlations among the days of consumption to estimate the "usual" intake of nutrients or contaminants using short-term consumption data (e.g. NAS, 1986; Slob, 1993, 1996; Carriquiry et al., 1995; Nusser et al., 1996). These models are most appropriate when the chemical of interest occurs in various basic food products, resulting in a nutrient intake or chemical dietary exposure different from zero for virtually each individual each day. Parametric and non-parametric methods are needed in order to better simulate, on a long-term basis, the frequency of consumption for occasionally eaten food.

Application of such methods results in a distribution of long-term nutrient intakes or food chemical dietary exposures that shows less variability than the distribution of dietary exposures directly derived from short-term food consumption data.

Lambe & Kearney (1999) warn against using short-term consumption data for estimating long-term or usual consumption and show that survey duration affects estimates of per cent consumers (the proportion of the population likely to consume the food), mean and high consumption of foods, and the classification of individuals as high or low consumers of foods or nutrients. Thus, data from these surveys need to be adjusted for use in the estimation of long-term consumption for use in chronic dietary exposure assessments.

2.2.5 Food consumption databases

2.2.5.1 Databases collected through population-based methods

FBS data are generally available for most countries. These data include the amounts of foods available for human consumption derived from national statistics on food production, disappearance, or utilization, such as those compiled by the United States Department of Agriculture's (USDA) Economic Research Service (Putnam & Allshouse, 1999) or the

Australian Bureau of Statistics (2000). The FAO's statistical database (FAOSTAT) is a compilation of similar statistics for more than 250 countries. The data are compiled or estimated, when official data from member countries are missing, from national food production and utilization statistics (FAO, 2004a).

The GEMS/Food regional diets are based on selected FAO FBSs and represent average per capita food consumption. To date, five regional diets have been used by JMPR and JECFA to estimate dietary exposure to pesticide residues and contaminants in food on an international basis (WHO, 1998, 2003). Using a cluster analysis approach, 13 consumption cluster diets have now been produced, based on all available FAO FBS data for the period 1997–2001, and are expected to be updated every 10 years. The 13 GEMS/Food consumption cluster diets are currently used as a tool for international chronic dietary exposure assessments. Further details on these diets are available on the WHO web site (http://www.who.int/foodsafety/chem/gems/en/).

2.2.5.2 Databases collected through individual-based methods

Some of the food consumption databases collected through individual-based methods include:

- the 1994–1996 and 1998 USDA Continuing Survey of Food Intakes by Individuals (CSFII) (USDA, 2000) and the 1999–2004 National Health and Nutrition Examination Survey (NHANES), , which provide two-day (CSFII) and one- or two-day (NHANES) food consumption data for individuals in the United States, along with corresponding demographic and anthropometric data (age, sex, race, ethnicity, body weight, height, etc.) for each individual;
- national dietary surveys from many European countries. Data from European FCSs with nutrient intake data reported on an individual level from 1985 onwards are summarized in Table 6;
- the 1995 Australian National Nutrition Survey, which collected data on one 24-h food recall for 13 858 individuals aged 2 years and older;
- the 1997 New Zealand National Nutrition Survey, which collected data on one 24-h food recall for 4636 individuals aged 15 years and older (New Zealand Ministry of Health, 1999), and the 2002 children's survey, for children aged 5–14 years (New Zealand Ministry of Health, 2003); and
- the 2002–2003 Brazilian Household Budget Survey, which provided the amount of food acquired during seven consecutive days by 48 470 households in all 27 Brazilian states (Pesquisa de Orcamentos Familiares 2002–2003; http://www.ibge.gov.br).

Table 6 Summary of national food consumption surveys in European countries with nutrient intake data on an individual level from 1985 to 2002[a,b,c]

Country	Year(s)	Survey	Population		Sample size (response, %)	Dietary method[d]	Food composition data	Reference
			Sex	Age (years)				
Austria	1991–1994	Austrian Study on Nutritional Status (ASNS)	F + M	6–18	2 173	7d Rcd	Austrian food composition database	Elmadfa et al. (1994)
Austria	1993–1997	Austrian Study on Nutritional Status (ASNS)	F + M	19–65	2 065	24h Rcl, DH	Austrian food composition database	Elmadfa et al. (1999)
Austria	1994–1997	Austrian Study on Nutritional Status (ASNS)	F	pregnant	350	7d Rcd	Austrian food composition database	Elmadfa et al. (1999)
			F	lactating	43	3d Rcd		
Austria	1995, 1998	Austrian Study on Nutritional Status (ASNS)	F + M	elderly	78	7d Rcd	Austrian food composition database	Elmadfa et al. (1999)
Belgium	1980–1985	Belgium Interuniversity Research on Nutrition and Health (BIRNH)	F + M	25–74	10 971	1d Rcd	Dutch food composition tables, *McCance & Widdowson's The Composition of Foods*	De Backer (1984)
Croatia	1997–1998	Croatian Study on Schoolchildren's Nutrition	F + M	12–14	348	24h Rcl + FFQ	National food composition tables	Anonymous
Denmark	1985	Dietary Habits in Denmark	F + M	15–80	2 242	DH	Danish Food Composition Data Bank	Haraldsdóttir et al. (1986)
Denmark	1995	National Dietary Survey	F + M	1–80	3 098 (65)	7d Rcd	Danish Food Composition Data Bank	Andersen et al. (1996)
Denmark	2000	National Continuous Dietary Survey	F + M	4–75	1 500	7d Rcd	Danish Food Composition Data Bank	
	2001				1 500			
	2002				1 000			
Finland	1992	Dietary survey of Finnish adults (FINDIET)	F + M	25–64	1 861 (60)	3d Rcd	Finnish food composition database	Kleemola et al. (1994)
Finland	1997	Dietary survey of Finnish adults (FINDIET)	F + M	25–64	2 862 (72)	24h Rcl	Finnish food composition database (Fineli)	Anttolainen et al. (1998)
			F + M	65–74	290	24h Rcl		
France	1985–1995	?	F + M	18–62	1 778	DH	French food composition database	Hercberg et al. (1994)

Country	Year(s)	Survey	Population		Sample size (response, %)	Dietary method[d]	Food composition data	Reference
			Sex	Age (years)				
							CIQUAL	
France	1993–1994	National Food Consumption Survey (ASPCC)	F + M	18+	1 229	7d Rcd	French food composition database (CIQUAL)	Jean-Luc Volatier et al(1999)
France	1993–1994	National Food Consumption Survey (ASPCC)	F + M	2–85	1 500	7d Rcd	French food composition database (CIQUAL)	Rigaud et al. (1997)
France	1998–1999	Individual National Food Consumption Survey (INCA)	F + M	3–14	1 018	7d Rcd	French food composition database (CIQUAL)	Volatier (2000)
			F + M	15+	1 985	7d Rcd		
Germany	1985–1989	National Nutrition Survey in former West Germany	F + M	4–70+	24 632 (71)	7d Rcd	German food composition database, Version 2.I	Heseker et al. (1992)
Germany	1991–1992	National Health Survey in former East Germany	F + M	18–79	1 897 (71)	DH	German food composition database, Version 2.II	Hermann-Kunz & Thamm (1999)
Germany	1998	German Nutrition Survey	F + M	18–79	4 030	DH	German food composition database, Version 2.III	Mensink et al. (1999)
Hungary	1985–1988	First Hungarian Representative Nutrition Survey	F + M	15–60+	16 641	2 × 24h Rcl + FFQ	Hungarian Food Composition Table	Biro (1992/93)
Hungary	1992–1994	Hungarian Randomized Nutrition Survey	F + M	18–60+	2 559	3 × 24h Rcl + FFQ	Hungarian Food Composition Table	Biro et al. (1996)
Iceland	1990	Icelandic National Nutrition Survey	F + M	15–80	1 240 (72)	DH	Icelandic Food Composition Table	Steingrimsdottir (1993)
Iceland	2001	Icelandic National Nutrition Survey	F + M	?	?	?	Icelandic Food Composition Table	
Ireland	1990	Irish National Nutrition Survey	F + M	8–18+	1 214	DH	*McCance & Widdowson's The Composition of Foods*, 4th edition	Lee & Cunningham (1990)

Country	Year(s)	Survey	Population		Sample size (response, %)	Dietary method[d]	Food composition data	Reference
			Sex	Age (years)				
Ireland	1998	North-South Food Consumption Survey	F + M	18–64	1 379 (66)	7 d Rcd	*McCance & Widdowson's The Composition of Foods*, 5th edition	Irish Universities Nutrition Alliance. (2001)
Italy	1994–1996	Italian National Institute of Nutrition Food Survey (INN-CA 1995)	F + M	0–94	3 600	7d Rcd	Italian Food Composition Table	Turrini et al. (1999)
Lithuania	1997	Baltic Nutrition and Health Survey	F + M	20–65	2 183 (73)	24h Rcl + FFQ	Russian Food Composition Table	Kadziauskiene et al. (1999)
Netherlands	1987–1988	Dutch National Food Consumption Survey	F + M	1–79	5 898 (79)	2d Rcd	Dutch Food Composition Table	Löwik et al. (1998)
Netherlands	1992	Dutch National Food Consumption Survey	F + M	1–92	6 218 (72)	2d Rcd	Dutch Food Composition Table	Löwik et al. (1998)
Netherlands	1997–1998	Dutch National Food Consumption Survey	F + M	1–97	6 250 (69)	2d Rcd	Dutch Food Composition Table	Anonymous (1998)
Norway	1993	National Dietary Survey	F + M	13	1 705	FFQ	Norwegian Food Composition Table	Andersen et al. (1995)
				18	1 564			
Norway	1993–1994	National Dietary Survey among Adults (Norkost)	F + M	16–79	3 144 (63)	FFQ	Norwegian Food Composition Table	Johansson et al. (1997)
Norway	1997	National Dietary Survey among Adults (Norkost)	F + M	16–79	2 672 (54)	FFQ	Norwegian Food Composition Table	Johansson & Sovoll (1999)
Norway	1999	National Dietary Survey	F + M	0.5 and 1	2 400 (80)	FFQ	Norwegian Food Composition Table	
Norway	1999	National Dietary Survey	F + M	2	2 010 (67)	FFQ	Norwegian Food Composition Table	
Poland	1991–1994	Dietary habits and nutritional status of selected populations	F + M	11–14	1 126	24h Rcl	Polish Food Composition Table	Szponar & Rydilik (1996a, 1996b)
				18	2 193	24h Rcl		
				20–65	4 945	24h Rcl		
Portugal	1980	National Dietary Survey	F + M	1–65+	13 080	1d Rcd	Portugese Food Composition Table	Gonçalves Ferreira et al. (1985, 1986, 1987)

Country	Year(s)	Survey	Population		Sample size (response, %)	Dietary method[d]	Food composition data	Reference
			Sex	Age (years)				
Slovakia	1991–1999	Assessment of food habits and nutritional status	F + M	11–14	3 337	24h Rcl and FFQ	Slovak Food Data Bank and other sources	Babinska et al. (1998); Béderova et al. (1998)
				15–18	4 556			
				19–88	4 807			
Sweden	1989	Swedish Household Food Survey (HULK)	F + M	1–74	2 036 (70)	7d Rcd	Swedish Food Composition Data Bank	Becker (1994)
Sweden	1997–1998	Food Habits and Nutrient Intake in Sweden (Riksmaten)	F + M	18–74	1 215 (60)	7d Rcd	Swedish Food Composition Data Bank	Becker (1999)
Switzerland	1992–1993	Swiss Health Survey	F + M	15–74	26 000 (71)	FFQ	No nutrient calculations	Eichholzer et al. (1995)
United Kingdom	1986–1987	The Dietary and Nutritional Survey of British Adults	F + M	16–64	2 197 (70)	7d Rcd	*McCance & Widdowson's The Composition of Foods* and other sources	Gregory et al. (1990)
United Kingdom	1992–1993	National Diet and Nutrition Survey: Children aged 1½–4½ years	F + M	1.5–4.5	1 675 (88)	4d Rcd	*McCance & Widdowson's The Composition of Foods* and other sources	Gregory et al. (1995)
United Kingdom	1994–1995	National Diet and Nutrition Survey: People aged 65 years and over	F + M	65+	1 687 (80?)	4d Rcd	*McCance & Widdowson's The Composition of Foods* and other sources	Finch et al. (1998)
United Kingdom	1997	National Diet and Nutrition Survey: Young people aged 4–18 years	F + M	4–18	1 701	7d Rcd	*McCance & Widdowson's The Composition of Foods* and other sources	Gregory et al. (2000)
United Kingdom	2000–2001	National Diet and Nutrition Survey: Adults aged 19–64 years	F + M	19–64	2 000	7d Rcd	*McCance & Widdowson's The*	Henderson et al. (2003)

Country	Year(s)	Survey	Population		Sample size (response, %)	Dietary method[d]	Food composition data	Reference
			Sex	Age (years)				
							Composition of Foods and other sources	

F, female; M, male

[a] In Belgium, the only nationwide individual dietary survey was conducted in the period 1980–1985, and in Portugal, in 1980.

[b] Countries not mentioned in Table 6:
Czech Republic: national household budget surveys (DAFNE); no national survey on the level of individuals in the Czech Republic during the 1990s.
Greece: national household budget surveys (DAFNE); European Prospective Investigation into Cancer (EPIC).
Spain: national household budget survey (DAFNE); individual surveys at regional level or age groups (SENECA).

[c] The present table is extracted from Verger et al. (2002).

[d] 24h Rcl, 24-hour recall; 1d Rcd, one-day record; FFQ, food frequency questionnaire; DH, dietary history method.

2.2.6 Additional data

2.2.6.1 Poundage data

Poundage data are estimates of the amount of a chemical substance available for use in food manufacturing in a country during a period of time, usually over one year, and, as such, are neither food concentration nor food consumption data. These estimates may take into account the import or export of the chemical and of foods containing it and the non-food uses. Surveys of poundage data are usually performed by the producer associations, which ask single producers to report their volumes of production. A very large year-to-year variability in poundage data may occur, especially for substances produced in low quantities. This limits the usefulness of poundage data surveyed on a single-year basis. Poundage data are sometimes divided by an estimate of the population in order to obtain an estimate of per capita availability of a specific chemical substance. Assessment of the quality of data, including a rigorous quantification of under-reporting by producers, is needed before poundage data can be used (see section 3.4.1.1).

2.2.6.2 Body weight

For the purposes of dietary exposure estimates, food consumption data should be presented such that individual consumer body weights are applied to the consumption figures for each consumer. If the individual body weight data are not available, or if the individual body weights have not been correlated to the food consumption figures, average body weights for the target population (e.g. adults, GEMS/Food Consumption Cluster Diet C) should be used. Average body weights of 60 kg for adults and 15 kg for children are assumed for most populations in the world; however, for certain regions, the average body weight of the population may differ significantly from 60 kg. For the adult Asian population, an average body weight of 55 kg is assumed. If the default 60-kg adult body weight underestimates the actual individual body weights, the dietary exposure estimate on a per kilogram body weight basis will be overestimated. Likewise, if the default 60-kg adult body weight overestimates the actual individual body weights, the dietary exposure estimate on a per kilogram body weight basis will be underestimated.

3. ESTIMATING DIETARY EXPOSURE

3.1 Introduction

In principle, international dietary exposure assessments need to be performed for all identified chemical hazards present in the diet, and the same concepts are appropriate for contaminants, pesticide and veterinary drug residues, nutrients, food additives (including flavourings), processing aids, and other chemicals in foods. The most appropriate method to use in estimating exposure will vary, depending upon a variety of factors. The following sections discuss the range of options, highlight some methods that are currently used, and summarize the advantages and disadvantages of those methods.

The methodology applied in any dietary exposure assessment should be clearly stated and reproducible. Information about the model and data sources used, assumptions, limitations, and uncertainties should also be documented.

A framework for conducting exposure assessments should be established that will allow the analyst to select the most appropriate methodology for the intended use of the assessment. A framework that includes a stepwise approach is recommended, noting that the "best estimate" in terms of the "most realistic" dietary exposure assessment may not always be the "best estimate" in terms of the "most appropriate" one to suit the purpose of the dietary exposure exercise. In general, the framework's early steps will include screening methods that use minimal resources and the shortest possible time (see Figure 2) to identify, among the large number of chemicals, those of no safety concern. No further (refined) exposure assessment is needed for substances that do not present safety concerns when analysed using screening methods that include conservative assumptions.

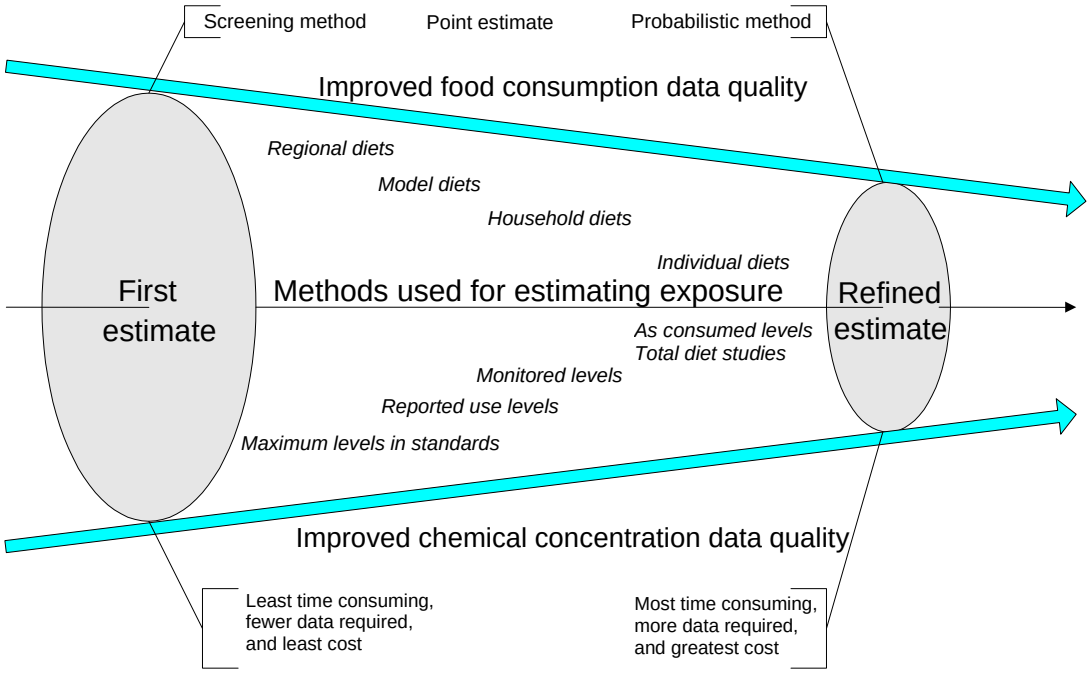

Figure 1 Stepwise approach to obtaining realistic dietary exposure assessments
Note: Data and methods selected from the right-hand side of the diagram are likely to result in a more realistic dietary exposure estimate or "refined estimate"; however, it may not be the "refined estimate" in terms of the "most appropriate" one to suit the purpose of a specific dietary modelling exercise.

In this chapter, the reader is provided with information to guide the selection of the most appropriate framework. The chapter also provides guidance in the selection of models and algorithms for various steps (tiers) in an exposure assessment framework and for different types of chemical substances. The data and resources that are required for each model/algorithm are also discussed.

3.2 Considerations when undertaking an exposure assessment

The specific approach that is most appropriate for estimating dietary exposure depends on several considerations, including (1) the type of substance being evaluated (food additive, pesticide, veterinary drug, contaminant, or nutrient) and whether the concern is the potential for too much or, for nutrients, too little intake, (2) the duration of exposure required to produce the toxic or beneficial effect, (3) the potential for different exposures in different subgroups or individuals within the population of consumers, and (4) the type of estimate needed (point estimate versus probabilistic characterization of the distribution of exposures). These considerations will be elaborated in conjunction with each of the methods discussed in the subsections of this chapter.

3.3 Stepwise approach to exposure assessment

Ideally, exposure assessments should aim to identify substances that may be of safety concern with the minimum expenditure of resources. Therefore, most exposure assessment frameworks will employ a stepwise or tiered approach. The initial steps will rely on conservative screening methods. If no safety concerns are identified, no additional exposure assessment is required. Where potential safety concerns are identified, the subsequent steps of the framework will provide methods that incorporate increasingly specific/refined data (and require more resources) (see Figure 2).

At step 1, dietary exposure can be assessed by using screening methods based on conservative assumptions. If the estimated dietary exposure to a given chemical substance exceeds its toxicological reference value (acceptable daily intake [ADI], provisional tolerable daily intake [PTDI], etc.) or is below the nutritional reference value (adequate intake [AI], recommended daily intake [RDI], etc.), a more accurate method of dietary exposure assessment should be applied. A stepwise approach is being used by JECFA for food additives, including flavourings, and contaminants. JMPR agreed in principle in 2003 to adopt a stepwise approach for acute dietary exposure estimates for pesticides. The possibility of using probabilistic modelling has been discussed by JMPR and CCPR, and some preliminary investigations of its use at an international level have been undertaken.

In the sections that follow, examples of the available methods have been organized (somewhat arbitrarily) into categories in order to assist the reader in selecting the most appropriate framework and the desired methods for each step of the framework. The methods are divided into those that provide single (point) estimates and those that characterize the full distribution of consumer exposures.

Point estimates include (1) screening methods, (2) exposure methods that rely on crude estimates of consumption (default factors based on physiological limits, food production data, or usage/poundage data), such as the theoretical added maximum daily intake (TAMDI) and other model diets (for veterinary drug residues and packaging materials), and (3) more refined exposure methods based on actual consumption data and chemical concentration data, such as TDSs, selective studies of individual foods, and duplicate portion diets.

Characterizing the full distribution of consumer exposures is the most resource-intensive assessment, since data are required that characterize the range of food consumption

practices as well as the range of chemical concentrations in the foods that are eaten. Therefore, such methods are usually reserved for later steps. When the methods are employed, appropriate statistical models are used to evaluate the data and to describe the range of consumer exposures and the associated probabilities of consumers having each level of exposure. These exposure assessments are generally referred to as probabilistic exposure estimates. Examples of probabilistic assessments are the Monte Carlo assessments that have been conducted to assess consumer exposure to acrylamide (FAO/WHO Acrylamide in Food Network: http://www.acrylamide-food.org/).

3.4 Point estimates of dietary exposure

A "point estimate" of dietary exposure is simply a single value that describes some parameters of consumers' exposure. For example, an average consumer's exposure is calculated as the product of the average consumption of the foods of interest and the average residues of the substance of interest in those foods. The resulting exposure estimate can be further modified by additional adjustment factors as appropriate (processing factors, etc.). A point estimate of a high consumer's exposure (such as the upper 90th percentile consumer) can also be calculated, provided the appropriate data are available.

A point estimate is not inherently "conservative" or "realistic". The conservatism incorporated into the analysis is determined by the data and assumptions that are used in calculating the estimate. Point estimates can range from initial screening methods that use very few data and generally include very conservative assumptions to refined exposure assessment that includes extensive underlying data in order to realistically calculate the actual exposure estimates.

Examples of the range of methods that are currently in use are presented below.

3.4.1 Screening methods

Screening methods should be designed to reflect the particulars of the exposures that are to be considered. The screening assessments currently performed by international organizations (e.g. those conducted by JECFA and JMPR) largely differ according to the category of substance and are different for food additives, pesticides, and veterinary drugs.

The screening method that is selected should be easy to use and pragmatic. Typically, screening methods should overestimate dietary exposure of high consumers using conservative assumptions in terms of food consumption and chemical concentration (e.g. budget methods) (section 3.4.1.2). This will avoid situations where the dietary exposure estimated by the screening process would erroneously indicate no safety concern (i.e. understate exposure). However, in order to effectively screen chemical substances and establish risk assessment priorities, the first steps of the procedure should not consider unsustainable diets, or the results will be too unrealistic to be useful. At a minimum, physiological limits of consumption should be taken into account.

Although screening methods are sometimes criticized as being "too conservative", it must be borne in mind that their aim is not to assess "true" dietary exposure but to screen food chemicals for which a refined dietary exposure assessment is necessary. This must be made clear when results are presented, as should all assumptions made (section 1.3).

Different screening methods are described below, together with a critical analysis of the assumptions on which they are based and of their fitness for purpose. There is a need for harmonization, where possible, of these methods.

Screening methods can be created that are appropriate for a worst-case assessment of compounds that are toxic as a result of either acute or chronic exposures, as well as for specific subpopulations of interest.

3.4.1.1 Poundage data (food additives, including flavourings)

Poundage data provide estimates of the amount of a chemical substance available in the marketplace (the amount available per capita can be calculated) for use in food manufacturing in a country during a period of time, usually over one year. The estimated dietary exposure that is provided with such a calculation is based neither on observed consumption patterns nor on data on the actual concentration of the chemical substance in foods. Estimates may be adjusted by the proportion of the population likely to consume the food (per cent consumers) in which the chemical may be present as well as for underreporting of the amount of chemical produced. Nonetheless, there is a very large uncertainty in a mean dietary exposure derived from poundage data, since typically no information is available that allows the user to identify the foods in which the substance is consumed, who is consuming the food, or how much of the substance is discarded without being consumed. Poundage data and derivative methods do not adequately describe highly exposed consumers and are therefore not sufficient to determine if their dietary exposure is within toxicological reference values. Additional methods based on use level data (e.g. budget method) should be used within the first step of the screening. Poundage data can be used to provide an indication of the historical and geographical trends in the use of a substance or as a comparative measure of overall population dietary exposure relative to other substances.

3.4.1.2 Budget method

A screening method referred to as the "budget method" has been used to assess the theoretical maximum daily dietary exposure to some food additives. The results are compared with the substances' ADIs. The budget method has been used at an early stage in assessments of food additives by JECFA (FAO/WHO, 2003) and assessments within the European Union (EU).

The method relies on assumptions regarding (1) the level of consumption of foods and of non-milk beverages, (2) the level of presence of the substance in foods and in non-milk beverages, and (3) the proportion of foods and of non-milk beverages that may contain the substance.

More specifically, the levels of consumption of foods and beverages considered are maximum physiological levels of consumption—that is, the daily consumption of 0.1 litre/kg body weight of non-milk beverages and the daily consumption of 100 kcal/kg body weight from foods (equivalent to 0.05 kg/kg body weight based on an estimated energy density of 2 kcal/g) (Hansen, 1979). In a 60-kg person, these levels correspond to the daily consumption of 6 litres of non-milk beverages and 3 kg of food.

The level contained in foods is assumed to be the highest maximum level of the food additive reported in any category, respectively, for foods and for beverages. When the level of a chemical is particularly high in a very specific category of food or beverage (e.g. chewing gums), the additive level considered is the highest maximum level among the other categories that are more "representative" in order to provide somewhat more realistic estimates. The proportion of, respectively, solid foods and beverages that may contain the substance is set arbitrarily. In the case of food additives, a default proportion that is often used for European assessments is 12.5% for solid foods and 25% for beverages (European Commission, 1998). For additives used in a wide range of foods, the proportion of solid foods may be set at 25%.

The overall theoretical maximum daily exposure to a chemical is calculated by summing the potential exposure from beverages and from foods:

Overall theoretical maximum daily exposure =
[maximum level of the chemical in beverages (mg/l) × 0.1 (litre/kg body weight) × percentage of beverages that may contain the substance] + [maximum level of the chemical in solid foods (mg/kg) × 0.05 (kg/kg body weight) × percentage of solid foods that may contain the substance]

The potential dietary exposure to the substance is expressed in milligrams per kilogram body weight per day.

For example, if a substance may be present at up to 350 mg/l in beverages and up to 1000 mg/kg in foods, and if the proportion of beverages and foods that may contain it is assumed to be, respectively, 25% and 12.5%, the theoretical maximum daily exposure to this substance will be:

$$[350 \times 0.1 \times 0.25] + [1000 \times 0.05 \times 0.125] = 8.75 + 6.25 = 15 \text{ mg/kg body weight}$$

In a 60-kg person, this daily exposure corresponds to 900 mg of the food additive deriving from the consumption of 1.5 litres of beverages and 375 g of food containing the substance at the maximum level.

The budget method may need to be applied to different consumption levels to provide similar levels of conservatism for adults and children. For example, when the budget method was applied to consider exposures to food additives authorized for use in the EU (European Commission, 1998), a specific budget calculation was performed for children by setting the proportion of beverages that could contain the additives at 100%. The level of consumption of beverages considered was therefore 0.1 litre/kg body weight (i.e. 1.5 litres in a typical 3-year-old child weighing 15 kg). This is a conservative assumption according to the results of a survey in the United Kingdom, which reported that the 97.5th percentile of consumption of beverages containing additives was 0.07–0.08 litres/kg body weight in children aged 1.5–4.5 years.

The budget method has the advantage of requiring virtually no product-specific data and of being very simple and rapid to perform. A disadvantage of the budget method is that the results largely depend on the proportion of foods and beverages that is assumed to contain the substance, and typically that proportion is set arbitrarily. The usefulness of the method can be improved if the proportions are chosen to be more realistic while ensuring that the estimate is still conservative. .

Another arbitrary assumption by analysts using the budget method is the identification of categories of foods and beverages with very high use levels that are considered not "representative", such as chewing gums. When such items are identified, a quick check of the quantity of the specific food item that would lead to exposure in excess of the toxicity reference value should be performed in parallel with the budget method in order to determine if the consumption of the specific item can lead to exposure in excess of the toxicological reference value.

The budget method, using the assumptions employed for EU assessments, has been applied in a case-study of food additives (Douglass et al., 1997). The assumptions for the energy density of foods were found to be only a slight overestimate, which would detract from the overall conservatism of the method. In contrast, the assumptions regarding energy intake and beverage consumption were overestimates of even high levels of consumption. Overall, the exposure to additives estimated with the budget method was found to be higher than the survey-based 95th percentile exposure to additives (Douglass et al., 1997).

The budget method is sometimes criticized as being "too conservative". For example, for an evaluation in Europe, the method was used as a screening for 58 additives. For 22 of the additives, the potential dietary exposure calculated with the budget methods was lower than the relevant ADI (European Commission, 1998), whereas 36 of these additives did not

"pass" the budget method. For the 36 that did not pass, it was recommended that more refined exposure assessments be conducted.

In summary, the budget method is a simple, inexpensive, and conservative screening method that can easily be applied to all chemicals intentionally added to food (additives, including flavourings, processing aids, etc.) for comparison with their relevant toxicological reference values, provided the maximum concentrations of the chemical in foods and beverages can be ascertained.

3.4.1.3 Model diets

Model diets are constructed from available information on food consumption and are designed to represent a typical diet for the population whose exposure is to be considered. A model diet can be constructed that reflects the diet of the general population or a specified subpopulation. For example, it may be of interest to evaluate the subgroup of the population that has the highest consumption of foods of interest and/or high consumption in relation to body weight.

Although model diets can be extremely useful, the models are only as good as the underlying data and assumptions, which should be stated for each model.

Some examples of model diets that have been used to evaluate consumer exposure are summarized below.

a) Theoretical added maximum daily intake model diet for flavourings

The TAMDI model diet was designed to provide a conservative estimate of potential exposure to a specific flavouring substance on the basis of proposed or allowed maximum (upper use) levels (UULs) in the different categories of foods and beverages that could be flavoured. The resulting exposure estimate is for a hypothetical consumer who consumes a fixed amount of flavoured foods and beverages every day, and those foods always contain the specific flavouring at its specified UUL (Cadby, 1996). The TAMDI is calculated by summing the exposures estimated for each individual food category (Table 7) to estimate total daily intake.

Table 7 Food consumption and concentration levels used in the TAMDI calculations[a]

Foods and beverages	Consumption (g/day)	Concentration (mg/g)
Beverages (not alcoholic)	324	UUL1
Foods	133	UUL2
Exceptions:		
Candy, confectionery	27	UUL3
Condiments, seasonings	20	UUL4
Alcoholic beverages	20	UUL5
Soups, savouries	20	UUL6
Other exceptions (e.g. chewing gums)	2	UUL7

TAMDI, theoretical added maximum daily intake; UUL, upper use level

[a] TAMDI (mg/day) = (324 × UUL1) + (133 × UUL2) + (27 × UUL3) + (20 × UUL4) + (20 × UUL5) + (20 × UUL6) + (2 × UUL7).

The consumption levels considered are aimed at representing typical portions of flavourable foods and beverages (e.g. a glass of non-alcoholic beverage, a piece of bakery ware). The portions are twice those that were used by the Codex Alimentarius Commission (1989) to provide an estimate of exposure to intense sweeteners in the absence of sufficient data relevant to the consumption of sugar-free products.

The TAMDI has been used by the European Scientific Committee on Food to assess potential exposure to single flavourings (European Commission, 2003a). A modified

TAMDI, in which typical use levels have been used instead of the UUL, has been applied in the evaluations of groups of chemically defined flavourings recently released by the European Food Safety Authority (EFSA, 2004). The selection of typical use level instead of UUL, as a general principle in a screening process, is not desirable, since consumers could be loyal to flavoured products containing the UUL.

The consumption levels considered in the TAMDI calculation may underestimate the average consumption of flavoured foods by some consumers. In contrast, the assumption that all flavoured foods consumed each day will contain the same flavouring at its UUL is obviously very conservative.

A major disadvantage of the TAMDI model is the arbitrary choice of food categories and portion size. TAMDI does not allow the analyst to easily determine whether it is assessing the exposure of the upper 90th or 95th or some other percentile consumer.

The advantages of TAMDI are that it is very easy to apply and the hypotheses on which it is based are transparent in terms of consumption level and concentrations. On the basis of some limited case-studies, the TAMDI appears to provide a conservative estimate of high exposure to flavourings. It can therefore be considered as a possible tool to prioritize dietary exposure assessments provided the underlying assumptions are clearly delineated. The TAMDI method may need to be supplemented with dietary exposure assessments targeted to high consumers of single categories of flavoured foods and beverages.

b) Model diet for veterinary drug residues

A model diet intended to cover high consumers of animal products is used by JECFA to establish MRLs for veterinary drug residues in foods of animal origin. The model diet consists of:

- 300 g meat;
- 100 g liver;
- 50 g kidney;
- 50 g animal fats;
- 100 g eggs; and
- 1.5 litres milk.

MRLs for a given chemical are set such that the dietary exposure estimated by the following calculation—(300 g × MRL in meat) + (100 g × MRL in liver) + (50 g × MRL in kidney) + (50 g × MRL in animal fats) + (100 g × MRL in eggs) + (1.5 litres × MRL in milk)—is lower than the relevant ADI.

Such a model clearly corresponds to a non-sustainable diet, but has been used as a conservative model.

At its 66th meeting (FAO/WHO, 2006), JECFA decided to use the median of the residue distribution to substitute for the MRL in the intake estimate, in order to reflect a better estimate of chronic dietary intake. The new estimate of intake is called “estimated daily intake” (EDI). In calculating the median from an array of results, including values below the LOQ or below the LOD, half of the respective limit is used for the calculation of median concentration of residues.

c) Model diet for chemical substances migrating from packaging materials

Currently, the EU and the United States each have methods developed for assessing dietary exposure to substances migrating from packaging materials. The methods are described below.

In the EU, a model diet for chemical substances migrating from packaging materials is used to establish the maximum limit of migration, the so-called "specific migration limit" (SML) (Barlow, 1994; European Commission, 2002, 2003b).

The maximum limit of migration is determined by assuming that a 60-kg person could ingest daily up to 1 kg of foodstuffs in contact with packaging material (600-cm^2 contact surface) that would always contain the substance under consideration at a concentration corresponding to the SML without exceeding the relevant toxicological reference value (i.e. tolerable daily intake [TDI]).

The assumption of repeated daily exposure to the same type of packaging material is conservative, but in some cases the other assumptions are not. For example, individuals may consume daily more than 1 kg of packaged food, especially if beverages are considered. Moreover, the default ratio of surface to mass (600 cm^2/kg) is that of a cube of 10-cm side width (total area 6 × 100 cm^2) containing 1 kg food; this ratio is low in comparison with that of foods in small packages (e.g. single portions, food in slices, some baby foods).

In the United States, the model diet used to evaluate food contact substances assumes a consumption of 3 kg of packaged foods and beverages and employs consumption factors that describe the fraction of the daily diet expected to be in contact with specific packaging material types (e.g. glass, plastic, paper) (http://www.cfsan.fda.gov/~lrd/foodadd.html). Migration levels are then assigned according to the nature of the food likely to be in contact with the packaging material (aqueous, acidic, alcoholic, and fatty). In order to assess high levels of exposure, the impact of consumer loyalty to certain specific brands and packages would need to be taken into account in such a dietary exposure assessment.

3.4.2 More refined deterministic/point estimates

Point estimate modelling may also be appropriate as a second step in a tiered approach. The model selected can be more or less conservative, depending upon the purpose and the available information.

As noted above, deterministic models use a single point estimate for each model parameter. For concentration data, the point estimate typically consists of the mean, the median, a high percentile of all observed values, or even the ML proposed by national or international food authorities. For food consumption data, the point estimate typically consists of the mean or a high percentile of all the consumption values of a considered food in a population of interest.

This type of deterministic modelling has the advantage of being relatively simple to implement. Models can often be "developed" by using tools such as spreadsheet or database programs. However, because such models generally contain limited information, interpretation of the results can be problematic. The results are dependent on the input data and their appropriate treatment, but the impact may not be readily apparent; for example, if the input value used is not representative of the underlying distribution, then the result is likewise not representative. If "conservative" values (e.g. high concentration and high consumption values) are used in the model, the resulting exposure estimates will overstate typical exposures. For this reason, use of point estimate modelling with conservative parameter values may be appropriate for screening-level assessments. Nonetheless, it is important to keep in mind that it is difficult to know just how conservative the result will be.

When high-percentile values for either food consumption levels or chemical concentrations in food are not known, there are default procedures that can be used to develop rough estimates for these points (see sections 2.2.3 and 3.5.3). Modelling dietary exposures for high consumers of a food chemical can be accomplished by conducting a full distributional analysis using Monte Carlo techniques (section 3.5). Where adequate data are not available to conduct a distributional analysis, arbitrary factors may be incorporated in a point estimate to simulate the upper end of the distribution of food chemical exposure; for example, by assuming that the distribution is lognormal, a factor of 2 or 3 might be applied to the mean to roughly estimate the dietary exposure of high consumers. Different assumptions may be appropriate when modelling acute and chronic dietary exposures, since the concentrations of the substances will not always be high.

3.4.2.1 Correction factors

This type of deterministic approach can also be refined by applying correction factors to the concentration data when based on raw commodities to reflect changes due to processing or to account for the portion that is actually consumed (see section 2.1.4).

The use of processing factors to reflect the concentrations of the substance in the portion of food that is consumed will provide more realistic estimates of exposure. Depending on the substance and the processing techniques used, the levels in the edible portion may be higher or lower than the concentration in the whole food. Edible portion concentration data are discussed in section 2.1.4.

In many cases, only a fraction of the total food or crop supply is anticipated to contain the substance being evaluated. Where data exist to quantify the percentage affected, these values can be applied to the concentration data as an adjustment factor in order to more accurately estimate consumer exposures; however, the possibility of consumer loyalty to specific brands also needs to be considered.

3.4.2.2 Handling of non-detects

In conducting dietary exposure assessments, the proportion of non-detected values in the data set of chemical concentrations is important. Assumptions about those values and their treatment may influence the result of the assessment (see section 2.1.5). The impact of the treatment of the non-detected or "censored" values should be tested by repeating the analyses with different assumptions as to the values in those samples without detectable residues (GEMS/Food-Euro, 1994).

Where feasible, it is appropriate to convey the degree of uncertainty in the input data sets (food consumption data, concentration data). A common method for describing uncertainty is to repeat the analysis using (1) bounding "high-end" estimates for all parameters, (2) bounding "low-end" estimates for all parameters, and (3) central tendency estimates (mean or median) for all parameters. Based on the implied uncertainty, the risk manager can then determine if the expenditure of time and resources necessary to gather additional information about these parameters is warranted.

3.4.2.3 Consumer loyalty

The tendency of consumers to repeatedly purchase and consume the same food products, termed consumer loyalty, has an effect on estimated dietary exposure. Thus, if a specific brand of processed food contains a high concentration of a substance, consumers of that brand would have higher dietary exposure of the substances than those consuming brands without, or with lesser amounts of, the substance. Consideration of consumer loyalty may be important when assessing high chronic dietary exposure to food chemicals present in

processed foods (e.g. food additives, including flavourings, processing aids, or chemicals migrating from packaging) (Arcella et al., 2003). Consumer loyalty may also warrant consideration in the dietary exposure assessments of other chemicals, such as pesticide residues and contaminants. Its impact may be lower in these cases, as there is frequent mixing of raw agricultural commodities before purchase by consumers. However, some segments of the population may still be systematically exposed to foods containing higher than average levels of these substances, particularly for pesticide and veterinary drugs, where only a proportion of the food commodity may be treated and the food is not mixed or blended.

3.4.3 Further examples of point estimates using model diets

Some examples of more refined point estimate models are summarized below.

3.4.3.1 GEMS/Food regional diets and consumption cluster diets

Data submitted on the priority contaminants/commodities in GEMS/Food have been used to assess the potential risk to human health from such exposures (UNEP/FAO/WHO, 1988; WHO, 1989b; UNEP, 1992; Bhat & Moy, 1997; Schutz et al., 1998). In these assessments, the estimated dietary exposures determined for each country are compared, when possible, with relevant ADIs or provisional tolerable weekly intakes (PTWIs) established by JMPR and JECFA. GEMS/Food provides relevant information to JMPR, JECFA, and the Codex Alimentarius Commission and its subsidiary bodies as appropriate.

The GEMS/Food regional diets, now replaced by the GEMS/Food consumption cluster diets (see section 2.2.5.1), are used as model diets by both JMPR and JECFA in chronic dietary exposure assessments. Following is an example of chronic dietary exposure estimates developed by JMPR at an international level using GEMS/Food consumption cluster diet. The methods initially recommended by the 1989 WHO guidelines for predicting chronic dietary exposure to pesticide residues (WHO, 1989a) relied heavily on a model diet approach to give a theoretical maximum daily intake (TMDI) or national TMDI, with calculations based on MRLs and the GEMS/Food consumption cluster diet. Since 1996, following the recommendations of the joint FAO/WHO consultation on guidelines for predicting dietary intake of pesticide residues, held in York, United Kingdom (WHO, 1995b), the dietary exposure estimates are performed using STMR levels in the calculation of international estimated daily intakes (IEDIs), instead of MRLs and TMDIs. The mean consumption levels in the GEMS/Food consumption cluster diet are used for all crops with recommended MRLs, and the individual intakes are summed. JMPR uses this procedure in a single-step approach, using the best available information, including median residue levels determined through supervised field trials. Whenever possible, residues are estimated for the edible portion. This may require the use of processing factors and consumption of processed food. Although it is appropriate to correct for the edible portion if the commodity is always prepared in some way, care should be taken with processes such as peeling, where it is often assumed that the commodity is always peeled before consumption, while in reality this may not be true.

One of the principles for international exposure assessment is that the underlying data should be conservative. Therefore, the GEMS/Food consumption cluster diet, which tend to overestimate mean food consumption, are valid data for dietary exposure assessment, especially since national FCS data are often lacking. The result of such a calculation is not intended to represent the dietary exposure of high consumers. Alternatively, national FCS data should be used when available. National FCS data may provide additional information, such as distributions of food consumption data, portion sizes, consumption by specific population groups, as well as brand name and food treatment information. If national data are

not available, in order to assess the dietary exposure to a food chemical for high consumers at an international level, a correction factor can be applied to mean consumption amounts to approximate the high percentiles of dietary exposure (WHO, 1985).

3.4.3.2 Total diet studies (TDSs)

TDSs are designed to assess chronic dietary exposure to food chemicals actually ingested by the population living in a country and, if possible, population subgroups (WHO, 1992). This is accomplished by measuring chemical concentrations in food (including drinking-water) "as consumed". While the traditional focus of TDSs has been on assessing dietary exposure to pesticide residues and contaminants, the advent of multi-element analyses has seen TDSs increasingly include selected nutrients. TDSs have also been used for estimating dietary exposure to food additives. TDSs differ from other chemical surveillance or monitoring programmes because they aim to assess dietary exposure to food chemicals across the total diet in one study. If conducted on a regular basis, TDS results can provide a continuous means of checking the effectiveness of regulatory systems that have been established to control the levels of chemicals in the food supply, as well as monitor trends in dietary exposures.

The majority of TDSs worldwide use the point estimate (deterministic) approach to assess mean dietary exposure for a whole population. In some studies, high consumer dietary exposures are estimated by applying specified factors to mean consumption data (WHO, 1985). Estimates for specific population subgroups (e.g. infants or young children) can also be determined if food consumption data are available. Some countries combine distribution of food consumption data at an individual level with one fixed value for the concentration of the chemical in the TDS foods or food groups (FSANZ, 2003; Food Standards Agency, 2004; Leblanc et al., 2005). TDSs are not suitable for the assessment of acute dietary exposures because of the high degree of compositing of samples.

3.4.3.3 Modelling high consumers of two food groups

Model diets can be developed on the basis of published data from FCSs as an alternative to the budget method or additional step in the screening process. For example, a model diet has been used in Europe to estimate chronic dietary exposure based on the assumption that a person might consume average amounts of several different foods but only one or two at a high level (European Commission, 1998). The behaviour of such a consumer is modelled by adding up potential dietary exposure to a food chemical at the 97.5th percentile of consumers of the two food categories that lead to the highest dietary exposure with the mean potential exposure for all other food categories. It has the advantage of being applicable to surveys for which only data on mean and high consumption of large food groups are available, without the need to have access to the raw data of individual dietary records. It can therefore be used on the basis of published data. This approach has usually been used for chronic dietary exposure assessments for additives where the food consumption data have been aggregated into fewer than 20 large food categories. The basic assumption of this model diet is considered valid if the number of food groups is limited.

3.4.4 Specialized studies designed to answer specific questions

If the situation warrants, studies may be designed to answer specific questions about consumer exposure. The study may directly measure exposure or may provide additional information about one or more parameters of the exposure assessment algorithm. Examples of specialized studies are given below.

3.4.4.1 Selective studies of individual foods

In some cases, surveys such as a TDS that encompass the whole diet may not be necessary. Surveys of specific foods are particularly useful if the dietary exposure of a chemical is predominantly influenced by one, two, or a limited range of foods and/or when food surveillance/monitoring has already established average chemical concentrations in the foods (WHO, 1985). For example, mercury in fish and seafood, persistent organic pollutants (POPs) in fat-containing foods (van Zoonen in WHO, 2002a; Baars et al., 2004), mycotoxins (Leblanc et al., 2005), food additives (Chen in WHO, 2002a; Yoon in WHO, 2005a), and veterinary drugs would all generally be best approached via a selected individual foods approach.

3.4.4.2 Duplicate portion studies

Duplicate portion studies may also be used to assess dietary exposures for population subgroups, as they provide dietary exposure information at the individual level, based on the diet "as consumed". This can be especially useful for well defined population subgroups, such as vegetarians (MAFF, 2000; Clarke et al., 2003), children (Wilhelm et al., 2002; Murakami et al., 2003), breastfeeding mothers (Gulson et al., 2001), adult women (Tsuda et al., 1995), or people who consume catering establishment meals (Leblanc et al., 2000). However, such studies are very costly in terms of participant involvement and management and are used for small groups of people only (IPCS, 2000). Nonetheless, such a study can be very useful, in that it can provide an estimate of total exposure that can act as a benchmark for estimating the degree of over- or underestimation of exposure when assessments are conducted with limited data. For example, in the early evaluations of dietary exposure to acrylamide, a TDS conducted by the Swiss government provided an estimate of total exposure that was used to assess whether the foods that had already been analysed were those that represented the most important sources of acrylamide, or whether other significant sources remained to be identified.

3.5 Refined dietary exposure assessments (probabilistic distributional analyses)

If the existence of a safety concern cannot be ruled out on the basis of dietary exposure assessed at the initial (screening-level) steps, more accurate assessments of dietary exposure may be needed. It should be noted that the consumer exposures are not changing; rather, the accuracy with which those exposures are estimated is improving by using more refined methods. In any case, it should be emphasized that the probabilistic assessment, although giving a better dietary exposure estimate than one calculated using the deterministic approach, would not necessarily give a lower estimate.

Refinements could include more defined information about the foods that are consumed (less conservative assumption about the amounts consumed, concentrations of the chemical in the foods, impact of processing and food preparation, etc.), or more complex exposure assessment models can be employed that allow more realistic simulation of consumer practices.

Nonetheless, further steps to allow the refinement of the dietary exposure assessment should be designed in such a way that potential high dietary exposures to a specific chemical are not underestimated. The methodologies should take into consideration non-average individuals, in particular those who consume large portions of specific food items, are loyal to those foods containing the highest concentration of the chemical of interest, or have low or infrequent consumption of foods with very high food chemical concentrations.

For the models to be accurate, the food consumption data and food chemical concentration data should be for the same food products (see section 2.2.3). Good estimates are derived from good data, and no complex/complete model will make insufficient or deficient data into good data. Additional data may need to be collected to adequately represent the actual exposure situations.

3.5.1 Overview of probabilistic estimates of exposure

For substances requiring further refinement beyond screening methods or point estimates of exposure, as described above, a probabilistic analysis of exposure variability can be conducted. Conceptually, population exposure must be thought of as a range of values, rather than a single value, because individual members of the population experience different levels of exposure. Factors that contribute to this "variability" include age (owing to differences in body weight and the type and amount of food consumed), sex, ethnicity, nationality, region, and personal preferences, among others. Variability in dietary exposure is often described using a "frequency distribution" (see Figure 3). Sometimes, the frequency distribution is approximated as a continuous probability distribution (see Figure 4). In both cases, the horizontal axis corresponds to the level of exposure, and the vertical axis corresponds to the relative proportion of the population.

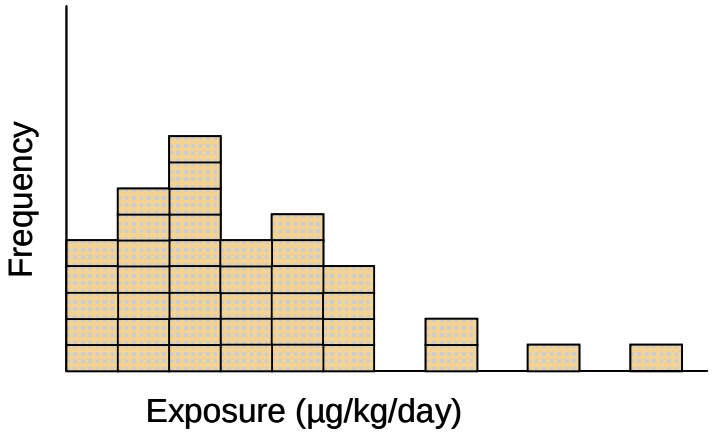

Figure 2 Frequency distribution

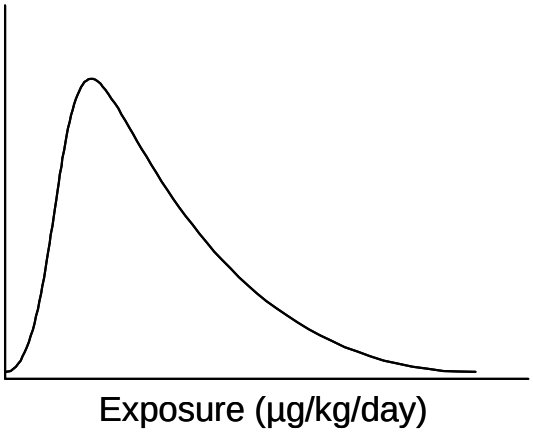

Figure 3 Continuous probability distribution

The variability distribution can be characterized by referring to representative members of the population. For example, the median individual has an exposure at the middle

of the distribution (i.e. half of the population has exposures that are less than that of the median individual, whereas the other half has exposure levels exceeding that of the median individual). The 95th percentile individual has an exposure that exceeds the levels experienced by 95 out of every 100 individuals in the population. The average or mean exposure is computed by summing the exposures of all individuals and dividing by the size of the population. Section 3.5.2 discusses some of the models that are available for conducting probabilistic assessments. Finally, in those cases warranting the greatest level of scrutiny, so-called two-stage simulation techniques can be used to characterize both uncertainty and variability (section 3.5.4). In all instances, adequate data must be available to allow meaningful assessment.

3.5.2 Probabilistic models

The structure of a probabilistic model is similar to that of the deterministic models described in section 3.4, in that it is based on the same basic equations. The fundamental difference is that at least one variable is represented by a distribution function instead of a single value. As for point estimates, it may be possible to further refine probabilistic models by taking account of factors such as edible portion, percentage crop treated, or consumer loyalty, where appropriate to do so (see section 3.4.2). Following is a discussion of approaches to developing probabilistic models for dietary exposure assessments.

3.5.2.1 Simple empirical distribution estimate

Dietary exposure assessments can be based on a food consumption distribution determined empirically from a FCS and a single point estimate to represent the chemical concentration in the relevant food product. Each point of the distribution curves of food consumption can be multiplied by the concentration in the relevant food commodity. Conversely, it is possible to have a single point estimate for consumption and an empirical distribution of chemical concentrations in that food. Finally, it is possible to have sufficient data to determine the distribution profile for both the amounts of food consumed and the levels of the chemical in those foods.

3.5.2.2 Random sampling estimate from food consumption and/or chemical concentration distributions

This approach requires data sets representing the distribution of concentrations in each relevant food category and, similarly, distributions of consumption for the same food categories for the population of interest. It explicitly takes into account the variability of input data, providing a more realistic result than that produced by simple deterministic scenarios, which generally are constrained by conservative default assumptions when a single value is selected to represent the entire distribution.

There are two general approaches to developing distributions for use in a probabilistic assessment. Non-parametric techniques can be used when actual data sets are available for a parameter. In these cases, the data sets can be assumed to represent the distribution of interest. The probabilistic assessment is implemented by randomly selecting one of the values from the parameter's data set for each iteration of the simulation. For example, if a data set with 100 concentration measurements contains two observations of 5 mg/kg, then the probabilistic assessment will effectively assume that there is a 2% frequency of the concentration being equal to this value.

Parametric techniques interpolate among the data points and extrapolate beyond them by assuming a particular distributional form. For example, standard techniques can be used to fit a normal, lognormal, or any other type of distribution to a data set. While the extrapolation

"fills in" gaps that may be particular to a specific data set, the elimination of these gaps comes at the cost of requiring an assumption to be made as to the functional form of the distribution. The assessor can evaluate the impact of the assumption by repeating the analysis assuming alternative (but plausible) functional forms.

Other methods, including iterative simulation methods, have been used in exposure assessment modelling but are beyond the scope of this guidance document. In general, the primary differences in the techniques are the methods that are employed to draw values from the data and in the evaluation of uncertainty and variability. Simple models of the multiplicative form may be appropriate for a variety of exposure assessments (Slob, 1994).

3.5.2.3 Stratified sampling

A stratified sampling method selects values at regular intervals throughout each distribution. For example, the mean or median of each quartile of each distribution is determined. The primary disadvantage of the single stratum calculation is that it produces no estimates for extreme values. This problem may be ameliorated, but never entirely overcome, by using more strata (e.g. estimating the mean of each decile instead of estimating a value for each quartile). Very detailed and accurate and entirely reproducible characterizations of the output distributions may be obtained by using many strata. The difficulty with stratified sampling is that the number of iterations required may get very large and may require additional computer software/expertise.

3.5.2.4 Random sampling (Monte Carlo simulation)

Monte Carlo simulation involves the use of random numbers to select values from the input distributions. The technique has been applied to a wide variety of modelling scenarios. As a result, it can be concluded that with appropriate data and when the simulation is conducted with a sufficiently large number of "iterations", the results will simulate the actual situation. The Monte Carlo simulation may be inaccurate at the extreme upper and lower ends of a distribution, which is particularly true if using a parametric distribution rather than non-parametric (empirical) distribution data are used. In such a case, when using a non-parametric approach for contamination data, a cut-off limit in the distribution tail may be introduced to avoid including "unrealistic" contamination levels in the model.

3.5.2.5 Latin hypercube

Latin hypercube is a statistical method that is essentially a hybrid of the stratified and random sampling methods. Distributions are divided into strata, and then random samples are drawn from each stratum in order to ensure that the iterations are balanced throughout the range of each concentration and food consumption data distribution. This method also allows for some samples to be drawn at the extremes of the distributions.

3.5.3 Applicability of a probabilistic approach at the international level

At an international level, time and resources should be dedicated to the application of probabilistic methodology only when there is a dietary exposure concern that cannot be refined using simpler and less resource-intensive methods. Where this is the situation, it may be useful to evaluate probabilistic exposure estimates derived for a representative selection of national populations to arrive at an understanding of the international situation.

It may be more feasible in many cases to refine the point estimate of dietary exposure than to use a probabilistic method, as described in section 3.4.2. For example, for contaminants, pesticide residues, and veterinary drug residues, the exposure assessment may be refined by incorporating processing factors that adjust the initial concentration data to

reflect the impact of processing (rice → polished rice; fruit → peeled fruit; potato → cooked potato). Likewise, the consumption data can be refined to provide estimates of intake of different forms of the food (raw, processed). This is the case for some pesticide residues. JMPR usually receives and reviews relevant data for food processing. If a processing factor is calculated from such data, the exposure assessment can be refined provided there is corresponding consumption information on the processed food item.

3.5.4 Uncertainty and variability analysis

Although both uncertainty and variability can be characterized using probability distributions, they are different concepts. Uncertainty corresponds to the assessor's level of knowledge about the data sets. Therefore, uncertainty can be decreased as the quantity or quality of the information available improves. In contrast, variability is a characteristic of the population and the population's behaviour. Its characterization can be improved by better information, but it cannot be decreased or eliminated.

Uncertainty refers to limitations in the knowledge of the exposure assessor about the data sets used. If the assessor's knowledge were perfect, then the exposure estimates for specific members of the population (e.g. the median individual or the 95th percentile individual) could be characterized as a single value. This is never the situation, so an uncertainty analysis is an important part of a probabilistic model and should portray the limits of current knowledge by generating a range of estimates that cover the range of plausible interpretation. More typically, knowledge is imprecise, and exposures for representative individuals must be reported as a range of values. The uncertainty analysis is ideally a quantitative exercise where feasible. This serves two basic purposes. First, it gives decision-makers an idea of the overall confidence associated with the estimation process. Second, it facilitates research planning by giving researchers a formal target.

A formal uncertainty analysis is not always necessary. Two good reasons for omitting a formal representation of uncertainty are that (1) the uncertainties involved are relatively small and (2) it is known beforehand that either a most likely case or worst-case scenario will drive the decision process.

The basic notion underlying a "statistical" uncertainty is that the uncertainty about an unidentified (or random) individual or event is characterized by the known frequency distribution of a population or series. Thus, the same distribution may function as either a frequency distribution or an uncertainty distribution, depending on whether it is being used to make a prediction about a population or an individual.

In an uncertainty analysis, each component of a model may have its own uncertainties.

The concept of statistical sampling error is another important frequency-based uncertainty. This involves the use of a statistical distribution to express the doubt that a small sample accurately represents a population. The underlying distribution used is speculative and is usually assumed to be the normal distribution. Confidence intervals for parameter estimates usually reflect sampling error.

Formal representation of uncertainty may utilize statistical concepts of uncertainty, such as measurement and sampling error. In addition, probability trees (Hacking, 1976; Rescher, 1993) may be used to represent uncertainties associated with the plausible use of alternative model forms or alternative surrogate data sets.

For many public health issues, it may desirable to characterize the uncertainty associated with population estimates for a value that varies among individuals. For example, dietary exposure estimates are often made for a series of individuals in a survey, and those population estimates are uncertain. In these circumstances, each inference may have distributions that describe the range of population values and distributions or probability trees

that represent uncertainty. An uncertainty analysis may also alleviate concerns over the accuracy of a simulation method for estimating the tails of the frequency distributions by demonstrating that the uncertainties associated with the extreme values are larger than the errors introduced by the simulation method. In order to integrate these different elements into the conclusions, a two-dimensional simulation is useful.

The discussion of variability and uncertainty here is intended to provide a general framework for thinking about the characterization of population dietary exposure. In practice, the emphasis of dietary assessments is on the characterization of population variability. Nonetheless, it is useful to keep in mind that the population estimates developed are not certain and that, ideally, the assessor should provide some indication of the plausible range of values for various representative members of the population.

3.5.5 Sensitivity analysis

Risk assessment models may become very complex. An uncertainty analysis (see section 3.5.4) may reveal that there are substantial uncertainties in an estimate without indicating where those uncertainties arise. That is, it may not be apparent which of the uncertainties in the assumptions give rise to the uncertainty in the model predictions. Sensitivity analysis refers to quantitative techniques that may be used to identify those aspects of the inputs (chemical concentration or food consumption data) that contribute the greatest extent to the uncertainty. Analyses that evaluate inputs identified as the most important sources of uncertainty may be expected to be the most useful.

There are many different sensitivity analysis techniques (Cullen & Frey, 1999; Frey & Patil, 2002). The simplest of these vary each input one at a time, with all the other values held at some nominal (i.e. central or most likely) value. The resulting range in the output is then compared for each of the inputs. Although they are invariably more calculation intensive, the more sophisticated sensitivity analysis methods analyse correlations among input distributions.

Sensitivity analysis is also sometimes used to evaluate frequency distributions (Frey & Patil, 2002). In this case, the relationship of the inputs used to describe population variability and the output distribution for the population estimate are examined. This type of analysis may be useful for identifying control strategies for food chemicals.

3.6 Specific considerations for modelling approaches for acute and chronic dietary exposure assessments

Different methods for conducting dietary exposure assessments may need to be selected based on the exposure durations required to elicit the toxic or beneficial effects. Two time frames—chronic (long-term) and acute (short-term; a single meal or over a whole day)—have been considered for some assessments at the international level and by some national governments. These time frames are discussed below; however, it should be noted that these are standard time frames, and other lengths of time may be more appropriate for some chemical substances. Different assumptions will be appropriate when modelling acute and chronic exposures.

3.6.1 Chronic dietary exposure assessments

Typically, toxicological studies carried out to examine the health effects resulting from consumption of a chemical substance in the diet are completed over a long period of time (e.g. a year or the lifetime of test animals). These health effects are understood to arise from long-term exposure to the substance being studied. Exposure assessments conducted to be

comparable to these long-term toxicological studies have been termed chronic dietary exposure assessments.

Chronic exposure assessments may be deterministic (point values) or distributional (also known as probabilistic or stochastic). Typically, a mean dietary exposure will be compared with a chronic (long-term) toxicological reference value (ADI, PTWI). The mean dietary exposure may be calculated by applying a deterministic model using average food consumption levels and the average concentrations in the relevant food products. Where desired, it is also possible to conduct this assessment using parameters that will compute the dietary exposure of consumers with high exposure. Where data are not available, as a rough approximation, exposures to individuals with high consumption can be estimated by using a fixed factor of multiplication to simulate an upper percentile.

For a chemical with long-term effects, the mean chemical concentration is typically used, assuming this value represents the long-term average of truly encountered concentrations. In the case of a non-staple food (i.e. a food not typically consumed every day by each consumer), high-percentile estimates based on the whole population "dilute" the quantities of food eaten and consequently underestimate the exposure of high consumers. However, excluding the individual non-consumers (those who do not report eating the food of interest during the survey duration) gives a conservative assessment of exposure, because the true number of consumers over a long period of time is underestimated by the short-term FCSs (see section 2.2.4) (IEFS, 1998; Tran et al., 2004).

If this first point estimate for dietary exposure is below the toxicological reference value, further refinement steps are not necessary, and the chemical is unlikely to be of safety concern. However, when the initial screening results in an estimate of the dietary exposure close to or above the toxicological reference value, a more accurate assessment will usually be necessary.

3.6.2 Acute dietary exposure assessments

The focus of dietary risk assessment has generally been on the risks arising from chronic (long-term) dietary exposure. However, in the early 1990s, it became apparent that in some cases, residues of a chemical substance could pose risks resulting from a single exposure or at most a few days of exposure.

Two developments have led to this recent change in focus. First, as chronic dietary exposure methodology has improved, there has been a move away from "worst-case" estimates of chronic dietary exposures. In the past, there were always large conservative assumptions to account for lack of data; now, with more data available, the chronic dietary exposures are more realistic, and this has directed more attention to a greater need for an explicit consideration of acute dietary exposure. Second, research on residues of acutely toxic pesticides (organophosphates and carbamates) in individual fruits and vegetables revealed random occurrences of comparatively high residue levels. Those people who consume significant amounts of such foods are at risk of eating such a "hot" commodity unit (Harris, 2000). As for chronic exposure, acute dietary exposure assessments may be deterministic (point values) or distributional. At an international level, a deterministic methodology was developed to address the calculation of the acute dietary exposure (Hamilton & Crossley, 2004).

3.6.2.1 Pesticide residues

The joint FAO/WHO consultation held in Geneva in 1997 (WHO, 1997b) recommended a procedure for performing acute dietary exposure assessment for compounds for which an ARfD was established. (For compounds with no acute toxicity, JMPR has concluded that an

ARfD is unnecessary, and assessing the acute exposure is irrelevant.) This was followed by the international conference on pesticide residues variability and acute dietary risk assessment, held in York, United Kingdom (MAFF, 1999), and the ad hoc expert meeting held before the 1999 CCPR (Annex V in FAO, 1999b). While it was recognized that probabilistic modelling would provide the most refined estimate, it was also recognized that this would be difficult at the international level, and a simpler method was developed.

At its 1999 meeting, JMPR performed acute dietary exposure assessments for the first time, by calculating IESTI. In the IESTI methodology, the estimates are performed for each crop individually, as it is assumed that it is unlikely that an individual will consume, within a meal or 24 h, two different commodities of LP weights that have the same pesticide at the highest residue level. This methodology has been further refined by subsequent JMPR meetings. The equations currently used by JMPR are shown in Annex 4 of this document.

A more detailed summary of the development of the method for assessing dietary exposure is given in Annex 4 Figure 5 shows the decision tree for acute dietary exposure assessment, which could be applied to any food chemical with an ARfD.

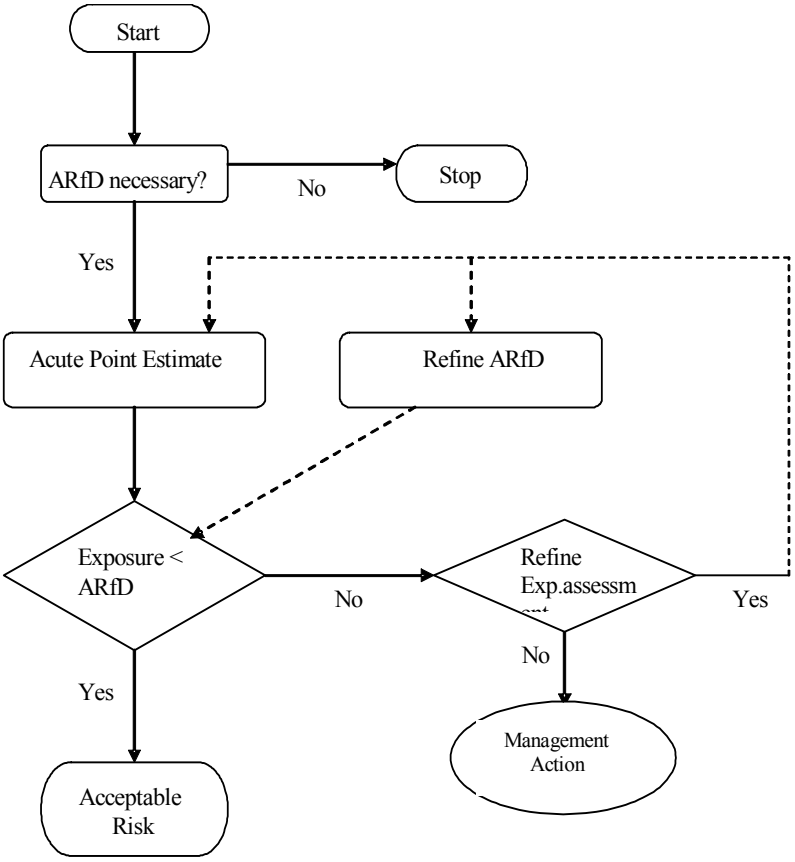

Figure 4 Decision tree for acute dietary exposure assessment

The concept of a variability factor was introduced by JMPR to take into account the different concentrations of residues in individual units of a composite sample. JMPR concluded in 2005 that due to the inevitable random nature of the variability factor derived from the combined uncertainty associated with sampling and analysis, the best estimate of the default variability factor is the mean of the variability factors derived from samples of various crops. The mean variability factor was found to be 3 (FAO, 2004b), and it has been used as a default

value by JMPR since 2003. It is important to note that the variability factor as described here can be applied only for samples coming from single lots. Analysts conducting acute exposure assessments for pesticides may want to select an appropriate variability factor for the specific evaluation.

3.6.2.2 Veterinary drug residues

For veterinary drug residues, some of which may also represent an acute hazard, the manner in which MRLs are established ensures that the ADI (which may be based on an acute end-point) in general is not exceeded. Substances with acute pharmacological or toxicological properties are of concern; these include classes such as β-blockers, β-agonists, anaesthetics, tranquillizers, vasodilators, and compounds that may trigger acute hypersensitivity reactions (e.g. penicillins). While the procedures for establishing MRLs appear to deal adequately with drug residues of non-acutely toxic compounds in the principal edible tissues, discussions are ongoing for the special case of injection site residues. These residues pose the potential problem of exceeding the guidance value even when residues in the other tissues are at or below their MRLs.

Owing to the nature of veterinary drugs, the ADI for those compounds is sometimes based on acute end-points. Furthermore, the model diet (see section 3.4.1.3) used by JECFA is considered to be rather conservative and to also cover acute dietary exposure (i.e. LP size). However, when these daily food consumption amounts are compared with the values that JMPR uses in its acute dietary exposure assessments, based on the highest available 97.5th percentile of consumption (WHO, 2004a), it can be seen that, in some cases, the veterinary drug dietary exposure estimates may be underestimating the acute dietary exposure.

3.6.2.3 Contaminants and food additives (including flavourings)

For contaminants, when the toxicological evaluation indicates a need for an acute dietary exposure assessment, the case 1 IESTI calculation can be used (see Annex 4 for details of the calculation), with the GEMS/Food value for the highest reported 97.5th percentile of consumption (WHO, 2004a).

For most food additives (including flavourings), no acute toxicity occurs at the potential level of exposure; therefore, no acute dietary exposure assessments are needed. For some chemicals, allergic reactions sometimes may be of concern. While exposures can be calculated, there is currently no clear toxicity value to use in evaluating the significance of those exposures. Research is under way to allow the development of thresholds for allergenicity of a variety of food allergens.

3.7 Aggregate/cumulative exposures

Historically, the safety of food additives and residues of pesticides and veterinary drugs and the risk of chemical contaminants have been evaluated on the basis of single-chemical and single-exposure pathway scenarios. That is, risk assessors generally performed risk assessments, and risk managers developed management options by examining each pathway separately. In general, exposures to a chemical through the food, drinking-water, and residential/occupational pathways were each assessed independently, and no concerted effort was made to evaluate potential exposures through multiple pathways simultaneously. This problem is often exacerbated, in that the responsibility for these different routes of exposure is often in different parts of national governments and international organizations.

Although different chemicals may act by the same mechanism and produce the same effect (e.g. organophosphate pesticides and acetylcholinesterase inhibition), little consideration was given to the fact that exposure could occur to multiple chemicals at the

same time and that the toxicological effects might be additive or even potentiated. For example, although two pesticides might act by a common mechanism of toxicity (e.g. acetylcholinesterase inhibition) and exposure on any given day might result in additive effects, standard or traditional exposure assessment methodologies did not consider this co-occurrence.

This concern was recognized in 1993 in a report issued by the United States National Research Council (NRC) entitled *Pesticides in the Diets of Infants and Children* (NRC, 1993). Similar reports were subsequently issued by the United Kingdom Food Standards Agency (2002) and the Health Council of the Netherlands (2004). These reports made several recommendations on how to improve the assessment of health risks posed by pesticides in the diets of infants and children. One recommendation was that consideration be given to all sources of dietary and non-dietary exposures to pesticides. Consideration of combined exposures to a single chemical across multiple routes (oral, dermal, inhalation) and across multiple pathways (food, drinking-water, residential/occupational) is known as "aggregate exposure". The reports also recommended that consideration be given to the assessment of risks from exposure to multiple pesticide residues that cause a common toxic effect. This consideration of risks associated with multiple chemicals that act by a common mechanism is termed "cumulative exposure".

The USEPA considers aggregate and cumulative exposures under the Food Quality Protection Act of 1996, which includes specific provisions with respect to consideration of the risk posed by the pesticide chemical on multi-pathway "aggregate" and multi-pathway, multi-chemical "cumulative" assessments.

This issue of aggregate and cumulative exposure assessments was also recognized and discussed during an FAO/WHO consultation held in Geneva during 1997 (WHO, 1997b). Specifically, the consultation noted that exposures to food chemicals through other routes may occur, and that co-exposures to chemicals or drugs sharing the same mechanism of action (toxicity) may also be encountered. These scenarios and the range of exposure assessments that can be developed were summarized during the meeting as shown in Table 8.

Table 8 Scenarios and the range of exposure assessments[a]

Toxic concern	Exposure route	Assessment type
Single chemical	Single food	–
	Multiple foods	Aggregate dietary
	Multiple media	Aggregate
Multiple chemicals with the same mechanism of action	Single food	–
	Multiple foods	Cumulative dietary
	Multiple media	Cumulative

[a] Table is modified somewhat from the table originally appearing in the report (WHO, 1997b) to clarify naming conventions.

The issue of aggregate risk associated with human exposure to pesticides from multiple sources is under review, with a focus on the use of probabilistic approaches. While exposures beyond food and water—for example, environmental (particularly residential) and occupational exposures—are not within the purview of the Codex Alimentarius Commission, all sources of exposure are within the human health mandates of FAO and WHO and other agencies.

The methodology for the cumulative dietary exposure to chemical substances in food with a common mechanism of action could be considered at an international level regardless of the development of probabilistic methods. One approach in cumulative risk assessment is the use of the toxicity equivalence factor (TEF). These factors, representing the toxicities relative to an "index compound", are applied to the concentration data of each compound

within a group with a common mechanism and a total exposure is calculated, expressed in terms of the "index compound". This approach was used by JMPR for dithiocarbamates (FAO, 1999a) and by JECFA for chlorinated dibenzo-*p*-dioxin congeners (FAO/WHO, 2002). The choice of the "index compound" is not trivial and will greatly depend on the toxicity database available and the toxicological end-point used. Data on the levels of compounds must be collected in a manner that determines the co-occurrence of residues.

3.8 Biomarkers of exposure

Biological markers or biomarkers are indicators of changes or events in biological systems. Biomarkers of exposure refer to "cellular, biochemical, analytical, or molecular measures that are obtained from biological media such as tissues, cells, or fluids and are indicative of exposure to an agent" (IPCS, 2004) or "agents or their metabolites either in tissues, secreta, excreta, expired air or any combination of these" (Berlin et al., 1984) that can be independently used to quantify overall exposure to a substance. These terms are further described by NRC (1987). Examples of biomarkers of exposure (Anwar, 1997; CDC, 2003) include the concentration of lead in blood (µg lead/dl blood) (CDC, 2004), the concentration of mercury in either blood (µg mercury/litre blood) or hair (µg mercury/g hair) (FAO/WHO, 2004), and the concentration of pesticides or their metabolites in serum, fat, urine, blood, or breast milk (Anwar, 1997).

Exposure biomarkers do not depend on estimating exposure from food consumption and chemical concentration data. They are "downstream" from consumption and hence causally closer to the health effects of interest, and they represent a more direct measure of internal exposure. Perhaps the greatest challenge associated with the use of biomarkers is interpreting their public health significance and particularly their quantitative relationship to adverse health effects. Biomarkers can be used effectively to evaluate whether a control measure has successfully altered the level of exposure in a population (Schulte, 1995) or to compare one consumer group with another non-exposed subpopulation. In contrast, it is often difficult to characterize the relationship between exposure biomarker levels and health risk.

A second challenge associated with the use of biomarkers relates to source attribution. Because biomarkers are integrative measures of exposure, they do not distinguish between alternative sources of exposure (Aitio & Kallio, 1999). For example, exposure to polycyclic aromatic hydrocarbons (PAHs) can result from smoking (or being in the vicinity of smokers), coal tar treatments, or occupational activities (e.g. road paving and work near coke ovens) (Strickland et al., 1996). Even among individuals with no apparent notable exposure to PAHs, low levels of PAH metabolites have been detected in urine (Strickland et al., 1996).

Relating changes in biomarker levels to changes in exposure is further complicated by analytical considerations (Aitio & Kallio, 1999). Of course, with measurement of the parent compound (e.g. benzene or lead in blood, mercury in hair or blood), specificity is precise. While some metabolic products are relatively specific (e.g. methylhippuric acids in the case of exposure to xylene or mandelic acid in the case of exposure to styrene or ethylbenzene) (Aitio & Kallio, 1999), in other cases specificity is limited. For example, phenol or hippuric acid concentrations in urine can be used as indicators of exposure to benzene or toluene, respectively, but these metabolites may also be generated by other parent compounds (Aitio & Kallio, 1999).

Differences in biomarker persistence pose a third challenge to their use. Although some biomarkers (e.g. bone lead concentrations) have a half-life of many years, others, such as the concentration of contaminants in blood, typically have much shorter half-lives. For example, the half-life of mercury in blood is approximately 60 days (Aitio & Kallio, 1999). In these cases, representative measurements of exposure depend on more frequent monitoring. In some extreme examples, such as urinary iodine, the half-life is on the order of

hours (Wild et al., 2001). In these cases, characterizing exposure for an individual would depend on making multiple measurements in a single day. Short of being able to do so, measurement results for a group of individuals (taken at different times of the day) might be interpreted as representing the distribution of biomarker levels for the population, even though such measurements are not adequate for the purpose of characterizing individual levels of exposure.

Finally, even if a biomarker with a long half-life is available, it is not always the case that it is the most relevant measure of exposure for the purpose of risk assessment. Aggregate exposure (the product of the average rate of exposure and time) is thought to be the most relevant measure of exposure in some cases, such as dioxin (Schulte, 1995). The assumption that toxicity depends on this aggregate measure is known as Haber's Law (Weller et al., 1999). In contrast, some acute toxicity effects may instead depend on the frequency of peak exposure levels (Lauwerys et al., 1995). In this case, levels of biomarkers with long half-lives may offer a misleading characterization of risk.

Human milk is a unique biological matrix for monitoring certain environmental contaminants, because it can provide exposure information about both the mother and the breastfed infant through a non-invasive method of collection. For some chemicals, levels in milk can provide an integrated assessment of exposure from multiple foods and multiple media. Although human milk is the natural food for infants, with the optimal composition to meet their nutritional needs in early life and providing associated immunological, psychological, and economic advantages (WHO, 2002c), it has been unintentionally compromised by chemicals from our environment. Nevertheless, the mere presence of an environmental chemical in human milk does not necessarily indicate a health risk for breastfed infants.

POPs in human milk are good examples of exposure biomarkers, since POPs are known to accumulate in the food-chain. Consequently, human milk monitoring can yield information about the kinds and quantities of POPs in the environment as well as in our bodies. Better understanding of our exposure to harmful environmental chemicals will help us to better manage them by eliminating or reducing their emissions or by limiting their presence in the food supply.

Over the past several decades, GEMS/Food, whose interest is in international studies on levels of contaminants in food, has collected information on the levels and time trends of many POPs in food, including human milk (e.g. WHO, 1989b, 1996; Van Leeuween & Malish, 2002). Results have shown a variety of contamination profiles, indicating different sources of exposure. Consistent with dietary exposure assessments submitted to GEMS/Food prior to 1992 and risk assessments of certain organochlorine compound in human milk performed in 1998, basic monitoring and assessment programmes in all countries for organochlorine compounds in food and human tissues are essential in order to appropriately protect public health from these risks.

In summary, use of exposure biomarkers offers some advantages over conventional measures of exposure expressed in terms of food consumption. Biomarkers integrate exposure over time from multiple sources. Moreover, they can be directly measured and hence do not rely on mathematical models developed using multiple uncertain assumptions to estimate exposure. They reflect internal exposure and, as such, are "closer" to adverse health effects of interest than are specific external exposure estimates. In contrast, their interpretation is complicated by the fact that linking exposure biomarkers to toxicity end-points is often difficult or impossible. In addition, because of their integrative nature, it can be difficult to attribute changes in biomarker levels to a particular exposure source, or even to a particular compound. Finally, use of biomarkers can be complicated if their half-life is

short. In these cases, multiple measurements are necessary to characterize an individual's exposure.

4. RECOMMENDATIONS

4.1 Data on chemical concentrations in food

1. For chemical concentration data to be most useful for dietary exposure estimates, it is important that, wherever possible, details be provided on data source, survey type/design, sampling, sample preparation, analytical methodology, LOD/LOQ, and quality assurance.

2. In all cases, as the chemical concentration value assigned to non-detected or non-quantified results in the data set for food chemicals may significantly influence the result of the dietary exposure assessment, the treatment of these results should be clearly stated.

4.2 Food consumption data

3. Given that the design of food consumption studies can have a critical impact on the results of any dietary exposure assessment, harmonization of study design should be achieved to the extent possible. Surveys should include drinking-water, beverage consumption, and food supplements (section 2.2.1).

4. All countries, including developing countries, should conduct FCSs on a periodic basis, preferably with individual dietary records (section 2.2.1).

5. Ideally, the food consumption values in the GEMS/Food LP database should be based on the 97.5th percentile of individual consumer days from national survey results. This database should be expanded to include data from additional countries to better represent all member countries (section 2.2.3).

6. If a FCS includes multiple days of record per participant, individual consumer days should be used when estimating upper and lower percentiles of dietary exposure from food chemicals, where multiple valid consumer days for a single survey participant should be considered as independent observations and not averaged (e.g. 97.5th percentile food consumption amounts for use in acute dietary exposure estimates) (section 2.2.3).

7. In estimating acute dietary exposures from chemical residues in a single commodity or food, it is appropriate to use food consumption data for only those people who consume the single food (consumers only). Estimations of chronic dietary exposures from chemical residues in multiple commodities or foods should be conducted for both consumers only and all respondents in the survey (total survey population) (section 2.2.3).

8. National data on 97.5th percentile levels of consumption derived from individual dietary records are collected by GEMS/Food through the Codex Alimentarius Commission. National governments should provide food consumption information to GEMS/Food with adequate documentation (section 2.2.3).

9. The 13 GEMS/Food consumption cluster diets should replace the currently used 5 regional diets as a tool for international chronic dietary assessments (section 2.2.5).

10. Food consumption and dietary exposure estimates should be expressed on the basis of individual body weights; if the latter are not available, then the appropriate default body weights should be used (60 kg for whole population, 55 kg for Asian populations) (section 2.2.6).

4.3 Estimating dietary exposure

11. Acute and chronic dietary exposure assessments undertaken for veterinary drug residues should be conducted according to a methodology used for exposure assessments for chemicals in general (e.g. food additives, pesticide residues, and contaminants) (section 3.1).

12. TDSs are useful tools for assessing mean chronic dietary exposures to chemical hazards and for identifying priorities. TDSs are not normally suitable for the assessment of acute dietary exposures because of the high degree of compositing of samples (section 3.4.3).

13. The methodology for the cumulative dietary exposure to food chemicals with a common mechanism of toxicity could be considered for use at the international level regardless of the development of probabilistic methods (section 3.7).

5. REFERENCES

Aitio, A. & Kallio, A. (1999). Exposure and effect monitoring: A critical appraisal of their practical application. *Toxicology Letters*, **108**, 137–147.

Andersen et al. 1995 [64. is it Andersen, L.F., Nes, M., Sandstad, B., Bjoerneboe, G.E., & Drevon, C. (1995). Dietary intake among Norwegian adolescents. European Journal of Clinical Nutrition, 49, 555–564.?]

Andersen et al. 1996 [65. is it Andersen, N. L., Fagt, S., Groth, M.V., Hartkopp, H.B., Moller, A., Ovesen, N.L., & Warming, D.L. (1996). Dietary intakes for the Danish population 1995. Søborg, Denmark, National Food Agency of Denmark (Publication No. 235).

Anonymous. Croatian Health Service Yearbooks.

Anonymous 1998 [67. is it Anonymous (1998). Zo eet Nederland. Resultaten von de Voedselcon-sumptie-peiling 1997–1998. The Hague, Netherlands, Voedingscentrum.?]

Anttolainen, M., Javanainen, J., Kaartinen, P., Lahti-Koski, M., Lauronen, J., Männistö, S., Ovaskainen, M., Paajanen, H., Pietinen, P., Roos, E., Valsta, L., & Virtanen, M. (1998) *The 1997 dietary survey of Finnish adults*. Helsinki, Finland, National Public Health Institute (Publication B8/1998).

Anwar, W.A. (1997). Biomarkers of human exposure to pesticides. *Environmental Health Perspectives*, **105**(Suppl. 4), 801–806.

Arcella, D., Soggiu, M.E., & Leclercq, C. (2003). Probabilistic modelling of human exposure to intense sweeteners in Italian teenagers: validation and sensitivity analysis of a probabilistic model including indicators of market share and brand loyalty. *Food Additives and Contaminants*, **20**(Suppl.), S73–86.

Australian Bureau of Statistics (2000). *Apparent consumption of foodstuffs, Australia, 1997–98 and 1998–99*. Canberra, Australia, Australian Bureau of Statistics (http://www.abs.gov.au/AUSSTATS/abs@.nsf/productsbytitle/123FCDBF086C4DAACA2568A90013939A?OpenDocument).

Baars, A.J., Bakker, M.I., Baumann, R.A., Boon, P.E., Freijer, J.I., Hoogenboom, L.A.P., Hoogerbrugge, R., van Klaveren, J.D., Liem, A.K.D., & de Vries, J. (2004). Dioxin, dioxin-like PCBs and non-dioxin-like PCBs in food stuffs: occurrence and dietary intake in the Netherlands. *Toxicology Letters*, **151**, 51–61.

Babinska, K., Bederova, A., & Bartekova, S. (1998). Dietary pattern in the adult population from selected areas of Slovac Republic. *European Journal of Epidemiology*, **52**, S59.

Barlow, S.M. (1994). The role of the Scientific Committee for Food in evaluating plastics for packaging. *Food Additives and Contaminants*, **11**, 249–259.

Becker, W. (1994). [*Dietary habits and nutrient intake in Sweden 1989*.] Uppsala, Sweden, National Food Administration (in Swedish with English summary).

Becker, W. (1999). Riksmaten 1997–1998. The Swedes eat more healthy.] Vår Föda, **51**(1), 24–27.

Béderova, A., Babinska, K., & Baretekova, S. (1998). Energy and nutrient intake in children and adolescents from eight socio-economically different regions of Slovakia. *European Journal of Epidemiology*, **52**, S59.

Berlin, A., Yodaiken, R.E., & Henman, B.A. (1984). *Assessment of toxic agents at the workplace: Roles of ambient and biological monitoring*. The Hague, Netherlands, Marinus Nijhoff.

Bhat, R.V. & Moy, G.G. (1997). Monitoring and assessment of dietary exposure to chemical contaminants. *World Health Statistics Quarterly*, **50**(1–2), 132–149.

Biro, G. (1992/93). *First Hungarian Representative Nutrition Survey 1985–1988. Results. Vols. I (1992) and II (1993)*. Budapest, Hungary, OTH, NEVI, OETI

Biro, G., Antal, M., & Zajkas, G. (1996). Nutrition survey of the Hungarian population in a randomized trial between 1992–1994. *European Journal of Clinical Nutrition*, **50**, 201.

Brunner, E., Stallone, D., Juneja, M., Bingham, S., & Marmot, M. (2001). Dietary assessment in Whitehall II: comparison of 7d diet diary and food-frequency questionnaire and validity against biomarkers. *British Journal of Nutrition*, **86**, 405–414.

Brussard, H.H., Lowik, M.R.H., Steingrimsdottir, L., Moller, A., Kearny, J., De Henauw, S., & Becker, W. (for the EFCOSUM group) (2002). A European food consumption survey method—conclusions and recommendations. *European Journal of Clinical Nutrition*, **56**(Suppl. 2), S89–S94.

Cadby, P. (1996). Estimating intakes of flavouring substances. *Food Additives and Contaminants*, **13**(4), 453–460.

Carrington, C.D. (1996). Logical probability and risk assessment. *Human and Ecological Risk Assessment*, **2**, 62–78.

Carriquiry, A.L. (2003). Estimation of usual intake distributions of nutrients and foods. *Journal of Nutrition*, **133**, 601–608.

Carriquiry, A.L., Goyeneche, J.J., Fuller, W.A., & Jensen, H.H. (1995). *Estimated correlations among days for the combined 1989–91 CSFII*. Ames, IA, USA, Iowa State University, Center for Agricultural and Rural Development, September (Staff Report 95-SR 77).

Carter, R.L., Sharaugh, C.O., & Stapell, C.A. (1981). Reliability and validity of the 24-hour recall. *Journal of the American Dietetic Association*, **79**, 542–547.

CDC (2003). *Second national report on human exposure to environmental chemicals*. Atlanta, GA, USA, United States Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Environmental Health, Division of Laboratory Sciences (NCEH Publication No. 02-0716).

CDC (2004). *A review of evidence of health effects of blood lead levels <10 µg/dL in children*. Atlanta, GA, USA, United States Department of Health and Human Services, Centers for Disease Control and Prevention, Work Group of the Advisory Committee on Childhood Lead Poisoning Prevention (http://www.cdc.gov/nceh/lead/ACCLPP/meetingMinutes/lessThan10MtgMAR04.pdf).

Clarke, D.B., Barnes, K.A., Castle, L., Rose, M., Wilson, L.A., Baxter, M.J., Price, K.R., and DuPont, M.S. (2003). Levels of phytoestrogens, inorganic trace-elements, natural toxicants and nitrate in vegetarian duplicate diets. *Food Chemistry*, **81**(2), 287–300.

Codex Alimentarius Commission (1989). *Guidelines for simple evaluation of food additive intake.* Supplement 2 to Codex Alimentarius Commission, 14, CAC/GL 3.

Codex Alimentarius Commission (2001). *Procedural manual*, 12th ed. Rome, Italy, Food and Agriculture Organization of the United Nations, Joint FAO/WHO Food Standards Programme (http://www.fao.org/DOCREP/005/Y2200E/y2200e00.htm).

Codex Alimentarius Commission (2003). *Revised guidelines on Good Laboratory Practice in residue analysis.* Rome, Italy, Food and Agriculture Organization of the United Nations, Joint FAO/WHO Food Standards Programme (http://www.codexalimentarius.net/download/standards/378/cxg_040e.pd).

Codex Alimentarius Commission (2006). *Procedural manual*, 15th ed. Rome, Italy, Food and Agriculture Organization of the United Nations, Joint FAO/WHO Food Standards Programme.

Cullen, A.C. & Frey, H.C. (1999). *Probabilistic techniques in exposure assessment*. New York, NY, USA, Plenum Press.

Dabeka, R.W., McKenzie, A.D., & Bradley, P. (2003). Survey of total mercury in total diet food composites and an estimation of the dietary intake of mercury by adults and children from two Canadian cities, 1998–2000. *Food Additives and Contaminants*, **20**(7), 629–638.

De Backer, G. (1984). Regional differences in dietary habits, coronary risk factors and mortality rates in Belgium. Design and methodology. An interuniversity study. *Acta Cardiologica*, **39**, 285–292.

Deharveng, G., Charrondiere, U.R., Slimani, N., Southgate, D.A.T., & Riboli, E. (1999). Comparison of nutrients in the food composition tables available in the nine European countries participating in EPIC. *European Journal of Clinical Nutrition*, **53**, 60–79.

Douglass, J.S., Barraj, L.M., Tennant, D.R., & Long, W.R. (1997). Evaluation of the budget method for screening food additive intakes. *Food Additives and Contaminants*, **14**, 791–802.

EFSA (2004). *Statement of the Scientific Panel on Food Additives, Flavourings, Processing Aids, and Materials in Contact with Food (AFC Panel) on estimation of intakes in the course of the safety assessment of chemically defined flavourings (expressed on 13 July 2004).* Minutes of the 7th plenary meeting of the AFC Panel held in Brussels, Belgium, on 12–13 July 2004. Parma, Italy, European Food Safety Authority (http://www.efsa.eu.int/).

Egan, S.K., Tao, S.S.H., Pennington, J.A.T., & Bolger, P.M. (2002). US Food and Drug Administration's Total Diet Study: intake of nutritional and toxic elements, 1991–1996. *Food Additives and Contaminants*, **19**(2), 103–125.

Eichholzer, M., Bisig, B., & Gutzwiller, F. (1995). *Ernährung in der Schweiz. Schweitzerische Gesundheitsbeefraging 1992/1993*. Bern, Switzerland, Bundesambt für Gesundheitswesen EDMZ.

Elmadfa, I., Godina-Zarfl, B., Dichtl, M., & König, J. (1994). The Austrian study on nutritional status of 6 to 18 years old pupils. *Biblio Nutritio et Dieta*, **51**, 62–67.

Elmadfa, I., Burger, P., Derndorfer, E., Kiefer, I., Kunze, M., König, J., Leimuller, G., Manafi, M., Mecl, M., Papathanasiou, V., Rust, P., Vojir, F., Wagner, K.-H., & Zarfl, B. (1999). *Österreichisher Ernährungsbericht 1998*. Wien, Germany, Bundesministerium für Gesundheit, Arbeit und Soziales und Bundesministerium für Frauenangelegenheiten und Verbraucherschutz (Hrsg.).

Eurachem (1999). *Guide to quantifying uncertainty in analytical measurements*, 2nd ed. (http://www.measurementuncertainty.org).

European Commission (1998). *Report on methodologies for the monitoring of food additive intake across the European Union.* Final report submitted by the Task Co-ordinator, 16 January 1998. Report of a Working Group on scientific co-operation on questions relating to food. Brussels, Belgium, European Commission Directorate General III Industry (Task 4.2; SCOOP/INT/REPORT/2).

European Commission (2002). Commission Directive 2002/72/EC of 6 August 2002 relating to plastic materials and articles intended to come into contact with foodstuffs. *Official Journal of the European Communities*, **L220**, 19–58 (http://eur-lex.europa.eu/LexUriServ/site/en/oj/2002/l_220/l_22020020815en00180058.pdf).

European Commission (2003a). *Opinion of the Scientific Committee on Food on glycyrrhizinic acid and its ammonium salt* (opinion expressed on 4 April 2003). Brussels, Belgium, European Commission, Scientific Committee on Food, 10 April (SCF/CS/ADD/EDUL/225, Final; http://europa.eu.int/comm/food/fs/sc/scf/index_en.html).

European Commission (2003b). *A practical guide for users of European directives* (updated to 15 April 2003). Brussels, Belgium, European Commission, Health & Consumer Protection Directorate-General (http://europa.eu.int/comm/food/food/chemicalsafety/foodcontact/practical_guide_en.pdf).

European Union (2004). *Monitoring of pesticide residues in products of plant origin in the European Union, Norway, Iceland and Lichtenstein, 2002 report, April 2004* (DG SANCO Report 17/04;

FAO (1999a). *Pesticide residues in food—1998*. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. Rome, Italy, Food and Agriculture Organization of the United Nations (FAO Plant Production and Protection Paper 148).

FAO (1999b). *Pesticide residues in food—1999*. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. Rome, Italy, Food and Agriculture Organization of the United Nations (FAO Plant Production and Protection Paper 153).

FAO (2001) Pesticide residues in food-2000. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Rome, Italy, Food and Agriculture Organization of the United Nations(FAO Plant Production and Protection Paper 163 http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/Download/2000_rep/cap2.pdf

FAO (2002a). Pesticide residues in food. Vol. 2, 2nd ed., 2000. *Manual on the submission and evaluation of pesticide residues data.* Rome, Italy, Food and Agriculture Organization of the United Nations (http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/JMPRguidance.htm)

FAO (2002b). *Pesticide residues in food—2002*. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. Rome, Italy, Food and Agriculture Organization of the United Nations (FAO Plant Production and Protection Paper 172).

FAO (2004a). *FAOSTAT database collections, including food balance sheets.* Rome, Italy, Food and Agriculture Organization of the United Nations (http://www.fao.org/GENDER/stats/genstats.htm).

FAO (2004b). *Pesticide residues in food—2003*. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues. Rome, Italy, Food and Agriculture Organization of the United Nations (FAO Plant Production Paper 176).

FAO (2004c). *Pesticide residues in food—2004*. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. Rome, Italy, Food and Agriculture Organization of the United Nations (FAO Plant Production Paper 178; http://www.fao.org/WAICENT/FAOINFO/AGRICULT/AGP/AGPP/Pesticid/JMPR/DOWNLOAD/2004_rep/report2004jmpr.pdf).

FAO (2005a). *Background to INFOODS.* Rome, Italy, Food and Agriculture Organization of the United Nations, Agriculture and Consumer Protection Department (http://www.fao.org/infoods/index_en.stm; accessed May 2005).

FAO (2005b). *Food nomenclature, terminology and classification systems.* Rome, Italy, Food and Agriculture Organization of the United Nations, Agriculture and Consumer Protection Department (http://www.fao.org/infoods/nomenclature_en.stm; accessed May 2005).

FAO (2005c). *Tagnames for food components.* Rome, Italy, Food and Agriculture Organization of the United Nations, Agriculture and Consumer Protection Department (http://www.fao.org/infoods/tagnames_en.stm; accessed May 2005).

FAO (2005d). *Food composition data interchange*. Rome, Italy, Food and Agriculture Organization of the United Nations, Agriculture and Consumer Protection Department (http://www.fao.org/infoods/interchange_en.stm; accessed May 2005).

FAO (2005e). *Pesticide residues in food—2005*. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. Rome,

Italy, Food and Agriculture Organization of the United Nations (FAO Plant Production Paper 183; http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/DOWNLOAD/2005_rep/report2005jmpr.pdf).

FAO/WHO (2002). *Safety evaluation of certain food additives and contaminants*. Geneva, Switzerland, World Health Organization (WHO Food Additives Series No. 48).

FAO/WHO (2003). *Guidelines for the preparation of working papers on intake of food additives for the Joint FAO/WHO Expert Committee on Food Additives*, 2nd ed. Rome, Italy, Food and Agriculture Organization of the United Nations; and Geneva, Switzerland, World Health Organization, February (1st edition, of January 2001, available at http://www.who.int/ipcs/food/jecfa/guidelines/en).

FAO/WHO (2004). *Safety evaluation of certain food additives and contaminants*. Geneva, Switzerland, World Health Organization (WHO Food Additives Series No. 52).

FAO/WHO (2006). *Evaluation of certain veterinary drug residues in food*. Sixty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives. Geneva, World Health Organization (WHO Technical Report Series No. 939).

Finch, S., Doyle, W., Lowe, C., Bates, C.J., Prentice, A., Smithers, G., & Clarke, P.C. (1998). *National Diet and Nutrition Survey: people aged 65 years and over. Vol. 1. Report of the Diet and Nutrition Survey*. London, United Kingdom, TSO.

Food Standards Agency (2002). *Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment—Risk assessment of mixtures of pesticides and similar substances.* London, United Kingdom, Food Standards Agency, September (FSA/0691/0902).

Food Standards Agency (2004). *Total Diet Study 2000 of 12 elements—aluminium, arsenic, cadmium, chromium, copper, lead, manganese, mercury, nickel, selenium, tin and zinc.* London, United Kingdom, Food Standards Agency (Food Survey Information Sheet 48/04; http://www.food.gov.uk/science/surveillance/fsis2004branch/fsis4804metals).

Frey, H.C. & Patil, S.R. (2002). Identification and review of sensitivity analysis methods. *Risk Analysis*, **22**, 553–578.

FSANZ (2001). *The 19th Australian Total Diet Survey—a total diet survey of pesticide residues and contaminants.* Food Standards Australia New Zealand (http://www.foodstandards.gov.au/newsroom/publications/19thaustraliantotaldietsurveyapril2001/19thaustraliantotaldietsurvey/).

FSANZ (2003). *The 20th Australian Total Diet Survey—a total diet survey of pesticide residues and contaminants.* Food Standards Australia New Zealand (http://www.foodstandards.gov.au/newsroom/publications/20thaustraliantotaldietsurveyjanuary2003/20thaustraliantotaldietsurveyfullreport/index.cfm).

GEMS/Food-Euro (1994). *Workshop on reliable evaluation of low-level contamination of food*. Kulmbach, Federal Republic of Germany, 3–5 March 1994 (EUR/ICP/EHAZ.94.12/WS03).

GEMS/Food-Euro (1995). *Second workshop on reliable evaluation of low-level contamination of food*. Kulmbach, Federal Republic of Germany, 26–27 March 1995 (EUR/ICP/EHAZ.94.12/WS04; http://www.who.int/foodsafety/publications/chem/lowlevel_may1995/en/).

Green, T.J., Allen, O.B., & O'Connor, D.L. (1998). A three-day weighed food record and a semiquantitative food-frequency questionnaire are valid measures for assessing the folate and vitamin B-12 intakes of women aged 16 to 19 years. *Journal of Nutrition*, **128**, 1665–1671.

Gregory, J., Foster, K., Tyler, H., & Wiseman, M. (1990). *The Dietary and Nutritional Survey of British Adults.* London, United Kingdom, HMSO.

Gregory, J.R., Collins, D.L., Davies, P.S.W., Hughes, J.M., & Clarke, P.C. (1995). *National Diet and Nutrition Survey: children aged 1 ½ to 4 ½ years. Vol. 1. Report of the Diet and Nutrition Survey.* London, United Kingdom, HMSO.

Gregory, J.R., Lowe, S., Bates, C.J., Prentice, A., Jackson, L.V., Smithers, G., Wenlock, R., & Farron, M. (2000). *National Diet and Nutrition Survey: young people aged 4 to 18 years. Vol. 1. Report of the Diet and Nutrition Survey.* London, United Kingdom, TSO (summary available at http://www.statistics.gov.uk/ssd/surveys/national_diet_nutrition_survey_children.asp).

Gulson, B.L., Mizon, K.J., Korsch, M.J., Mahaffey, K.R., & Taylor, A.J. (2001). Dietary intakes of selected elements from longitudinal 6-day duplicate diets for pregnant and nonpregnant subjects and elemental concentrations of breast milk and infant formula. *Environmental Research*, **87**(3), 160–174.

Hacking, I. (1976). *The emergence of probability.* Cambridge, United Kingdom, Cambridge University Press.

Hamilton, D. & Crossley, S., eds. (2004). *Pesticide residues in food and drinking water: Human exposure and risks*. John Wiley & Sons (Wiley Series in Agrochemicals and Plant Protection).

Hamilton, D.J., Ambrus, A., Dieterle, R., Felsot, A., Harris, C., Petersen, B., Racke, K., Wong, S., Gonzalez, R., Tanaka, K., Earl, M., Roberts, G., & Bhula, R. (2004). Pesticide residues in food—acute dietary exposure. *Pest Management Science*, **60**, 311–339.

Hansen, S.C. (1979). Conditions for use of food additives based on a budget method for an acceptable daily intake. *Journal of Food Protection*, **42**, 429–434.

Haraldsdóttir, J. et al. (1986). *Danskernes Kostvaner 1. Hovedresultater*. Soborg, Denmark, Levnedsmiddelstryrelsen.

Harris, C.A. (2000). How the variability issue was uncovered ; the history of the UK residue variability findings. *Food Additives and Contaminants*, **17**, 491–495.

Health Council of the Netherlands (2004). *Pesticides in food: assessing the risk to children*. The Hague, Netherlands, Health Council of the Netherlands (No. 2004/11E).

Helsel, D.R. (1990). Less than obvious—statistical treatment of data below the detection limit. *Environmental Science and Technology*, **24**(12), 1766–1774.

Henderson, L., Irving, K., Gregory, J., et al. (2003). *The National Diet & Nutrition Survey: adults aged 19 to 64 years. Vol. 3. Vitamin and mineral intake and urinary analytes.* London, United Kingdom, HMSO. Hercberg, S., Preziosi, P., Galan, P., Devanlay, M., Keller, H., Bourgeois, C., Potier de Courcy, G., & Cherouvrier, F. (1994). Vitamin status of a healthy French population: dietary intakes and biochemical markers. *International Journal for Vitamin and Nutrition Research*, **364**, 220–233.

Hermann-Kunz, E. & Thamm, M. (1999). Dietary recommendations and prevailing food and nutrient intakes in Germany. *British Journal of Nutrition*, **8**, S61–S69.

Heseker, H., Adolf, T., Eberhardt, W., Hartmann, S., Herwig, A., Kübler, W., Matiaske, B., Moch, K.J., Schneider, R., & Zipp, A. (1992). *Lebensmittel- und Nährstoffaufnahme Erwachsener in der Bunderrepublik Deutschland. VERA-Schriftenreihe*. Niederkleen, Germany, Wissenschaftlicher Fachverlag Dr Fleck.

IEFS (1998). *The effect of survey duration on the estimation of food chemical intakes*. Institute of European Food Studies (Food Additive Intake Series Report No. 3).

International Accreditation New Zealand (2004). *Uncertainty of measurement, precision and limits of detection in chemical and microbiological testing laboratories.* Auckland, New Zealand, International Accreditation New Zealand (Technical Guide AS TG5; http://www.ianz.govt.nz/publications2/pdfs/AS_TG5_uncert_of_measure.pdf).

IPCS (2000). *Human exposure assessment*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 214; http://www.inchem.org/pages/ehc.html).

IPCS (2004). *IPCS risk assessment terminology*. Geneva, Switzerland, World Health Organization, International Programme on Chemical Safety (Harmonization Project Document No. 1; http://www.who.int/ipcs/methods/harmonization/areas/ipcsterminologyparts1and2.pdf).

Irish Universities Nutrition Alliance (2001). North/South Ireladn food consumption survery .(http://www.safefoodonline.com/Uploads/North%20South%20Ireland%20Food%20Consumption%20Survey.pdf)

Johansson, L., Solvoll, K., Bjorneboe, G.-E.A., & Drevon, C.A. (1997). Dietary habits among Norwegian men and women. *Scandinavian Journal of Nutrition*, **4**, 63–70.

Johansson, L. & Sovoll, K. (1999). [*National dietary survey among men and women 16–79 years of age*.] Oslo, Norway, National Council on Nutrition and Physical Activity (Report 3/1999) (in Norwegian).

Kadziauskiene, K., Bartkeviciute, R., Olechnovic, M., Viseckiene, V., Abaravicius, A., Stukas, R., & Robertson, A. (1999). *Health behaviour and nutritional status of Lithuanian population, 1997–1998.* Vilnius, Lithuania, Ministry of Health, National Nutrition Centre, Medical Faculty of Vilnius University.

Karvetti, R.L. & Knuts, L.R. (1985). Validity of the 24-hour recall. *Journal of the American Dietetic Association*, **85**, 1437–1442.

Keith, L.H., Crummett, W., Deegan, J., Jr, Libby, R.A., Taylor, J.K., & Wentler, G. (1983). Principles of environmental analysis. *Analytical Chemistry*, **55**, 2210–2218.

Kleemola, P., Virtanen, M., & Pietinen, P. (1994). *The 1992 dietary survey of Finnish adults*. Helsinki, Finland, National Public Health Institute (Publication B2/1994).

Klensin, J.C. (1992). *INFOODS: food composition data interchange handbook.* Tokyo, Japan, United Nations University Press (http://www.unu.edu/unupress/unupbooks/80774e/80774E00.htm).

Klensin, J.C., Feskanich, D., Lin, V. Truswell, A.S., & Southgate, D.A.T. (1989). *Identification of food components for INFOODS data interchange*. Tokyo, Japan, United Nations University (http://www.unu.edu/unupress/unupbooks/80734e/80734E00.htm).

Kroes, R., Müller, D., Lambe, J., Löwik, M.R.H., van Klaveren, J., Kleiner, J., Massey, R., Mayer, S., Urieta, I., Verger, P., & Visconti, A. (2002). Assessment of intake from the diet. *Food and Chemical Toxicology*, **40**(2–3), 327–385.

Kroke, A., Klipstein-Grobusch, K., Voss, S., Möseneder, J., Thielecke, F., Noack, R., & Boeing, H. (1999). Validation of a self-administered food-frequency questionnaire administered in the European Prospective Investigation into Cancer and Nutrition (EPIC) Study: comparison of energy, protein, and macronutrient intakes estimated with the doubly labeled water, urinary nitrogen, and repeated 24-h dietary recall methods. *American Journal of Clinical Nutrition*, **70**, 439–447.

Lambe, J. & Kearney, J. (1999). The influence of survey duration on estimates of food intakes—relevance for food-based dietary guidelines. *British Journal of Nutrition*, **81**(Suppl. 2), S139–S142.

Lauwerys, R.R., Bernard, A., Roels, H., & Buchet, J.P. (1995). Health risk assessment of long-term exposure to non-genotoxic chemicals: Application of biological indices. *Toxicology Letters*, **77**(1–3), 39–44.

Leblanc, J.-C., Malmauret, L., Guérin, T., Bordet, R., Boursier, B., & Verger, P. (2000). Estimation of the dietary intakes of pesticides residues, lead, cadmium, arsenic and radionuclides in France. *Food Additives and Contaminants*, **17**, 925–932.

Leblanc, J.C., Tard, A., Volatier, J.L., & Verger, P. (2005). Estimated dietary exposure to the principal food mycotoxins from the 1st French Total Diet Study. *Food Additives and Contaminants*, **22**(7), 652–672.

Lee, P. & Cummingham, K. (1990). *The Irish National Nutrition Survey (INNS)*. Dublin, Ireland, Irish Nutrition and Dietetic Institute.

Löwik, M.R.H., Hulshof, K.F.A.M., van der Heijden, L.J.M., Brussaard, J.H., Burema, J., Kistemaker, C., & deVries, P.J.F. (1998). Changes in the diet in the Netherlands: 1987–88 to 1992. *International Journal of Food Sciences and Nutrition*, **49**, S1–S64.

Madden, J.P., Goodman, S.J., & Guthrie, H.A. (1976). Validity of the 24-hr recall. Analysis of data obtained from elderly subjects. *Journal of the American Dietetic Association*, **68**, 143–147.

MAFF (1999). *Report of the international conference on pesticide residues variability and acute dietary risk assessment, 1–3 December 1998, York, United Kingdom*. London, United Kingdom, Ministry of Agriculture, Fisheries and Food, Pesticides Safety Directorate.

MAFF (2000). *Duplicate diet study of vegetarians—dietary exposures to 12 metals and other elements*. London, United Kingdom, Ministry of Agriculture, Fisheries and Food, Food Standards Agency, January (Joint Food Standards Group Food Surveillance Information Sheet No. 193; (http://archive.food.gov.uk/maff/archive/food/infsheet/2000/no193/193vege.htm).

Mensink, G.B.M., Thamm, M., & Haas, K. (1999). Die Ernährung in Deutschland (1998). *Gesundheitswesen*, **61**, S201–S206.

Murakami, T., Narita, N., Nakagaki, H., Shibata, T., & Robinson, C. (2003). Fluoride intake in Japanese children aged 3–5 years by the duplicate-diet technique. *Fluoride*, **36**(1), 49.

NAS (1986). *Nutrient adequacy: Assessment using food consumption surveys*. National Academy of Sciences, Subcommittee on Criteria for Dietary Evaluation. Washington, DC, National Academy Press.

New Zealand Ministry of Health (1999). *NZ food: NZ people. Key results of the 1997 National Nutrition Survey.* Wellington, New Zealand, New Zealand Ministry of Health, August (http://www.moh.govt.nz/moh.nsf/49b6bf07a4b7346dcc256fb300005a51/8f1dbeb1e0e1c70c4c2567d80009b770?OpenDocument).

New Zealand Ministry of Health (2003). *NZ food, NZ children. Findings of the 2002 National Children's Nutrition Survey.* Wellington, New Zealand, New Zealand Ministry of Health, November (http://www.moh.govt.nz/moh.nsf/49b6bf07a4b7346dcc256fb300005a51/064234a7283a0478cc256dd60000ab4c?OpenDocument).

NRC (1987). Biological markers in environmental health research. National Research Council, Committee on Biological Markers. *Environmental Health Perspectives*, **74**, 3–9.

NRC (1993). *Pesticides in the diets of infants and children*. National Research Council, Committee on Pesticides in the Diets of Infants and Children. Washington, DC, National Academy Press.

Nusser, S.M., Carriquiry, A.L., Dodd, K.W., & Fuller, W.A. (1996). A semiparametric approach to estimating usual intake distributions. *Journal of the American Statistical Association*, **91**, 1440–1449.

Petersen, B.J., Chaisson, C.F., & Douglass, J.S. (1994). Use of food-intake surveys to estimate exposures to nonnutrients. *American Journal of Clinical Nutrition*, **59**(Suppl.), 240S–243S.

Putnam, J.J. & Allshouse, J.E. (1999). *Food consumption, prices, and expenditures, 1970–97*. Washington, DC, United States Department of Agriculture, Economic Research Service, Food and Rural Economics Division (Statistical Bulletin No. 965).

Raper, N., Perloff, B., Ingwersen, I., Steinfeldt, L., & Anand, J. (2004). An overview of USDA's dietary intake data system. *Journal of Food Composition and Analysis*, **17**, 545–555.

Renwick, A.G., Barlow, S.M., Hertz-Picciotto, I., Boobis, A.R., Dybing, E., Edler, L., Eisenbrand, G., Greig, J.B., Kleiner, J., Lambe, J., Muller, D.J.G., Smith, M.R., Tritscher, A., Tuijtelaars, S., van den Brandt, P.A., Walker, R., & Kroes, R. (2003). Risk characterisation of chemicals in food and diet. *Food and Chemical Toxicology*, **41**, 1211–1271.

Rescher, N. (1993). Probability logic: A non-truth-functional system. In: *Many-valued logic*, 2nd ed. Aldershot, United Kingdom, Gregg Revivals, pp. 184–187.

Rigaud, D., Giachetti, I., Cassuro, D.A., Deheeger, M., Borys, J.M., Lemoina, A., & Volatier, J.L. (1997). Enquête nationale de consommation alimentaire. ASPCC/DGALL: étude des apports en énergie et en macronutriment de la population française auprès de 1500 personnes 2 sexes agées de 2 à 85 ans. 1. Energie et macronutriments. *Cahiers de Nutrition et de Dietetique*, **32**, 379–389.

Rimm, E.B., Giovannucci, E.L., Stampfer, M.J., Colditz, G.A., Litin, L.B., & Willett, W.C. (1992). Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. *American Journal of Epidemiology*, **135**, 1114–1126.

Schaefer, E.J., Augustin, J.L., Schaefer, M.M., Rasmussen, H., Ordovas, J.M., Dallal, G.E., & Dwyer, J.T. (2000). Lack of efficacy of a food-frequency questionnaire in assessing dietary macronutrient intakes in subjects consuming diets of known composition. *American Journal of Clinical Nutrition*, **71**, 746–751.

Schulte, P.A. (1995). Opportunities for the development and use of biomarkers. *Toxicology Letters*, **77**(1–3), 25–29.

Schutz, D., Moy, G.G., & Käferstein, F.K. (1998). *GEMS/Food International Dietary Survey: infant exposure to certain organochlorine contaminants from breast milk—a risk assessment.* Geneva, World Health Organization (Document WHO/FSF/FOS/98.4).

Slimani, N., Deharveng, G., Charrondiere, R.U., van Kappel, A.L., Ocke, M.C., Welch, A., Lagiou, A., van Liere, M., Agudo, A., Pala, V., Brandstetter, B., Andren, C., Stripp, C., van Staveren, W.A., & Riboli, E. (1999). Structure of the standardized computerized 24-h diet recall interview used as reference method in the 22 centers participating in the EPIC project. European Prospective Investigation into Cancer and Nutrition. *Computer Methods and Programs in Biomedicine*, **58**(3), 251–266.

Slimani, N., Ferrari, P., Ocke, M., Welch, A., Boeing, H., van Liere, M., Pala, V., Amiano, P., Lagiou, A., Mattison, I., Stripp, C., Engeset, D., Charrondiere, U.R., Buzzard, M., van Staveren, W., & Riboli, E. (2000). Standardization of the 24-hour diet recall calibration method used in the European Prospective Investigation into Cancer and Nutrition (EPIC): General concept and preliminary results. *European Journal of Clinical Nutrition*, **54**, 900–917.

Slob, W. (1993). Modeling long-term exposure of the whole population to chemicals in food. *Risk Analysis*, **13**, 525–530.

Slob, W. (1994). Uncertainty analysis in multiplicative models. *Risk Analysis*, **14**, 571–576.

Slob, W. (1996). A comparison of two statistical approaches to estimate long-term exposure distributions from short-term measurements. *Risk Analysis*, **16**, 195–200.

Steingrimsdottir, L. (1993). Nutrition in Iceland. *Scandinavian Journal of Nutrition*, **37**, 10–112.

Strickland, P., Kang, D., & Sithisarankul, P. (1996). Polycyclic aromatic hydrocarbon metabolites in urine as biomarkers of exposure and effect. *Environmental Health Perspectives*, **104**(Suppl. 5), 927–932.

Szponar, L. & Rydilik, E. (1996a). Nutrition mode and nutritional status of boys and men in Poland. *Zymienie Cztonieko i Metaboliszm (Polish Journal of Human Nutrition and Metabolism)*, **23**(Suppl. 2), 3–37.

Szponar, L. & Rydilik, E. (1996b). Nutrition mode and nutritional status of girls and women in Poland. *Zymienie Cztonieko i Metaboliszm (Polish Journal of Human Nutrition and Metabolism)*, **23**(Suppl. 2), 38–70.

Thompson, F.E., Kipnis, V., Subar, A.F., Krebs-Smith, S.M., Kahle, L.L., Midthune, D., Potischman, N., & Schatzkin, A. (2000). Evaluation of 2 brief instruments and a food frequency questionnaire to estimate daily number of servings of fruit and vegetables. *American Journal of Clinical Nutrition*, **71**, 1503–1510.

Tran, N.L., Barraj, L.M., Smith, K., Javier, A., & Burke, T.A. (2004). Combining food frequency and survey data to quantify long-term dietary exposure; a methyl mercury case study. *Risk Analysis*, **24**(1), 19–30.

Tsuda, T., Inoue, T., Kojima, M., & Aoki, S. (1995). Market basket and duplicate portion estimation of dietary intakes of cadmium, mercury, arsenic, copper, manganese, and zinc by Japanese adults. *Journal of AOAC International*, **78**(6), 1363–1368.

Turrini, A., Leclercq, C., & D'Amicis, A. (1999). Patterns of food and nutrient intakes in Italy and their application to the development of food-based dietary guidelines. *British Journal of Nutrition*, **81**(Suppl. 2), 83–89.

UNEP (1992). *The contamination of food*. Nairobi, Kenya, United Nations Environment Programme (UNEP/GEMS Environmental Library No. 5).

UNEP/FAO/WHO (1988). *Assessment of chemical contaminants in food*. Report on the results of the UNEP/FAO/WHO programme on health-related environmental monitoring (prepared in cooperation with the UNEP Monitoring and Research Centre, London), Geneva, Switzerland, World Health Organization.

USDA (2000). *1994–96, 1998 Continuing Survey of Food Intakes by Individuals (CSFII) and the Diet and Health Knowledge Survey (DHKS)* [CD-ROM]. Washington, DC, United States Department of Agriculture; Springfield, VA, USA, National Technical Information Service (NTIS Accession No. PB2000-500027).

USDA (2004). *Pesticide Data Program annual summary calendar year 2002*. Washington, DC, United States Department of Agriculture (http://www.ams.usda.gov/science/pdp/Summary2002.pdf).

USEPA (1996). *Residue chemistry test guidelines*. Washington, DC, United States Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances (OPPTS 860.1520 Processed Food/Feed; EPA 712-C-96-184).

USEPA (2000). *Assigning values to non-detected/non-quantified pesticide residues in human health food exposure assessments.* Washington, DC, USA, United States Environmental Protection Agency, Office of Pesticide Programs, 23 March 2000 (Item 6047; http://www.epa.gov/fedrgstr/EPA-PEST/2000/March/Day-31/6047.pdf).

USFDA (2004a). *Total Diet Study*. Rockville, MD, USA, United States Department of Health and Human Services, Food and Drug Administration, Center for Food Safety and Applied Nutrition (http://vm.cfsan.fda.gov/~comm/tds-toc.html).

USFDA (2004b). *Pesticide Program residue monitoring 2002*. Rockville, MD, USA, United States Department of Health and Human Services, Food and Drug Administration, Center for Food Safety and Applied Nutrition (http://vm.cfsan.fda.gov/~dms/pes02rep.html).

Van Leeuween, F.X.R. & Malish, R. (2002). Results of the third round of WHO-coordinated exposure study on the levels of PCBs, PCDDs and PCDFs in human milk. *Organohalogen Compounds*, **56**, 311–316.

Vannoort, R.W. (2003). *2003/04 New Zealand Total Diet Survey analytical results—1st quarter*. Wellington, New Zealand, New Zealand Food Safety Authority, 20 November (http://www.nzfsa.govt.nz/science-technology/research-projects/total-diet-survey/index.htm).

Vannoort, R.W. (2004a). *2003/04 New Zealand Total Diet Survey analytical results—2nd quarter*. Wellington, New Zealand, New Zealand Food Safety Authority, 20 April (http://www.nzfsa.govt.nz/science-technology/research-projects/total-diet-survey/index.htm).

Vannoort, R.W. (2004b). *2003/04 New Zealand Total Diet Survey analytical results—3rd quarter.* Wellington, New Zealand, New Zealand Food Safety Authority, 8 July (http://www.nzfsa.govt.nz/science-technology/research-projects/total-diet-survey/index.htm).

Vannoort, R.W. (2004c). *2003/04 New Zealand Total Diet Survey analytical results—4th quarter.* Wellington, New Zealand, New Zealand Food Safety Authority, November (http://www.nzfsa.govt.nz/science-technology/research-projects/total-diet-survey/index.htm).

Vannoort, R.W., Cressey, P.J., & Silvers, K. (2000). *1997/98 New Zealand Total Diet Survey, Part Two: Elements*. Wellington, New Zealand, New Zealand Food Safety Authority (http://www.moh.govt.nz/moh.nsf/49ba80c00757b8804c256673001d47d0/a48868055568b2814c2568b100823cef?OpenDocument).

Verger, P., Ireland, J., Moller, A., Abravicius, J.A., de Henauw, S., & Naska, A. (for the EFCOSUM Group) (2002). Improvement of comparability of dietary intake assessment using currently available individual food consumption surveys. *European Journal of Clinical Nutrition*, **S2**, S18–24.

Volatier, J.L. (2000). *Enquête INCA individuelle et nationale sur les consommations alimentaires*. London, United Kingdom, Technique & Documentation.

Weller, E., Long, N., Smith, A., Williams, P., Ravi, S., Gill, J., Henessey, R., Skornik, W., Brain, J., Kimmel, C., Kimmel, G., Holmes, L., & Ryan, L. (1999). Dose-rate effects of ethylene oxide exposure on developmental toxicity. *Toxicological Sciences*, **50**, 259–270.

WHO (1979). *Guidelines for establishing or strengthening national food contamination monitoring programmes*. Prepared under the joint sponsorship of the United Nations Environment Programme, the Food and Agriculture Organization of the United Nations, and the World Health Organization. Geneva, Switzerland, World Health Organization (Document WHO/HCS/FCM/78.1).

WHO (1985). *Guidelines for the study of dietary intakes of chemical contaminants*. Geneva, Switzerland, World Health Organization (WHO Offset Publication No. 87).

WHO (1989a). *Guidelines for predicting dietary intake of pesticide residues*. Geneva, Switzerland, World Health Organization, Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme in collaboration with the Codex Committee on Pesticide Residues.

WHO (1989b). *Levels of PCBs, PCDDs, and PCDFs in breast milk.* Copenhagen, Denmark, World Health Organization Regional Office for Europe (Environmental Health Series No. 34).

WHO (1992). *Assessment of dietary intake of chemical contaminants*. Geneva, Switzerland, World Health Organization, Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme (WHO/HPP/FOS/92.6).

WHO (1995a). *Application of risk analysis to food standard issues*. Report of a FAO/WHO consultation, Geneva, Switzerland, 13–17 March 1995. Geneva, Switzerland, World Health Organization (WHO/FNU/FOS/95.3).

WHO (1995b). *Guidelines for predicting dietary intake of pesticide residues*. Report of a Joint FAO/WHO Consultation, York, United Kingdom, 2–6 May 1995. Geneva, Switzerland, World Health Organization, Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme (Document WHO/FNU/FOS/95.11).

WHO (1996). *Levels of polychlorinated dibenzo*-p-*dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) in human milk: Second round of WHO-coordinated exposure study*. Copenhagen, Denmark, World Health Organization Regional Office for Europe (Environmental Health Series No. 3).

WHO (1997a). *Food consumption and exposure assessment of chemicals*. Report of a FAO/WHO consultation, Geneva, Switzerland, 10–14 February 1997. Geneva, Switzerland, World Health Organization (WHO/FSF/FOS/97.5).

WHO (1997b). *Guidelines for predicting dietary intake of pesticides residues (revised)*. Geneva, Switzerland, World Health Organization, Programme of Food Safety and Food Aid, Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme in collaboration with the Codex Committee on Pesticide Residues (http://www.who.int/foodsafety/publications/chem/en/pesticide_en.pdf).

WHO (1998). *GEMS/Food regional diets. Regional per capita consumption of raw and semi-processed agricultural commodities.* Geneva, Switzerland, World Health Organization (WHO/FSF/FOS/98.3; http://www.who.int/foodsafety/chem/en/).

WHO (2000). *Methodology for exposure assessment of contaminants and toxins in food.* Report of a Joint FAO/WHO workshop, World Health Organization, Geneva, Switzerland, 7–8 June 2000. Geneva, World Health Organization (WHO/SDE/PHE/FOS/00.5; http://www.who.int/foodsafety/publications/chem/en/).

WHO (2002a). *GEMS/Food total diet studies*. Report of the 2nd international workshop on total diet studies, Brisbane, Australia, 4–15 February 2002. Geneva, Switzerland, World Health Organization (http://www.who.int/foodsafety/chem/en/).

WHO (2002b). *Latin American total diet study workshop, 8–13 July 2002, Buenos Aires, Argentina*. Geneva, Switzerland, Pan American Health Organization, World Health Organization, and Pan American Institute for Food Protection and Zoonoses (INPPAZ) (http://www.who.int/foodsafety/chem/en/).

WHO (2002c). *The optimal duration of exclusive breastfeeding. Report of an expert consultation.* Geneva, Switzerland, World Health Organization (WHO/NHD/01.09).

WHO (2003). *GEMS/Food regional diets: Regional per capita consumption of raw and semi-processed agricultural commodities*, rev. ed. Geneva, Switzerland, World Health Organization, Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme (http://www.who.int/foodsafety/chem/gems/en/index1.html).

WHO (2004a). *Highest reported 97.5th percentile consumption figures (eaters only) for various commodities by the general population and children ages 6 and under, January 2004*. Geneva, Switzerland, World Health Organization, Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme.

WHO (2004b). *Guidelines for drinking-water quality*, 3rd ed. Geneva, World Health Organization (http://www.who.int/water_sanitation_health/dwq/en).

WHO (2005a). *GEMS/Food total diet studies.* Report of the 3rd international workshop on total diet studies, Paris, France, 14–21 May 2004. Geneva, Switzerland, World Health Organization (http://www.who.int/foodsafety/chem/en/).

WHO (2005b). *GEMS/Food instructions for electronic submission of data on chemical contaminants in food.* Geneva, Switzerland, World Health Organization (http://www.who.int/foodsafety/publications/chem/gems_instructions/en/).

Wild, C.P., Andersson, C., O'Brien, N.M., Wilson, L., & Woods, J.A. (2001). A critical evaluation of the application of biomarkers in epidemiological studies on diet and health. *British Journal of Nutrition*, **86**(Suppl. 1), S37–S53.

Wilhelm, M., Wittsiepe, J., Schrey, P., Budde, U., & Idel, H. (2002). Dietary intake of cadmium by children and adults from Germany using duplicate portion sampling. *Science of the Total Environment*, **285**, 11–19.

Winter, C.K. & Francis, F.J. (1997). Assessing, managing and communicating chemical food risk. *Food Technology*, **51**(5), 85.

Ysart, G., Miller, P., Crews, H., Robb, P., Baxter, M., De L'Argy, C., Lofthouse, S., Sargent, C., & Harrison, N. (1999). Dietary exposure estimates of 30 elements from the UK Total Diet Study. *Food Additives and Contaminants*, **16**(9), 391–403.

ANNEX 1: GLOSSARY

Acute reference dose (ARfD)
The estimate of the amount of a substance in food or drinking-water, expressed on a body weight basis, that can be ingested in a period of 24 h or less, without appreciable health risk to the consumer on the basis of all the known facts at the time of the evaluation. It is expressed in milligrams of the chemical per kilogram of body weight. (WHO, 1997a)

Exposure, acute
A contact between an agent and a target occurring over a short time, generally less than a day. Other terms, such as "short-term exposure" and "single dose", are also used. (IPCS, 2004)

Exposure, chronic
A continuous or intermittent long-term contact between an agent and a target. Other terms, such as "long-term exposure", are also used. (IPCS, 2004)

Highest residue (HR)
The highest residue level (expressed as milligrams per kilogram) in a composite sample of edible portion of a food commodity when a pesticide has been used according to maximum GAP conditions. The HR is estimated as the highest of the residue values (one from each trial) from supervised trials, conducted according to maximum GAP conditions, and includes residue components defined by JMPR for estimation of dietary intake. When the HR is corrected using processing factors, it is referred to as highest residue level with processing (HR-P). (FAO, 1999b)

International estimated daily intake (IEDI)
A prediction of the long-term daily intake of a pesticide residue on the basis of the assumptions of average daily food consumption per person and median residues from supervised trials (STMR), allowing for residues in the edible portion of a commodity and including residue components defined by JMPR for estimation of dietary intake. Changes in residue levels resulting from preparation, cooking, or commercial processing are included. When information is available, exposure to residues from other sources should be included. The IEDI is expressed in milligrams of residue per person per day. (WHO, 1997a)

International estimate of short-term intake (IESTI)
A prediction of the short-term intake of a pesticide residue on the basis of the assumptions of high daily food consumption per person and highest residues from supervised trials, allowing for residues in the edible portion of a commodity and including residue components defined by JMPR for estimation of dietary intake. The IESTI is expressed in milligrams of residue per kilogram body weight. (FAO, 2004c)

Maximum residue limit (MRL) (for pesticides and veterinary drugs)
A Codex MRL for pesticide residues is the maximum concentration of a pesticide residue (expressed as milligrams per kilogram) recommended by the Codex Alimentarius Commission to be legally permitted in or on food commodities and animal feed. MRLs are based on GAP data, and foods derived from commodities that comply with the respective MRLs are intended to be toxicologically acceptable. Consideration of the various dietary residue intake estimates and determinations at both national and international levels in

comparison with the ADI should confirm that foods complying with Codex MRLs are safe for human consumption.

A Codex MRL for veterinary drug residues for animal-derived foods is the maximum concentration of veterinary drug residue (usually expressed in milligrams per kilogram) recommended by the Codex Alimentarius Commission to be legally permitted in or on such food. (WHO, 1997a)

National estimate of short-term intake (NESTI)

A prediction of the short-term intake of a pesticide residue carried out at the national level on the basis of the assumptions of high daily food consumption per person and highest residues from supervised trials, allowing for residues in the edible portion of a commodity and including residue components defined for estimation of dietary intake. The NESTI is expressed in milligrams of residue per kilogram body weight. (WHO, 1997a)

Processing factor

The residue level in the processed commodity divided by the residue level in the initial commodity. (WHO, 1997a)

Provisional tolerable daily intake (PTDI)

The reference value, established by JECFA, used to indicate the safe level of intake of a contaminant. The PTDI is calculated on a daily basis for contaminants that do not accumulate in the human body, such as arsenic. The PTDI is a primary health standard that applies to total exposure (i.e. both food and non-food sources). The contribution from non-food exposure therefore has to be taken into account when comparing food sources with the PTDI. The tolerable intake is also generally referred to as "provisional", since there is often a paucity of data on the consequences of human exposure at low levels, and new data may result in a change to the tolerable level. (WHO, 1997a)

Provisional tolerable weekly intake (PTWI)

The reference value, established by JECFA, used to indicate the safe level of intake of a contaminant. The PTWI is calculated on a weekly basis for contaminants that may accumulate in the human body over time, in order to minimize the significance of daily variations in intake. This value generally applies to contaminants such as lead, cadmium, and mercury. The PTWI is a primary health standard that applies to total exposure (i.e. both food and non-food sources). The contribution from non-food exposure therefore has to be taken into account when comparing food sources with the PTWI. The tolerable intake is generally referred to as "provisional", since data on the consequences of human exposure at low levels are often insufficient, and new data may result in a change to the tolerable level. (WHO, 1997a)

Supervised trials

Scientific studies in which pesticides are applied to crops or animals according to specified conditions intended to reflect commercial practice, after which harvested crops or tissues of slaughtered animals are analysed for pesticide residues. Usually specified conditions are those that approximate existing or proposed GAP. (WHO, 1997a)

Supervised trials median residue (STMR)

The expected residue level in the food commodity (expressed in milligrams of residue per kilogram of commodity) when a pesticide has been used according to maximum GAP conditions. The STMR is estimated as the median of the residue values (one from each trial)

from supervised trials conducted according to maximum GAP conditions and includes residue components defined by JMPR for estimation of dietary intake. For some commodities, such as banana, STMR levels may be determined directly from levels measured in the edible portion when data are available. (WHO, 1997a)

Supervised trials median residue in processed commodity (STMR-P)

The expected residue level in the food commodity (expressed in milligrams of residue per kilogram of commodity) when a pesticide has been used according to maximum GAP conditions and the commodity is processed according to the main GAP practice used to prepare the food prior to consumption. (WHO, 1997a)

Theoretical maximum daily intake (TMDI)

A prediction of the maximum daily intake of a pesticide residue, assuming that residues are present at the MRLs and that average daily consumption of foods per person is represented by regional diets. The TMDI is calculated for the various GEMS/Food consumption cluster diet in milligrams of residue per person and is expressed as a percentage of the ADI. (WHO, 1997a)

Theoretical added maximum daily intake(TAMDI)

The TAMDI model diet was designed to provide a conservative estimate of potential exposure to a specific flavouring substance on the basis of proposed or allowed maximum (upper use) levels (UULs) in the different categories of foods and beverages that could be flavoured. The resulting exposure estimate is that of a hypothetical consumer who consumes every day one standard portion of food/beverage from each of these categories, and those foods/beverages always contain the specific flavouring at its specified UUL. The TAMDI is calculated by summing the exposures estimated for each individual food/beverage category to estimate total daily intake.

Uncertainty

Imperfect knowledge concerning the present or future state of an organism, system, or (sub)population under consideration. (IPCS, 2004)

ANNEX 2: LIST OF ACRONYMS AND ABBREVIATIONS

ADI	acceptable daily intake
AI	adequate intake
ARfD	acute reference dose
CCCF	Codex Committee on Contaminants in Foods
CCFA	Codex Committee on Food Additives
CCFAC	Codex Committee on Food Additives and Contaminants
CCPR	Codex Committee on Pesticide Residues
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Foods
CSFII	Continuing Survey of Food Intakes by Individuals
EAR	estimated average requirement
EDI	estimated daily intake
EFCOSUM	European Food Consumption Survey Method
EU	European Union
EuroFIR	European Food Information Resource Network
FAO	Food and Agriculture Organization of the United Nations
FAOSTAT	FAO statistical database
FBS	food balance sheet
FCS	food consumption survey
FFQ	food frequency questionnaire
GAP	good agricultural practice
GEMS/Food	Global Environment Monitoring System Food Contamination Monitoring and Assessment Programme
HR	highest residue level from trial
HR-P	highest residue level from trial in processed commodity
IEDI	international estimated daily intake
IESTI	international estimate of short-term intake
INFOODS	International Network of Food Data Systems
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LOD	limit of detection
LOQ	limit of quantification
LP	large portion
ML	maximum level
MRL	maximum residue limit
MRL-P	maximum residue limit in processed commodity
ND	not detected
NESTI	national estimate of short-term intake
NHANES	National Health and Nutrition Examination Survey (USA)
NQ	not quantified
NRC	National Research Council (USA)
OPAL	Operating Program for Analytical Laboratories
PAH	polycyclic aromatic hydrocarbon
POP	persistent organic pollutant
PTDI	provisional tolerable daily intake
PTWI	provisional tolerable weekly limit
RDI	recommended daily intake
SIGHT	Summary Information on Global Health Trends
SML	specific migration limit

STMR	supervised trials median residue
STMR-P	supervised trials median residue in processed commodity
TAMDI	theoretical added maximum daily intake
TDI	tolerable daily intake
TDS	total diet study
TEF	toxicity equivalence factor
TMDI	theoretical maximum daily intake
USDA	United States Department of Agriculture
UUL	upper use level
USA	United States of America
USEPA	United States Environmental Protection Agency
WHO	World Health Organization

ANNEX 3: LIST OF PARTICIPANTS

International Expert Workshop on Exposure Assessment, 2–6 May 2005, Annapolis, MD, USA

Dr Arpad Ambrus, Food Safety Program, Central Service for Plant Protection and Soil Conservation, Budapest, Hungary

Ms Janis Baines, Food Standards Australia New Zealand, Barton, Australia *(Rapporteur)*

Dr Leila Barraj, Exponent, Washington, DC, USA

Dr P. Michael Bolger, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA

Dr Eloisa Caldas, University of Brasilia, Brasilia, Brazil

Dr Clark Carrington, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA

Dr Joshua Cohen, Harvard Center for Risk Analysis, Boston, MA, USA

Dr Michael DiNovi, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA

Ms S. Kathleen Egan, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA *(Rapporteur)*

Dr Stephen R. Funk, United States Environmental Protection Agency, Washington, DC, USA

Dr Jean-Charles Leblanc, Department for the Evaluation of Nutritional and Health Risks, French Food Safety Agency (AFSSA), Maisons Alfort, France

Dr Catherine LeClerq, National Institute for Food and Nutrition Research (INRAN), Rome, Italy

Mr David J. Miller, United States Environmental Protection Agency, Washington, DC, USA

Dr Bernadette C. Ossendorp, Centre for Substances and Integrated Risk Assessment, National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands

Dr Barbara Petersen, Exponent, Washington, DC, USA *(Chair)*

Dr Janet C. Rühl, DuPont Crop Protection, Newark, NJ, USA

Dr Richard W. Vannoort, Christchurch Science Centre, Christchurch, New Zealand

Dr Philippe Verger, National Institute for Agricultural Research (INRA), Paris, France

Secretariat

World Health Organization: **Dr Sam Page**

Food and Agriculture Organization of the United Nations: **Dr Ruth Charrondiere**, **Dr Amelia Tejada**

ANNEX 4: ACUTE DIETARY EXPOSURE ASSESSMENT ESTIMATES CURRENTLY USED BY JMPR

As described in section 3.6.2, the methodology for calculating the acute dietary exposure to pesticide residues was initially developed by several international meetings (WHO, 1997a; FAO, 1999a). Subsequently, the methodology was refined by JMPR (FAO, 2002b, 2004b, 2004c). The calculated exposure is called the international or national estimate of short-term intake (IESTI or NESTI). In this methodology, the estimates are performed for each crop individually, as it is unlikely that an individual will consume, within a meal or 24 h, a large portion of more than one food containing the highest residue level (the one that incorporates the variability factor).

Current equations

Calculations of the acute dietary exposure recognize four different cases: 1, 2a, 2b, and 3. Case 1 is the simple case where the residue in a composite sample reflects the residue level in a meal-sized portion of the commodity. Case 2 is the situation where the meal-sized portion as a single fruit or vegetable unit might have a higher residue level than the composite. Case 2 is further divided into case 2a and case 2b, where the unit size is less than or greater than the large portion size, respectively. Case 3 allows for the likely bulking and blending of processed commodities such as flour, vegetable oils, and fruit juices.

The following definitions apply to all equations:

LP	Highest large portion provided (97.5th percentile of eaters), in kg food/day
HR	Highest residue level in composite sample of edible portion found in the supervised trials used for estimating the maximum residue level, mg/kg
HR-P	Highest residue level in a processed commodity, mg/kg, calculated by multiplying the highest residue level in the raw commodity by the processing factor
bw	Mean body weight, kg, provided by the country from which the LP was reported
U	Unit weight of the edible portion, kg, median[1] value provided by the country where the trials that gave the highest residue level were carried out
v	Variability factor, the factor applied to the composite residue to estimate the residue level in a high-residue unit; defined as the residue level in the 97.5th percentile unit divided by the mean residue level for the lot
STMR	Supervised trials median residue, mg/kg
STMR-P	Supervised trials median residue in processed commodity, mg/kg
P	Processing factor, the ratio of the residue level found in the processed commodity to the residue level in the raw commodity before processing.

It should be noted that the LP should be matched to the Codex commodity to which the HR or STMR relates. In the case of commodities that are predominantly eaten as the fresh fruit or vegetable, the LP should relate to the raw agricultural commodity. However, when major portions of the commodity are eaten in a processed way (e.g. grains), and when information on the residue in the processed commodity is available, the LP should relate to the processed commodity (e.g. flour or bread).

[1] Although it was decided at the International Conference on Pesticide Residues Variability and Acute Dietary Risk Assessment in York in 1998 (MAFF, 1999) that the median unit weight should be used in the IESTI equation, this value is not always available. Countries frequently use other values, such as the mean or an approximate value. JMPR uses the values that were submitted by Codex Member States to WHO GEMS/Food, assuming these values represent median unit weights.

Case 1

The residue in a composite sample (raw or processed) reflects the residue level in a meal-sized portion of the commodity (unit weight is below 0.025 kg). Case 1 also applies to meat, liver, kidney, edible offal, and eggs, and for grains, oil seed, and pulse commodities when the estimates are based on post-harvest use of the pesticide.

$$\text{IESTI} = \frac{\text{LP} \times (\text{HR or HR-P})}{\text{bw}}$$

Case 2

The meal-sized portion, such as a single fruit or vegetable unit, might have a higher residue level than the composite (whole fruit or vegetable unit weight is above 0.025 kg).

Case 2a

Unit edible weight of raw commodity is less than LP weight.

$$\text{IESTI} = \frac{\text{U} \times (\text{HR or HR-P}) \times v + (\text{LP-U}) \times (\text{HR or HR-P})}{\text{bw}}$$

The Case 2a formula is based on the assumption that the first unit contains residues at the [HR × *v*] level and the next ones contain residues at the HR level, which represents the residue in the composite from the same lot as the first one.

Case 2b

Unit edible weight of raw commodity exceeds LP weight.

$$\text{IESTI} = \frac{\text{LP} \times (\text{HR or HR-P}) \times v}{\text{bw}}$$

The Case 2b formula is based on the assumption that there is only one consumed unit and it contains residues at the [HR × *v*] level.

Case 3

Case 3 is for those processed commodities where bulking or blending means that the STMR-P represents the likely highest residue level. Case 3 also applies to milk and to grains, oil seeds, and pulses for which the estimates were based on pre-harvest use of the pesticide.

$$\text{IESTI} = \frac{\text{LP} \times \text{STMR-P}}{\text{bw}}$$

History of IESTI equations: changes since 1997

The changes introduced in the IESTI equations since their introduction in 1997 are described below.

Case 1: MRL was replaced by HR

As was already suggested by the previous FAO/WHO consultation (WHO, 1997a) and confirmed by the York consultation (MAFF, 1999) and the ad hoc expert meeting (FAO, 1999a), in case 1, the MRL-P (MRL in processed commodity) was replaced with the HR (or HR-P) (FAO, 1999b). The main reasons for this change are the following: MRLs may be significantly higher than the highest composite residue level in the residue trials, because of the

JMPR practice of using a geometric progression when recommending MRLs. This may lead to the IESTI not being sufficiently discriminatory to be used as a screening technique. Also, it was considered to be undesirable to round off values at an intermediate stage in the calculation.

Another advantage of using the HR instead of the MRL is the fact that this gives the opportunity to take into account the total toxicologically relevant residue. To enforce MRLs, as many pesticide residues as possible are measured in one single analytical run ("multi-residue methods"). Therefore, the residue definition (indicating the residue of concern) describing the MRL should be as simple as possible. In practice, the residue definition used for enforcement often equals the mother compound, which serves as an "indicator molecule" but does not necessarily encompass the total residue level, since a significant part of the compound may degrade or metabolize following application. In contrast, for dietary intake calculations, one is interested in the exposure to the total amount of toxicologically relevant residue. Therefore, if necessary, a separate residue definition for dietary risk assessment is defined in which metabolites or degradation products are also included. The HR relates to this residue definition.

Case 2a: STMR-P in the second part of the equation was replaced by HR or HR-P

In cases where a large portion consumed contains more than one individual unit (case 2a equation), it was initially assumed that the units comprising a portion may be derived from different lots. In that case, the first unit would contain residues at the level of HR × ν, and the subsequent ones would contain residues at the STMR level, which is the median value of residues in different lots. JMPR agreed at its 2000 meeting (FAO, 2001) that this assumption might not reflect the actual situation, in which the supply available for consumption is likely to be derived from a single lot. Therefore, the meeting decided to replace the STMR-P in the second part of the IESTI equation by the HR or HR-P.

Case 3: MRL was replaced by STMR or STMR-P

As was suggested by the York consultation (MAFF, 1999), a case 3 was introduced to account for the likely bulking and blending of processed commodities and milk. In these cases, the STMR (or STMR-P) is used in the calculation instead of the MRL (FAO, 1999b, FAO, 2001).

Variability factor

The concept of the variability factor ν was introduced to take into account the different concentrations of residues in the individual units of which a composite sample is composed. The definition of the variability factor changed from "the ratio of a highest level of residue in the individual commodity unit to the corresponding residue level seen in the composite sample" to "the 97.5th percentile of the residues presented in crop units divided by the mean residue of the lot residue population" (MAFF, 1999). The default variability factors of 5 and 10 were replaced by a common default factor of 3 (FAO, 2004b).

The decision to use a variability factor ν of 3 for all commodities was reached by JMPR (FAO, 2004b) after discussing a paper (Hamilton et al., 2004) in which available data for a number of pesticides over a range of crops showed an average variability factor of 2.7 (range 1.5–7.2) for supervised trials involving approximately 8000 unit analyses. The paper describes a method to derive the 97.5th percentile of the residue concentration distribution with 95% confidence from the data sets available. This value was then used to calculate the variability factor. The data presented showed that the best estimate of the variability factor is 3. In 2005, JMPR reconfirmed that owing to the inevitable random nature of the variability factor derived from the combined uncertainty associated with sampling and analysis, the best

estimate of the default variability factor is the mean of the variability factors derived from samples of various crops (FAO, 2005e).

ISBN 978 92 4 159747 0