

Guidance of the Scientific Committee on a request from EFSA related to Uncertainties in Dietary Exposure Assessment

Request No EFSA-Q-2004-019

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SUMMARY

The Scientific Committee has been asked by the European Food Safety Authority (EFSA) to advise on harmonisation of risk assessment methodologies in the fields falling within its mission. This opinion addresses the issue of scientific uncertainties in dietary exposure assessment. Every dietary exposure assessment is affected by scientific uncertainties and it is important for assessors to characterise the extent of uncertainty, so that it can be taken into account by risk managers.

Many exposure assessments follow standard screening procedures that are intended to produce conservative estimates of exposure. These screening assessments do not require an analysis of uncertainty on every occasion, provided that they include appropriate conservative assumptions and default values to take account of uncertainty. The Scientific Committee recommends that each Panel considers reviewing whether this requirement is satisfied by the assumptions and default values used in screening assessments in its area of work.

If screening assessments indicate exceedance (or in the case of nutrients, failure to attain) health-based guidance values, then more refined assessments may be needed. Some evaluation of uncertainty is required in all refined assessments. The Scientific Committee recommends that dietary exposure assessments should start with a systematic examination of potential sources and types of uncertainty, to maximise the likelihood that important uncertainties are recognised. The use of tables is suggested to help with this task.

The Scientific Committee recommends a tiered approach to analysing uncertainties. Each uncertainty in an assessment may be analysed at one of three tiers: qualitative, deterministic or probabilistic. Bearing in mind that it is not practical to treat all uncertainties quantitatively, initially, all significant uncertainties may be analysed qualitatively. This may be sufficient, if the outcome is clear enough for risk managers to reach a decision. Otherwise, those uncertainties that appear critical to the outcome may be analysed deterministically or probabilistically.

Communicating uncertainty to other scientists, risk managers and wider audiences is a key challenge. A tabular format is proposed to facilitate qualitative evaluation and communication of uncertainties. Treating the most significant uncertainties at higher tiers progressively refines the characterisation of uncertainty, and provides an increasingly clear picture of the likelihood of exceeding (or in the case of nutrients, failure to attain) a health-based guidance value.

It is important to communicate the strengths of the exposure assessment (what is known) as well as the uncertainties, and also to discuss the uncertainty affecting exposure compared to

that affecting other parts of the overall risk assessment (e.g. toxicity). The aim should be to provide a balanced picture of what is known and what is uncertain, and avoid giving an exaggerated impression of either certainty or uncertainty.

Sources and types of uncertainty affecting areas of dietary exposure assessment in the work of EFSA are reviewed in Annex 2. They illustrate the relevance of the approaches discussed in this opinion and provide a starting point for use in assessments by EFSA Panels.

It would be premature to give prescriptive guidance on which specific approaches to use for dealing with uncertainty in dietary exposure assessment until more experience is gained with their use in this field. The Scientific Committee therefore recommends that EFSA Panels identify which approaches appear promising for their particular needs and context, and review the usefulness and application to their work. The Scientific Committee strongly encourages the Panels to incorporate the systematic evaluation of uncertainties in their risk assessments and to communicate this clearly in their opinions.

KEY WORDS

Uncertainty, dietary exposure, exposure assessment, qualitative risk assessment, deterministic risk assessment, probabilistic risk assessment

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BACKGROUND

The European Food Safety Authority (EFSA) shall, according to the legislation (Article 23 of Regulation (EC) No 178/2002), “(a) provide the Community institutions and the Member States with the best possible scientific opinions in all cases provided for by Community legislation and on any question within its mission”, and “(b) promote and coordinate the development of uniform risk assessment methodologies in the fields falling within its mission”. In Article 3 of this regulation risk assessment is defined as “a scientifically based process consisting of four steps: hazard identification, hazard characterization, exposure assessment and risk characterization”.

The Scientific Committee of EFSA realised at an early stage the need for harmonisation of the work on exposure in the Scientific Panels and received a mandate¹ from EFSA to advise on this. Consequently, the Scientific Committee adopted an opinion in June 2005 (EFSA, 2005d), providing advice on how to improve the procedure and the way exposure assessments are performed within EFSA and referring to a number of internationally accepted guidelines. In addition, the Scientific Committee identified a need for more guidance for dealing with uncertainty in exposure assessment. Therefore, with the help of its Working Group for Exposure Assessment, the Scientific Committee prepared this second opinion, proposing an approach for the improvement and harmonisation of the treatment of uncertainty in dietary exposure assessments performed within EFSA.

TERMS OF REFERENCE

The Scientific Committee is asked by EFSA to advise on how to improve the harmonisation of methods used for the assessment of dietary exposure.

ASSESSMENT

1. INTRODUCTION

The requirement for increased transparency in risk assessment of food and feed has highlighted the issue of scientific uncertainty. Publications from the European Commission (European Commission, 2000, p 3.) and the former Scientific Steering Committee (European Commission, 2003a, pp. 17-19 and 87-88) have emphasised the need for risk assessors to characterise uncertainties and communicate them to risk managers. The Director-General of SANCO has said “Even though it is not a subject that lends itself easily to quantification, I would urge you to take account of the risk manager’s need to understand the level of uncertainty in your advice and to work towards a systematic approach to this problem” (Madelin, 2004). Furthermore, it is necessary to characterise scientific uncertainty so that risk managers can determine when to take appropriate measures.

¹ See Annex 1 of http://www.efsa.europa.eu/en/science/sc_committee/sc_documents/620.html

The consideration and expression of uncertainty is given particular attention in the Working Principles for Risk Analysis recently adopted by the Codex Alimentarius Commission: “Constraints, uncertainties and assumptions having an impact on the risk assessment should be explicitly considered at each step in the risk assessment and documented in a transparent manner. Expression of uncertainty or variability in risk estimates may be qualitative or quantitative, but should be quantified to the extent that is scientifically achievable. Responsibility for resolving the impact of uncertainty on the risk management decision lies with the risk manager, not the risk assessors” (Codex, 2003, p.45).

In practice, scientists have usually been mindful of the uncertainties in risk assessment and frequently include some discussion of uncertainties in risk assessment reports. However, only a small proportion of risk assessment reports have considered and expressed uncertainties in the systematic way implied by the above quotations, and very few have attempted to quantify uncertainty.

It is important to distinguish uncertainty from variability. Variability refers to variation that exists in the real world, e.g. individual variation in food consumption, or varying concentrations of contaminants in different food items. Uncertainty is often reducible through research, whereas variability is not. Research can reduce our uncertainty about a variable assessment input (e.g. provide more precise estimates of its mean and variance) but not actually reduce its variability.

This opinion has been produced with the aim of improving and harmonising the treatment of uncertainty in dietary exposure assessment. The opinion reviews the types of uncertainties that may affect dietary exposure assessment. It suggests some approaches to identifying and characterising uncertainties, which could be easily implemented. In addition, it outlines some more sophisticated approaches, and refers the reader to other sources for more detailed guidance on these.

2. SOURCES AND TYPES OF UNCERTAINTY IN DIETARY EXPOSURE ASSESSMENT

In dietary exposure assessment, uncertainty results from limitations in scientific knowledge, including the factors that determine exposure, and data availability. Examples include inaccuracies in 24-hour recall data on food consumption, and analytical measurement errors in data on the levels of chemicals in food.

The term “**sources of uncertainty**” refers to components of exposure assessment that can contribute to overall uncertainty in the output. There are five main sources: the assessment objectives, the exposure scenario(s), the exposure model, the model inputs, and the performance of the assessment².

The term “**type of uncertainty**” refers to the nature of the uncertainty. Different types of uncertainty that may affect exposure assessment include ambiguity (due to vagueness or imprecise description), measurement uncertainty, sampling uncertainty (due to limited sample sizes), default value uncertainty, extrapolation uncertainty, uncertainty about model structure, uncertainty about correlations or dependencies between inputs, differences in expert opinion, excluded factors, and ignorance (the possibility that unknown factors may influence exposure).

² This classification of sources of uncertainty is similar to the “locations” of uncertainty in Walker et al. (2003).

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

Each source of uncertainty can contribute more than one type of uncertainty, as shown in the first two columns of Table 1. To illustrate this, the third column of Table 1 contains some examples from an assessment of dietary exposure to ochratoxin A (OTA).

For the source model inputs, the main types of uncertainty need to be considered repeatedly for each input to the assessment, as illustrated in Table 2 (again for the example of OTA).

Annex 2 provides an overview of uncertainties arising in other areas of dietary exposure assessment that are relevant to EFSA Panels.

Table 1. Major sources and types of uncertainty in dietary exposure assessment, together with examples relating to an assessment of Ochratoxin A (EFSA, 2006)

Source of uncertainty	Types of uncertainty	Examples for an assessment of Ochratoxin A (OTA)
Assessment objectives	Ambiguity/imprecise description	Should be minimised by careful specification of objectives or terms of reference, in consultation with risk managers.
Exposure scenario	Ambiguity/imprecise description	Should be minimised by careful definition.
	Extrapolation	Extrapolation from 3 countries to other EU Member States.
	Excluded factors	Possible effects of regional variation in OTA levels on exposure for consumers of local produce. Consumption of children not considered.
	Expert disagreement	Experts might disagree on what factors should be included in scenario.
Exposure model	Ambiguity/imprecise description	Should be minimised by careful description.
	Model structure	Use of broad categories, combining foods with different contamination levels (e.g. grape and orange juice). Model assumes maximum of 2 foods are taken at 97.5 th percentile.
	Extrapolation	(e.g. use of a model outside the conditions it was developed for)
	Excluded factors	Possible effects of regional variation in OTA levels on exposure for local consumers. Foods with low consumption (e.g. dried fruit) or concentrations (e.g. poultry) are ignored.
	Expert disagreement	Experts might disagree on model structure.
Model inputs	<i>See Table 2 for more types</i>	
Performance of assessment	Non-conformance of assessment with objectives and scenario	Should be reduced by good practice and quality assurance (e.g. checking and peer review).
	Errors in data entry, calculations & programming	
	Errors in reporting results	

Table 2. Example of a tabular approach for systematic identification of uncertainties affecting the model inputs to exposure assessment. The example relates to an assessment of ochratoxin A exposure (EFSA, 2006)

Model input	Data	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/imprecise description
Concentration of OTA in food	SCOOP and JECFA reports	Any information on this? Limits of Detection? Treatment of Non-Detects?	Large samples, but details of sample selection not reported Weather conditions?	-	Extrapolation between foods (e.g. cocoa and chocolate to all confectionary)	Used mean concentrations (no distribution assumed)	Consumption of locally-produced food with high OTA levels?	Limited information on sampling methods and sources
Consumption	EFSA concise database: mean and 97.5 th percentile consumption for France, Italy and Sweden	Under-reporting of consumption. Reporting food in wrong categories.	Large surveys, representative of national adult populations	Values are based on broad categories, combining foods with different contamination levels (e.g. grape and orange juice). Model assumes 2 foods taken at 97.5 th percentile.	Extrapolation to other EU countries. Extrapolation from 7d surveys to long term consumption.	97.5 th percentiles estimated empirically from large samples (no distribution assumed).	Consumption of locally-produced food with high OTA levels?	Broad food categories and imprecisely identified food types
Conversion of solid coffee to liquid	Assumed dilution factor of 18	n.a. ³	n.a.	Uncertain how this relates to the true distribution of dilution factors.	n.a.	n.a.	n.a.	n.a.
Body weight	Default value of 60kg	n.a.	n.a.	Majority of EU adults are heavier than default value. Children are much lighter.	n.a.	n.a.	n.a.	n.a.

³ n.a. = not applicable

3. SCREENING ASSESSMENTS

The majority of dietary exposure assessments are screening procedures that are done in a standard way as a first step in the exposure assessment process. Typically screening assessments include the use of conservative assumptions and default values that have been established for a particular class of problems, scenarios or legislation (e.g. pesticides, additives). In the present context, conservative assumptions and default values describe assumptions, scenarios, models or exposure assessments that intentionally err on the side of over-estimation of exposure. Examples of conservative assumptions and default values currently used in the various legislative categories of food chemicals are given in Annex 2. They are intended to provide an appropriate level of protection for consumers, with an acceptable degree of certainty. Screening assessments that account for uncertainty in this way do not require an explicit analysis of uncertainty each time they are performed, provided that the process that established the conservative assumptions and default values included a systematic uncertainty analysis.

Many of the conservative assumptions and default values that are currently used in screening assessments were established some time ago, when there was less focus on the explicit or quantitative treatment of uncertainty. In some cases, they were originally based on subjective or arbitrary estimates, which are themselves uncertain. Therefore, the Scientific Committee recommends that every Panel considers reviewing the appropriateness of the conservative assumptions and default values that are used in screening assessments in its area of work. If this were to result in proposals for changing current procedures, there would need to be discussion between risk assessors and risk managers.

Conservative assumptions and default values have the important advantages of being quick and easy to use, and removing the need for detailed consideration of uncertainty at the screening stage. In addition, they may be harmonised within the EU and internationally.

If screening assessments indicate exceedance of health-based guidance values, then more refined assessments may be needed, as discussed below.

4. REFINED ASSESSMENTS

When an exposure assessment goes beyond standard scenarios, conservative assumptions and procedures, or uses non-standard input data, it is described as a refined assessment. The purpose of the assessment often changes, from ensuring a general level of protection (in a screening assessment) to providing a more realistic estimate of exposure, for example, for a specific population or scenario. The focus of uncertainty analysis therefore changes from ensuring a general level of certainty in a screening assessment to evaluating the uncertainty associated with a specific, refined assessment.

4.1. Identification of uncertainties in refined assessments

In cases where a refined assessment is required, the essential first step is to identify the potential sources and types of uncertainty so that they can be considered. The Scientific Committee recommends a systematic approach, examining each part of the assessment, to maximise the likelihood that significant uncertainties that might influence the assessment outcome are identified.

The task of systematically considering uncertainties in an assessment may be facilitated by using tabular formats, like Tables 1 and 2. This can be done reasonably easily; for example, producing Tables 1-3 for ochratoxin A took one person a couple of hours.

It is advisable to start this systematic process at the very beginning of the exposure assessment, to check for and correct uncertainties arising in the specification of the assessment objectives and exposure scenario. However, when communicating with risk managers and stakeholders, it may be better to focus on the subset of uncertainties that have most influence on the assessment outcome (see Table 3, below).

4.2. Tiered approach for uncertainty analysis

Uncertainty analysis does not itself require additional data; instead, it characterises the uncertainty associated with the existing data. It helps to identify data gaps, but this does not necessarily mean that extra data must be provided.

It is not practical or necessary to conduct an equally detailed analysis of uncertainties in every exposure assessment. On the contrary, the amount of effort and detail should be proportionate to the needs. The Scientific Committee therefore recommends a tiered approach to uncertainty analysis.

The tiered approach may begin by treating all uncertainties qualitatively (Tier1); this may be sufficient, if the outcome is clear enough for risk managers' purposes. Otherwise, those uncertainties which appear critical to the outcome may be analysed quantitatively; at first this can be done deterministically (Tier 2) and then, if necessary and feasible, probabilistically (Tier 3).

The benefits of progressing from lower to higher tiers of uncertainty analysis are illustrated for a hypothetical example in Figure 1. Higher tiers of uncertainty analysis lead to better understanding and characterisation of uncertainty; this may show that the uncertainty is less than was assumed at lower tiers, but it may also be greater. Higher tiers progressively refine the characterisation of uncertainty, and enable the assessor to give the risk manager a more realistic estimate of the likelihood of a health-based guidance value being exceeded, or in the case of nutrients, not being attained.

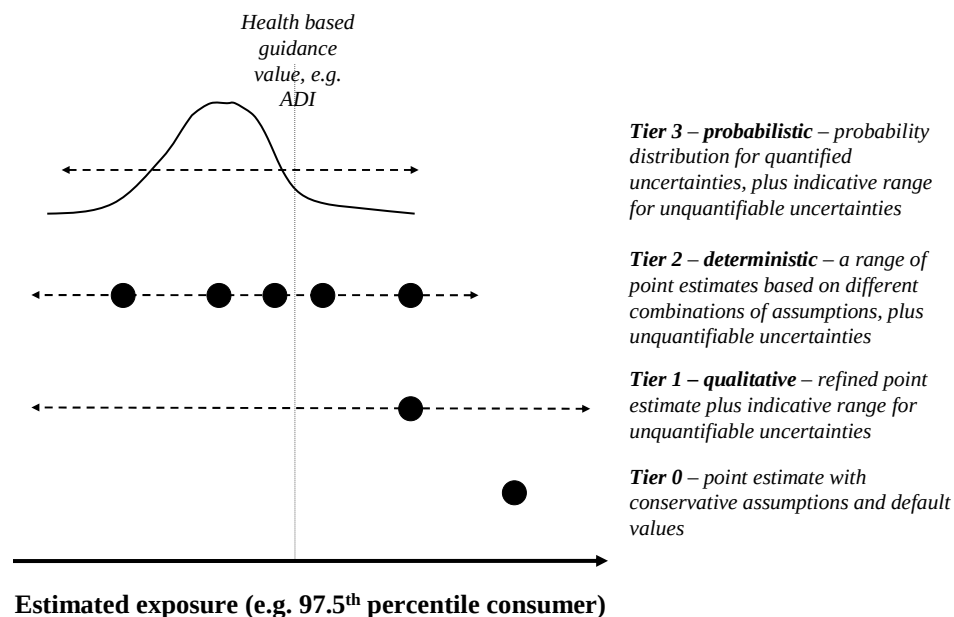


Figure 1. Graphical illustration of the benefits of progressing from lower to higher tiers of uncertainty analysis. The solid circles represent point estimates of exposure. The dotted lines represent the indicative range of exposure.

4.2.1. Qualitative analysis of uncertainties (Tier 1)

Having listed or described the uncertainties affecting a dietary exposure assessment, it is important to bear in mind that what the risk manager really needs to know is the combined effect of the uncertainties on the assessment outcome. Therefore it is desirable, even in a qualitative assessment, to give some indication of:

- the direction and magnitude of each individual uncertainty;
- the combined effect of all the uncertainties considered.

“Direction” refers to any directional influence of an uncertainty on the assessment outcome. For example, if the assessment uses a conservative assumption for a particular input, then the distribution of possible true values falls predominantly below the assumed value and will tend to make the outcome of the exposure assessment more likely (but not certain) to over-estimate true exposure.

The most obvious way to evaluate the “magnitude” of uncertainty of a parameter is to express it relative to a central estimate, e.g. measurement uncertainty is often expressed as “ $\pm 5\%$ ”. This is useful when the measure itself is the primary interest. However, when considering uncertainties in an exposure assessment, the primary interest is in how much they contribute to uncertainty in the resulting estimate of exposure. This is because it is the uncertainty of the final estimate that matters to the risk manager.

Therefore the magnitude of each uncertainty should be assessed based on its contribution to the assessment outcome. This can be done using a qualitative scale, e.g. low, medium and high, however it is essential to define whatever scale is used. A potentially useful way of defining a qualitative scale is as follows:

- The magnitude of the contribution of each uncertainty could be expressed relative to the margin between the estimated dietary exposure and the health-based guidance value. For example, an uncertainty that by itself causes the exposure estimate to rise above the health-based guidance value could be classified as “high”, and the magnitudes of other uncertainties could be expressed relative to that.

An example of this approach is shown in Table 3. This summarises an analysis of the uncertainties that were considered most important in the assessment of Ochratoxin A (EFSA, 2006). In Table 3, the analysis of direction and magnitude have been combined into a single measure using plus and minus signs^{4,5}. Plus signs for an uncertainty indicate that it could have caused small (+), medium (++) or large (+++) over-estimation of exposure, minus signs that it could have caused small (-), medium (- -) or large (- - -) under-estimation of the exposure. Some uncertainties are evaluated as potentially causing either over- or under-estimation (e.g. ++/- -).

Consideration should then be given to estimating the combined effect of the uncertainties on the assessment outcome, as has been done in the bottom row of Table 3. It is emphasised that this was not obtained by any mathematical combination of the individual uncertainties. Instead, the overall uncertainty was evaluated by considering subjectively the magnitudes and directions of the individual uncertainties. In doing this, the assessor should try to take account of any correlations or dependencies that might exist between different uncertainties.

One advantage of the approach illustrated in Table 3 is that it provides a concise summary of the most important uncertainties and the relative magnitude of their influence on the assessment output (a qualitative sensitivity analysis). This could then be used to target data collection or further analysis at Tier 2, if needed. It also provides a basis for some qualitative statements about the overall uncertainty, such as in the example in Table 3, where the estimate of exposure of adults is probably conservative, but the exposure of children may be underestimated.

Using an approach of the type illustrated in Table 3, makes explicit the judgements that have been made and has the important advantage of recording the basis for the conclusions and opening them to wider scrutiny and peer review.

⁴ Some assessors may prefer to separate the representation of direction and magnitude (e.g. EFSA, 2005a).

⁵ Some assessors may prefer to give only a textual evaluation of the combined uncertainties (e.g. EFSA, 2006b)

Table 3. Qualitative evaluation of influence of uncertainties on an assessment of ochratoxin A exposure for high consumers of foods contaminated with this substance (EFSA, 2006)

Source of uncertainty	Direction & magnitude *
Moderate under reporting of consumption is known to occur	- -
Misreporting: some subjects will have reported the food that they ate in a wrong food category	+/-
Use of broad food categories causes over-estimation of exposure (e.g. assuming all juice is contaminated at same level as grape juice, all hot drinks at same level as coffee)	+++
Extrapolation from food consumption during 7-day survey over-estimates long term consumption for high consumers	+++
Extrapolation of food consumption from France, Italy and Sweden to the other 22 EU Member States of the EU	++/- -
The possibility of large regional and temporal differences in OTA levels may lead to under-estimation of exposure for consumers eating locally-produced food	- -
Default body weight of 60 kg over-estimates average exposure for European adults	++
Exclusion of some foods with low contamination (e.g. poultry meat) or consumption (e.g. dried fruit) will cause slight under-estimation of exposure	-
Factor of 18 used to convert from solid coffee to liquid	?
Conservative assumption that individual consumers consume 2 broad food categories at 97.5 th percentile	+ ?
Exposure of children likely to be under-estimated due to smaller body weight and higher consumption of juices and cereals	- - -?
Qualitative evaluation of overall effect of identified uncertainties: estimates for high consumers are likely to over-estimate adult exposure by a moderate amount, but might be under-estimates for regional populations consuming locally-produced food and are probably under-estimates for children.	++ adults +/- local populations - - children

* Key to direction and magnitude:

+, ++, +++ = uncertainty likely to cause small, medium or large over-estimation of exposure;

-, - -, - - - = uncertainty likely to cause small, medium or large under-estimation of exposure.

4.2.2. Deterministic analysis of uncertainties (Tier 2)

When a qualitative assessment indicates a sufficient likelihood that the combined uncertainties could give rise to concern, then it may be useful to examine them quantitatively. This can be done deterministically, by calculating different point estimates to explore the range of possible values for uncertain inputs in the assessment (e.g. best case, worst case), and calculating their effect on the assessment outcome. A similar approach can be used for uncertainties concerning the exposure scenario or the exposure model, as opposed to its

inputs. The aim is to evaluate whether the uncertainties might be large enough to alter the assessment outcome and change the risk management decision; i.e. a form of sensitivity analysis.

Choosing the values to be used for deterministic calculations can be difficult.

- Often there are definite lower and upper bounds for the possible values (e.g. concentrations in a beverage must lie between zero and the saturation point). However, these are often much wider than the range of values which is really plausible, leading to extremely unrealistic exposure estimates.
- If measurements are available, it must be remembered that they will usually represent a mixture of true variability, sampling uncertainty and measurement uncertainty, and that the minimum and maximum recorded values will generally underestimate the true range of possible values because the true minimum and maximum are very unlikely to be observed in a limited sample.
- Often, data will be lacking, limited, poor in quality, or only indirectly relevant (e.g. measured for a different population or in different conditions). In these cases it may still be possible to identify a plausible range of values, based on the available data, expert judgement and common sense.

It is important for the assessor to try a range of input values and report the resulting range of exposure estimates to the risk manager, together with an evaluation of their relative plausibilities. This allows risk managers to base their decisions on the exposure estimate that provides the level of certainty which they judge to be appropriate⁶.

If ranges of values are being considered for several different assessment inputs, repeated calculations can be used to show the effect of each uncertainty on its own. In addition, it is essential to consider the potential combined effects of the different uncertainties. However, combining multiple conservative assumptions can quickly lead to a scenario that is extremely conservative, or even beyond the bounds of possibility. It is therefore important to consider which combinations are reasonably plausible. The most objective approach would be to use probabilistic methods (Tier 3) to estimate the probabilities of different combinations. At Tier 2, the plausibility of different combinations of input values can be assessed subjectively, taking account of any relevant data or evidence, expert judgement and common sense. Again, the subjective nature of this assessment makes it essential to report the rationale for the evaluation of plausibility in detail, so that others can review and evaluate the judgements that have been made.

As well as exploring the effects of alternative input values, deterministic calculations can be also used to examine the effects of various types of uncertainty that may arise concerning the assessment scenario or exposure model (see Table 1). Alternative scenarios or models can be explored by carrying out parallel calculations and comparing the results. In addition, it would be desirable to evaluate the relative plausibility of the different scenarios or models, in order to inform risk managers on the relative likelihood of the exposure estimates they produce.

As well as exploring the range of possible exposures, deterministic sensitivity analysis can be used to identify which input uncertainties contribute most to uncertainty in the exposure

⁶ "Responsibility for resolving the impact of uncertainty on the risk management decision lies with the risk manager, not the risk assessors." (Codex, 2003).

estimate⁷. This information can be very useful to assessors and risk managers, because consideration can then be given to analysing the key uncertainties probabilistically (Tier 3), or collecting appropriate data to reduce them.

Since it is never practical to quantify all uncertainties, it will always be necessary to consider Tier 2 results together with Tier 1 qualitative analysis of the uncertainties that remain unquantified. If this suggests that some unquantified uncertainties may be more important than those already quantified, then it may be desirable to expand the Tier 2 analysis to include them.

4.2.3. Probabilistic evaluation of uncertainties (Tier 3)

If analysis at Tiers 1 and 2 suggests that the combined uncertainty is such that unacceptable exposures cannot be ruled out, it may be helpful to estimate the probability that such exposures will actually occur, and also how frequent and how large they will be. To obtain such estimates, it is necessary to use probabilities or probability distributions to quantify the relative likelihood or frequencies of different exposures, i.e. “probabilistic” methods.

The main steps of a probabilistic analysis are:

- Define the assessment scenario (e.g. population or sub-population, routes of exposure considered, time scale), the probabilistic exposure estimate that is required, the structure of the model that will be used to obtain it, and the model inputs; identify which inputs are variable and/or uncertain and which of these are to be treated probabilistically; and identify important dependencies between inputs. Most of this should already have been done, as part of the Tier 1 and 2 evaluations described earlier.
- Specify appropriate distributions and dependencies to represent variability and uncertainty in the model inputs. This involves identifying available data, checking that they are appropriate for the purposes of the model, fitting appropriate distributions, and estimating dependencies.
- Carry out appropriate computations to “propagate” the variability and uncertainty through the exposure model and quantify the resulting variability and uncertainty in the output.
- Carry out a sensitivity analysis to examine the contribution of each model input to variation and uncertainty in the output. This may help to identify sources of variability that could be manipulated (e.g. by regulation or consumer advice) to reduce exposure, or identify which inputs would benefit most from collection of additional data to reduce uncertainty (if required).
- Produce appropriate graphics, tables and text to communicate the analysis and its results to peer-reviewers, risk managers and other stakeholders.

Probabilistic methods are more often used to quantify uncertainty in model inputs, rather than uncertainties in the scenario or the model. In principle, alternative models could be included within a single probabilistic assessment by assigning probabilities representing their relative plausibilities. An alternative is to produce a series of probabilistic assessments representing the different scenarios or models.

⁷ Results of sensitivity analysis should be interpreted with care if there are potential correlations or dependencies between different uncertainties, as this could cause alter their relative contributions to overall uncertainty.

A variety of approaches exist for probabilistic analysis, including one-dimensional and two-dimensional Monte Carlo simulation, bootstrapping and Bayesian analysis (e.g. European Commission, 2003b; Cullen and Frey, 1999; Vose, 2000; US Environmental Protection Agency, 1997) and fuzzy arithmetic and probability bounds (Ferson, 2002). This opinion does not attempt to describe or evaluate these methods in detail; instead the reader is referred to the sources cited above. The Scientific Committee is aware that the World Health Organization's International Programme on Chemical Safety is also preparing a guidance document on characterising and communicating uncertainty in exposure assessment, which will address all routes of exposure.

Each probabilistic approach has strengths and weaknesses, and there is no general consensus on which approaches should be preferred. This is especially true with regard to quantifying uncertainty. While probabilistic approaches are becoming increasingly accepted as part of routine regulatory practice, there is a lack of guidance on how to use them. In a report on quantitative microbial risk assessment, the former EC Scientific Steering Committee (SSC) stressed the need for further evolution of the methodology of quantitative risk assessment, and of criteria for the appropriate use of different probabilistic approaches. The SSC concluded that “a quick harmonisation at the present state-of-the-art should be avoided” (European Commission, 2003c). This implies that prospective users need to be aware of new developments, and consider carefully which approaches to use.

Probabilistic exposure modelling requires a high level of expertise in statistics as well as exposure assessment and the disciplines relevant to the types of data under consideration (e.g. analytical chemistry, microbiology, food consumption, etc.).

Finally, because it is never practical to treat all uncertainties probabilistically, it should always be accompanied by deterministic or qualitative evaluation of other uncertainties.

5. REPORTING AND COMMUNICATION OF RESULTS

Effective communication of risk is difficult, partly because the information that needs to be communicated is sometimes complex, and partly because perception of risk is influenced by a range of other factors including the context and preconceptions of the audience. Furthermore, it is generally necessary to communicate with several different audiences that require different information and different communication formats (e.g. scientists, risk managers and the public).

Communicating uncertainty adds complexity because it involves communicating ranges or distributions of possible risks, rather than single estimates. However, research studies have indicated that the majority of people do understand the difference between interval and point estimates of risk (Johnson and Slovic, 1995, 1998). Among those respondents who understood the concept, reporting of uncertainty had mixed effects. On the one hand, discussion of uncertainty appeared to signal more honesty. On the other hand, discussion of uncertainty led to lower competence ratings of the institutions responsible for risk assessment. Graphical presentation of uncertainty produced higher comprehension ratings, but lower trustworthiness ratings. The potential for such responses needs to be considered by scientists and risk managers when deciding how to communicate with consumers. However, the main

focus in this section is on finding effective ways for scientists to communicate uncertainty to risk managers.

Uncertainties analysed at different tiers produce different outputs and require different formats for communication.

Screening assessments at Tier 0 account for uncertainty by using conservative assumptions and default values. In these cases, it is sufficient to give the result, state that the standard default values were applied, and refer the reader to other sources (e.g. an official guidance document) for their derivation and justification. If there could be questions about the applicability of the conservative assumptions and default values to the case in hand (e.g. for a novel contaminant) then the decision to use them should be justified.

Uncertainties assessed at Tier 1 (qualitative) may be communicated by listing or tabulating them, together with an indication of their direction and magnitude. One possible format for this is illustrated in Table 3. In addition, it will generally be desirable to give a more detailed discussion in the text of the more important uncertainties, and of their combined effect on the assessment outcome.

Uncertainties assessed at Tier 2 (deterministic) generate alternative point estimates for exposure, and may be communicated in various ways depending on the particular methods used for sensitivity analysis. As a minimum, this should:

- identify which uncertainties have been treated at Tier 2,
- if only one uncertainty is quantified, present the alternative input values used, describe their relative plausibilities and give the corresponding exposure estimates,
- if more than one uncertainty is quantified, present the alternative combinations of input values used, their relative plausibilities and the corresponding exposure.

In addition, it will be useful (especially if upper estimates exceed levels of concern) to show which of the quantified uncertainties have most influence on the outcome.

When uncertainty is considered deterministically for a small number of assessment inputs, it may be helpful to summarise the results as a graph, showing the relationship between the input values and the resulting exposure (e.g. EFSA, 2004⁸).

Uncertainties assessed at Tier 3 (probabilistic) produce probability distributions as outputs. Probability distributions can be communicated in many ways, including:

- probability density function, showing the relative probability of different values,
- cumulative distribution, showing the probability of values below any given level,
- exceedance (inverse cumulative) distribution, showing the probability of values above any given level,
- summary statistics, e.g. mean or median estimates for the 97.5th percentile exposure together with one or more confidence intervals (e.g. 75, 90, 95 or 99% intervals); these may be presented numerically or graphically (e.g. box and whisker plots).

In addition, output from a probabilistic assessment will often include a sensitivity analysis, identifying major contributors to variability and uncertainty in the estimated exposure.

⁸ EFSA(2004) is an Opinion on the exposure of birds to the pesticide methamidophos. Figure 1 on page 21 in that Opinion shows how the exposure of birds increases with (a) the proportion of time birds spend feeding in crops treated with methamidophos, and (b) the proportion of small insects in their diet. However, in this example the relative plausibility of different input values was not evaluated.

It is essential to provide risk managers with an assessment of the overall degree of uncertainty in the dietary exposure assessment outcome. For example, if the assessment aggregates exposure via more than one source then the combined effect of uncertainties affecting the different sources of exposure should be considered. Similarly, if the uncertainties for an assessment have been analysed at different tiers (qualitatively, deterministically and probabilistically), it is necessary to find a way of presenting the results together and arriving at an overall characterisation of uncertainty. This is difficult and subjective but unavoidable, since it is never practical to quantify all uncertainties objectively. Few assessments have attempted to do this in a systematic way, and it would be premature to give firm recommendations. However, a combined presentation should include:

- A list of any uncertainties that have been treated probabilistically (Tier 3), and appropriate graphical, numerical and textual presentation of the results.
- A list of any uncertainties treated deterministically (Tier 2), showing the results obtained with alternative assumptions and relative plausibilities.
- A list of the uncertainties treated qualitatively (Tier 1), together with an evaluation of the direction and magnitude of their impact on the assessment outcome (e.g. in the form of Table 3).

Examples of some types of graphical presentation for probability distributions are provided in Annex 1.

In addition, it will generally be desirable to produce a concise textual and numerical summary of the results, e.g. for use in the executive summary of an exposure assessment. The appropriate format for this will vary from case to case. For the ochratoxin A (OTA) example in Tables 1-3, the exposure assessment and its associated uncertainties could be summarised as follows:

In conclusion, the use of more recent and accurate data (individual food consumption data from 3 EU countries and more than 15,000 analytical results) allows estimating the exposure of high consumers to OTA at between 40 and 60 ng/kg b.w./week which is about 30 % lower than the previous assessment (90 ng/kg b.w./week). Qualitative evaluation of uncertainties affecting the assessment indicates that exposure for adult high consumers is likely to be over-estimated by a moderate amount. However, the assessment might under-estimate exposure for regional populations consuming locally-produced food and probably under-estimates exposure for children.

A possible format for a Tier 3 assessment might be:

“The median estimate of the 97.5th percentile exposure is x, but this is affected by a number of uncertainties. Uncertainties A, B, C... were analysed probabilistically, resulting in a p% confidence interval of y – z. This included reasonable worst-case assumptions for uncertainties D, E, F..., which were treated deterministically. Evaluation of further, unquantified uncertainties suggests that the true 97.5th percentile exposure could be higher/is unlikely to be higher, because...”

A range of confidence intervals (p%) should be reported, e.g. using a table, so that risk managers can choose the level of confidence they wish to apply.

In addition to communicating results, it is essential to communicate sufficient information about the methods used so that reviewers can fully evaluate them, and so that other experts could repeat the assessment if desired. This is especially important for sensitivity analysis and probabilistic approaches, although it may be sufficient to describe them in outline if the reader can be referred to other sources for detail.

Finally, it is important to communicate the strengths of the exposure assessment (what is known) as well as the uncertainties, and also to discuss the uncertainty affecting exposure compared to that affecting other parts of the overall risk assessment (e.g. toxicity). The aim should be to provide a balanced picture of what is known and what is uncertain, and avoid giving an exaggerated impression of either certainty or uncertainty.

6. UTILITY OF RESULTS FOR RISK MANAGEMENT

The approaches discussed in this opinion are intended to be useful to risk managers by providing a better understanding of the degree of uncertainty associated with exposure estimates and, consequently, a better basis for risk management.

Each tier gives the risk manager an indication (qualitative, deterministic or probabilistic) of the likelihood that exposure will exceed, or in the case of nutrients be below, an acceptable level, such as a health-based guidance value.

In addition to providing a better description of uncertainty, each of the three tiers also adds to understanding by identifying (qualitatively, deterministically or probabilistically) which aspects of the assessment model are contributing most to overall uncertainty. This can help optimise the use of resources, by enabling further data collection to be targeted on reducing the largest uncertainties. Therefore, information on uncertainty is not simply useful but in many cases necessary to make rational choices between the various options open to risk managers - whether to take action to reduce exposure, and whether to request more data or analysis.

Figure 2 illustrates the role of qualitative and refined uncertainty analysis in relation to other aspects of the overall process of risk assessment (including both exposure and toxicity assessment) and risk management. As previously explained, an analysis of uncertainty is not required for screening assessments if they include conservative assumptions and default values to take account of uncertainty, but at least a qualitative uncertainty analysis should be done for every refined assessment.

The assessment is refined iteratively, as shown by the feedback loop in Figure 2, until a risk management decision can be made with adequate certainty. When the assessment indicates too high a likelihood of exceeding (or in the case of nutrients, falling below) an acceptable level of exposure, four options may be considered:

1. Refine either the exposure or effects assessment (e.g. use more realistic assumptions, or use probabilistic methods to quantify variability),
2. Refine the assessment of uncertainty (i.e. assess more uncertainties at Tiers 2 and 3), to get a clearer picture of the likelihood of exceeding an acceptable exposure,
3. Collect new data to reduce uncertainty, guided by sensitivity analysis,

4. Evaluate options for management action to reduce exposure (e.g. give advice to consumers, impose restrictions on substance, refuse authorisation, etc.).

A refined assessment may include one or more of these options. The choice between them might be influenced by consideration of their cost and difficulty, and of their potential contribution to reaching a decision. If uncertainty is high, then improving the characterisation of uncertainty might be more attractive than collecting further data or action to reduce exposure. However, if the potential consequences of exceeding an acceptable exposure were serious or irreversible, the risk manager might consider taking precautionary action to reduce exposure while also initiating research to reduce uncertainty (i.e. invoking the precautionary principle, European Commission, 2000). Deciding between these options therefore involves a risk management judgement, as does deciding whether there is adequate certainty that the exposure (or risk) is acceptable. Therefore interaction between risk assessors and risk managers is likely to be needed at these decision points, indicated by shaded diamonds in Figure 2.

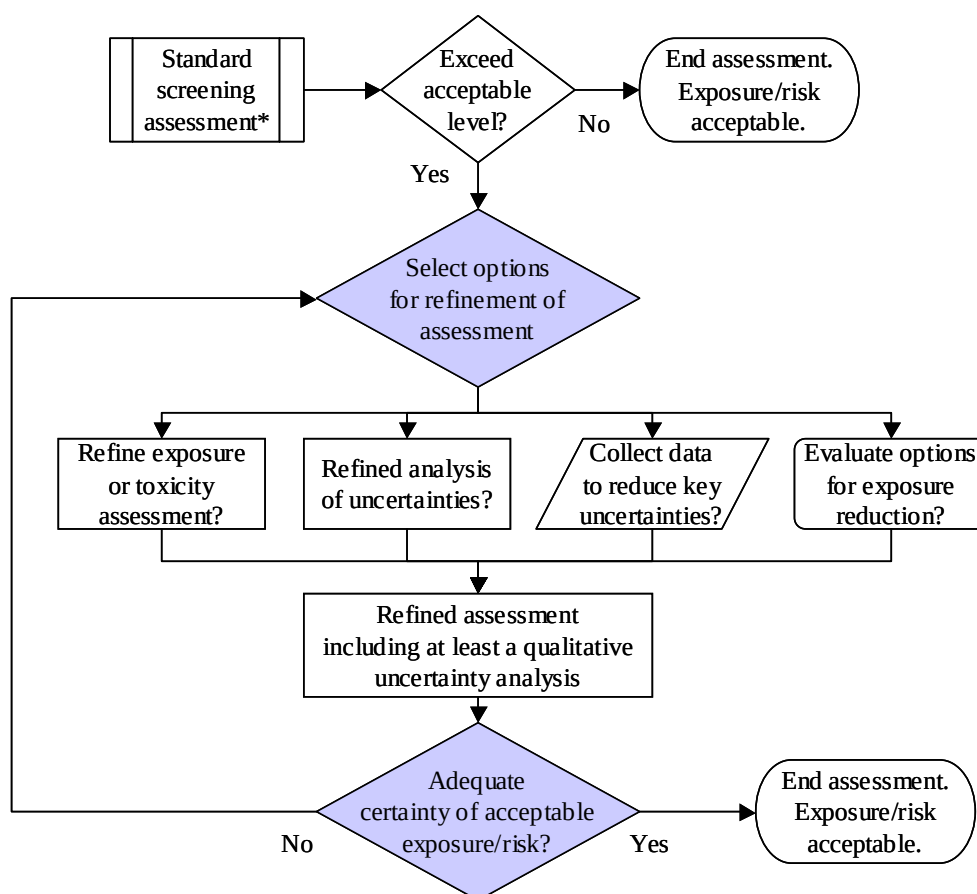


Figure 2. Flowchart illustrating the potential role of qualitative and refined uncertainty analysis within an overall process of risk assessment and risk management. Shading indicates decision steps that involve risk management judgements (see text).

7. CONCLUSIONS AND RECOMMENDATIONS

Each step in dietary exposure assessment is affected by scientific uncertainties, which contribute to the overall uncertainty of risk estimates provided to risk managers. It is important for assessors to characterise the extent of uncertainty, so that it can be taken into account by risk managers.

Analysis of uncertainty may not be required at all in screening assessments, provided they include conservative assumptions and default values to take account of uncertainty. However, it is especially important that such assumptions and default values are soundly-based, as they will be used repeatedly in many assessments. Therefore, the Scientific Committee recommends that each Panel should review the appropriateness of the assumptions and default values used in screening assessments in its area of work and inform the Scientific Committee of the outcome of the review.

Some evaluation of uncertainty is required in all refined assessments. This should start with a systematic examination of potential sources and types of uncertainty, to maximise the likelihood that important uncertainties are recognised.

Methods available for analysing uncertainties fall into 3 broad categories: qualitative, deterministic (using alternative point estimates,) and probabilistic (using probabilities or probability distributions). Qualitative and deterministic approaches are described in the opinion, but readers are referred to other sources for detailed information on sensitivity analysis and probabilistic methods.

The amount of effort and detail devoted to analysing uncertainties should be proportionate to the needs, so the Scientific Committee recommends a tiered approach. Each uncertainty in an assessment may be analysed at one of three tiers: qualitative (Tier 1), deterministic (Tier 2) or probabilistic (Tier 3). It is never practical to treat all uncertainties quantitatively. Instead, assessments may begin by treating all uncertainties qualitatively. This should not impose a major burden in most cases. A qualitative assessment of this type may be sufficient, if the outcome is clear enough for risk managers' purposes. Otherwise, those uncertainties which appear critical to the outcome may be analysed deterministically or probabilistically.

Communicating uncertainty effectively to other scientists, risk managers and wider audiences is a key challenge. Quantitative and probabilistic assessments can characterise uncertainty using ranges, confidence intervals and distributions, but these always need to be accompanied by good explanatory text and by a qualitative analysis of uncertainties that remain unquantifiable. A tabular format is proposed to facilitate the evaluation and communication of qualitative uncertainties. Suggestions are made for ways of evaluating the overall degree of uncertainty in the estimated exposure, taking account of uncertainties analysed at different tiers (qualitatively, deterministically and probabilistically).

Characterising uncertainty always involves some degree of subjective evaluation. It is essential to ensure that the subjective elements are based on, and limited to, what can be supported by scientific evidence; and that they are documented in sufficient detail that others can evaluate the judgements involved.

The approaches discussed in this opinion are expected to provide a better understanding of the degree of uncertainty associated with exposure estimates and, consequently, a better basis for risk management. Even the simplest approaches (Tier 1, qualitative) will improve the detection and understanding of uncertainty compared to most current practice. Treating selected uncertainties at Tiers 2 and 3 progressively refines the characterisation of uncertainty, and provides an increasingly clear picture of the likelihood of an acceptable exposure being exceeded.

Sources and types of uncertainty affecting key areas of dietary exposure assessment in the work of EFSA are given in Annex 2. They illustrate the relevance of approaches discussed in this opinion and offer a starting point for use in assessments by EFSA Panels.

It would be premature to give prescriptive guidance on which specific approaches to use for dealing with uncertainty in dietary exposure assessment until more experience is gained with their use in this field. The Scientific Committee therefore recommends that EFSA Panels identify which approaches appear promising for their particular needs and context, and review the usefulness and application to their work. The Scientific Committee strongly encourages the Panels to incorporate the systematic evaluation of uncertainties in their risk assessments and to communicate this clearly in their opinions.

8. SELECTED FURTHER READING

The handling of uncertainty in exposure assessment is also considered by IPCS/WHO (in preparation), which includes a more detailed discussion of probabilistic approaches.

Uncertainties in food consumption data are discussed by Kroes et al. (2002); uncertainties in other aspects of exposure assessment (and in toxicology and epidemiology) are discussed by Renwick et al. (2003).

Probabilistic approaches to exposure assessment are treated in detail by Cullen and Frey (1999). US Environmental Protection Agency (2001) describes probabilistic approaches for exposure assessment for contaminated land (Superfund sites). US EPA has also published a general policy for Monte Carlo analysis (US Environmental Protection Agency 1997).

Morgan and Henrion (1990) is a comprehensive general text on uncertainty and uncertainty analysis; Saltelli et al. (2000) is a general text on sensitivity analysis. Mokhtari & Frey (2005) provide guidance on selection sensitivity analysis methods for use in microbial food safety models.

Vose (2000) provides an accessible general account of probabilistic methods including Monte Carlo, bootstrapping and some Bayesian methods.

Ferson (2002) provides text and software for interval analysis and probability bounds analysis.

Van der Sluijs et al. (2005) describe the NUSAP approach to uncertainty evaluation including the qualitative “pedigree” measure. IPCC (2005) gives an overview of qualitative and quantitative approaches to uncertainty for use in climate change assessments.

Van der Sluijs et al. (2003) review a range of quantitative and qualitative methods and procedures for uncertainty assessment.

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ANNEX 1

EXAMPLES OF GRAPHICAL REPRESENTATIONS FOR PROBABILITY DISTRIBUTIONS

Examples of the three types of graphical representation for probability distributions are shown in Figure 1. These hypothetical examples show uncertainty distributions for the exposure of the 97.5th percentile consumer; this could equally be done for other percentiles or for the average consumer.

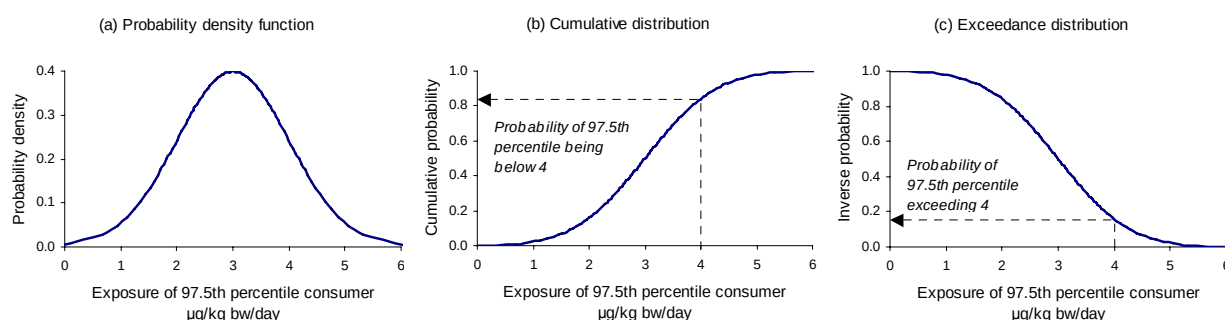


Figure 1. Examples of 3 different formats for presenting probability distributions

A more complex graphical format can be used to show a distribution for variability of exposure across the whole population, together with confidence intervals to show uncertainty (e.g. Figure 2). This can be used to read off confidence intervals for the exposure of any given percentile consumer.

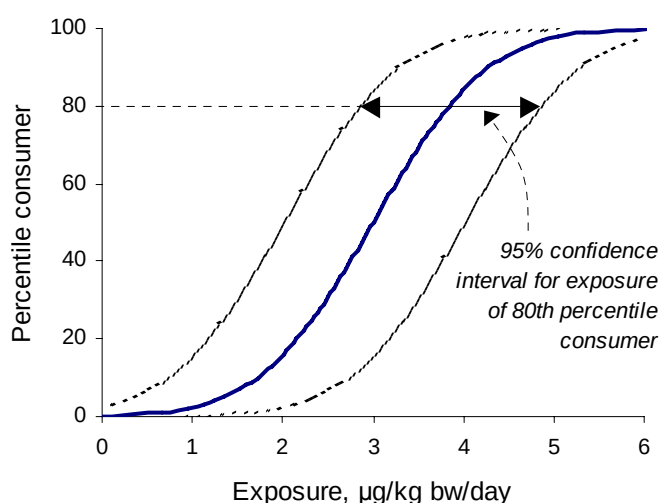


Figure 2. Example of cumulative distribution for variability of exposure between consumers (thick curve), with 95% confidence intervals (thin curves) showing uncertainty for each percentile consumer. Other confidence intervals (e.g. 90 or 99%) should also be shown, so that risk managers can choose the level of confidence they wish to apply.

Cumulative distributions have been found to be more intuitive for non-technical audiences than other kinds of display (Morgan and Henrion, 1990), and are convenient for reading off different percentiles (e.g. median, 95th percentile, etc.). Cumulative distributions are especially useful when interest is focussed on low values (e.g. intake of nutrients), while exceedance distributions may be more intuitive when the interest is in high values (e.g. exposure to contaminants). However, the most likely value (mode) and shape of the distribution are shown more clearly by a probability density function, and the US Environmental Protection Agency (1997) recommends showing both cumulative distributions and probability density functions side-by-side. Whichever methods are used for presenting the results, it is helpful to provide a textual explanation as well.

ANNEX 2

CONSIDERATION OF MAJOR SOURCES AND TYPES OF UNCERTAINTIES IN DIETARY EXPOSURE ASSESSMENTS

The following sections briefly review major sources and types of uncertainties affecting different areas of dietary exposure assessment. It starts by discussing uncertainties affecting food consumption and body weight, which are common inputs in all types of dietary risk assessment, and also some general uncertainties affecting concentrations in foods. Subsequent sections focus on different types of dietary exposure assessment (nutrients, contaminants, additives, etc.). In each section, the tabular format proposed in Table 2 of the main opinion is used to summarise the uncertainties affecting concentrations, while model uncertainties are discussed in the text. These sections and tables are not intended to be comprehensive or definitive, but rather to offer a starting point which may help the relevant EFSA Panels when discussing particular assessments.

i) Food consumption

Assessments of dietary exposure generally require information on food consumption. The specific information required depends on the context: in some cases an estimate of total food consumption might suffice, while other assessments may require a detailed breakdown of the diet into many detailed categories including information on the source and processing of the food (e.g. fried fillets of farmed salmon from a particular region).

There are various types of data describing food consumption, including the following:

- Household budget surveys generally measure amounts of foods brought into the household and refer to the food as purchased, i.e. no information on preparation methods and actually consumed (ingested) amounts.
- Individual dietary surveys aim is to measure the amounts of food and drink actually consumed. Different methods are used covering periods from 1 day to more long-term habitual consumption up to a year. A very detailed review of the existing individual dietary surveys in Europe was performed in the frame of the European programme EFCOSUM (Brussard et al. 2002).
- EFSA is currently developing a food consumption database integrating individual food consumption data from various Member States in a concise database.
- The only other estimates for international food consumptions are the so-called WHO/GEMS Food diets (<http://www.who.int/foodsafety/chem/gems/en/index1.html>) based on the FAO food balances and representing 13 diets around the world.

Some other types of food consumption data and uncertainties affecting them are shown in Table A1⁹.

Some potentially important extrapolation and model uncertainties arise when individual surveys of food consumption are used to estimate individual variation in consumption and dietary exposure over timescales shorter or longer than the survey duration. In general,

⁹ Tables numbered A1, A2 etc are presented in Annex 2.

averaging individual daily exposures over a survey of several days is likely to over-estimate between-individual variation in long-term (e.g. lifetime) exposure, but under-estimate individual variation in acute (1 day) exposures. This is conservative for long-term exposure (over-estimates high consumers), but non-conservative for acute exposure. In addition, a short survey tends to under-estimate the proportion of individuals who consume particular food types. Statistical methods are available to separate within- and between-individual variation (e.g. Slob, 1993, Nusser et al., 1996), but they require various assumptions which themselves are uncertain.

When accurate information is not available from the survey or in case of need for an international assessment, screening assessments may use estimates of consumption that are thought to represent a realistic worst case, e.g. assuming that an individual consumes 1 kg packaged food per day.

It is unusual for dietary surveys to include detailed information on the origin, processing, packaging, storage and preparation of food items, and indeed some of the details that may be required for refined dietary exposure assessments (e.g. the chemical composition of packaging) may not be available to survey respondents or interviewers. This leads to uncertainty in the identification of food items (see Table A1). It may be possible to augment the information provided in surveys using other data or expert knowledge (e.g. on the composition of different forms of packaging, and their market shares for different types of food). However, this is affected by different types of uncertainty (e.g. in estimating market shares) and dependencies (e.g. loyalty of some consumers to specific brands and therefore to specific types of packaging).

There are often uncertainties about the extent to which available consumption data represent different population groups. For instance, SCOOP data on consumption of food commodities may not be fully adequate to cover the consumption patterns of such age groups as children or adolescents. Moreover, the European society is increasingly complex from cultural, ethnic and religious standpoints. It is not just a matter of different amounts consumed, but also of the distribution of consumption of particular types of foods. Consequently there may be higher uncertainty in dietary exposure assessments for particular population groups, than for the so-called “general” population.

Further uncertainties affecting food consumption data are discussed by Kroes et al. (2002). Recommendations for the use of various food consumption data for risk assessment purposes were discussed in 2005 in a Joint FAO/WHO workshop on exposure assessment for chemicals in food report, held in Annapolis, Maryland, USA (report in preparation).

ii) Body Weight

Many assessments require dietary exposure to be estimated relative to body weight (e.g. mg/kg body weight/day). When individual consumption data are taken from surveys, ideally they should be paired with data on body weights for the same individuals. This builds in to the assessment the expected dependency between body weight and consumption (Table A2).

If the individual body weight data are not available, or if the individual body weights are not paired with the food consumption figures, average body weights for the target population are often used. Default 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, a default average body weight of 55 kg is assumed. If the default adult body weight underestimates the actual individual body weights, the dietary exposure estimate on a per kg body weight basis will be overestimated. Likewise, if the default adult body weight overestimates the actual individual body weights, the dietary exposure estimate on a per kg body weight basis will be underestimated. Furthermore, if average body weights are combined with individual data on consumption, the assessment may over-estimate the degree of individual variation in dietary exposure for some foods, if their consumption is correlated with body weight.

Table A1. Uncertainties affecting the estimation of *food consumption*, using different types of data.

Data	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/imprecise language
Individual food surveys based on diaries, e.g. 7 days	Uncertainty in recording of food types. Measurement error in weights. Under-reporting, especially of fatty foods. Incomplete information about e.g. packaging & processing.	Could be significant if survey is small or estimates for extreme consumers are required.	-	Extrapolation to other years, seasons, populations, or regions. Extrapolation from recipes to their ingredients.	Choice of fitted distributions (unless survey data are bootstrapped).	Uncertainty about degree of serial autocorrelation is important if assessing long-term exposure. Uncertainty about dependencies between food types (unless survey data are bootstrapped).	Definition of food categories. Definition of "adults". Ambiguity about the ingredients of recipes. Ambiguity about processing & packaging.
Recall/history surveys	As above plus recall errors and subjective estimation of quantities.	As above		As above	As above	As above	As above
Household budget surveys	As above	As above		As above plus extrapolation from household purchases to individual consumption.	As above	As above, plus non-random allocation of foods between household members.	As above
Assumption of 1kg/person/day of packaged food consumed			Uncertainty about how "conservative" the assumption really is, in particular for		-	-	

Data	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/ imprecise language
in 60 kg adult (model used for residues of packaging materials).			children.				
Food supply data calculated from food balance sheets e.g. GEMS Food diets	Uncertainty on global figures for production, import, export and quantities not consumed by humans	Uncertainty on the correct aggregation of statistics from several countries		Uncertainty on the representativeness of one or few countries for a region. Uncertainty on the level of conservatism of the average availability compared with the high consumption.			
Market shares of specific food types or brands relevant to the assessment	Subjective uncertainty when estimated from expert judgement.	Sampling uncertainty when estimated from market surveys.		Extrapolation from expert judgement or a limited survey to the overall market.		Brand may be associated with other product features such as source, unit weight, packaging, processing etc.	Imprecise identification of brands in survey data.
Place of production				Uncertainty on the population exposed to a food produced in a specific place (contaminated) or with specific means (bad practices)			

Table A2. Uncertainties affecting the estimation of *body weight*, using different types of data.

Assessment input	Data	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/ imprecise language
Individual body weights	Reported body weights of individuals in dietary survey,	Measurement error. Diurnal variation. Possible deliberate mis-reporting.	Could be significant if survey is small or estimates for extreme consumers are required.	-	Extrapolation to other regions.	Not relevant if original weights are used.	Correlation with consumption incorporated if individual records kept together in calculation.	-
Default average body weight	60 kg adult,, 15 kg for children.		-	Relation to true distribution for target population.		-	May over-estimate individual variation of exposure, if combined with individual data on consumption.	-

iii) Uncertainties concerning chemicals in foods – general issues

For most of the EFSA Panels, exposure assessments require inputs on the concentrations in food of various types of chemicals, including nutrients, additives, flavourings, pesticides, chemicals migrating from packaging materials, and other contaminants. There are some general uncertainties which affect most or all of these concentrations, as follows:

- measurement uncertainty (analytical variation, and measurements below the limit of detection or quantification)
- sampling uncertainty, due to limited numbers of samples analysed
- bias, if sampling for chemical analysis is targeted or non-random
- uncertainty about the representativeness of default values, when used (e.g. maximum permitted levels)
- extrapolation of concentrations from analysed foods to other foods for which data are lacking.
- extrapolation of concentrations between countries, regions, years, seasons, etc.
- uncertainty about the shape of distributions used to represent variation in concentrations
- uncertainty about the effects on concentrations of processing, storage and preparation procedures
- correlations in concentrations experienced by individual consumers over time: this can arise in various ways including consistent preferences for particular foods or products (consumer loyalty), home storage conditions, cooking methods, etc.

The specific nature of these uncertainties varies according to the types of chemicals involved, as discussed in the following sections. For some types of chemicals, there are differences in the nature and degree of uncertainty between exposure assessments conducted prior to authorisation or marketing, and assessments of chemicals already on the market (e.g. due to the availability of monitoring data).

iv) Nutrients

Food composition data on nutrients are needed for a variety of exposure/intake assessments. They are primarily needed in calculations of nutrient intakes from food consumption surveys in order to assess the adequacy of the diet of groups, and the proportion of different groups that have a risk of inadequate or excessive intakes. Such data are also used in evaluating effects on nutrient intakes of fortification, processing etc. of specific foods. Intake assessments are also used in studies on the relation between nutrient intakes and health outcomes

Food composition data on nutrients are primarily derived from direct analysis of foods. Due to high analytical costs and the large number of products available on the market, including different brands and varieties, direct analysis is generally limited to cover major food commodities or products. Moreover, analysis is often done on representative, bulked samples of a specific commodity or product type, e.g. milk from several regions, a mixture of different brands of breads, etc. Few data are available on the nutrient content of prepared foods in the form they are eaten. Various types of calculations and imputations are used to estimate the compositional values of similar types of foods. Examples include extrapolation of values for dairy milk to processed milk products using algorithms based on composition criteria, imputations based on ingredient lists of similar types of manufactured foods, calculations using recipes and qualified guesses. Recipe calculation is the main tool for estimating nutrient

composition of dishes and mixed foods including allowance for effects of food preparation and processing. These are based on available information on weight changes and losses/gains of nutrients under various conditions.

A number of factors influence the nutrient composition of foods, e.g. cultivars or breed, geographical origin, fertilization, feed, season of harvest or catch (for fish), storage time and conditions, maturity, formulation, fortification, preparation and processing. Analysed data on nutrient composition will rarely be available for all the combinations of the factors that are relevant to a specific exposure assessment. In some assessments these factors might be ignored, implying an assumption that they have negligible influence on exposure. Unless there is evidence that confirms this assumption, it will introduce uncertainty into the assessment.

Since analytical data on the composition of different types of manufactured foods and dishes are less abundant, allowance is generally made for the effect of food preparation or processing using standard extrapolation factors or equations. Most assessments are not based on original analytical data, but instead rely on nutrient concentrations from standard food composition tables or databases. Such data collections include a mixture of analytical, calculated and imputed values, for which the degree of uncertainty is generally not reported. All of these approaches imply various types of extrapolation uncertainty. These uncertainties can be reduced by conducting studies, e.g. duplicate portion or market basket studies, to compare estimated and measured nutrient levels in selected foods (e.g. Becker 1996) and then using the results to refine the extrapolation factors or composition tables, but some degree of uncertainty will always remain.

Table A3. Uncertainties affecting the estimation of **nutrient content of foods**, using different types of data.

Data	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Model uncertainty	Correlations between inputs	Ambiguity/ imprecise description
Direct analysis	Analytical bias and variation. Treatment of non-detects. Validity of outlying values.	Importance depends on sample size and representativity and whether average or extreme values are required.	-	Extrapolation or adjustment may be needed to allow for effects of cultivars or breed, geographical origin, fertilization, feed, season, storage time and conditions.	Choice of distribution for concentrations (e.g. lognormal). Selection of samples may not be random.	May be correlations between foods for same consumer (e.g. due to similar patterns of home processing)	May be uncertain which precise types of food were sampled, or what other conditions applied (if original records not available)
Calculations based on extrapolations from similar foods	Measurement uncertainty in data used as basis for extrapolation	Dependent on original analytical data	-	See above. May also be needed to allow for formulation, fortification, processing or preparation method.	Algorithm, e.g. use of dependent criteria, nutrient factor(s)	See above.	See above
Calculations based on ingredients (Recipes)	Inaccuracies in data on recipe composition	Representativity of recipe for the actual food item	-	Specificity of retention factors for process or preparation method applied.	Algorithm, e.g. extent of use of retention factors, etc.	Similar factors used for combination process-food group	See above. Imprecise description of recipe and conditions applied
Imputations	Bias due to choice of dependent criteria, e.g. type of food and/or nutrient	Dependent on original analytical data	-		Logical basis of imputations may be incorrect or speculative		

v) Additives and flavourings

Dietary exposure to additives/flavourings can be assessed through combination of data on food consumption with data on occurrence of additives/flavourings in foods and beverages. Different models are used to estimate either current or potential exposure. In the case of additives, the estimated exposure to the substance will usually be compared with an Acceptable Daily Intake, which refers to the total exposure from all sources. In the case of chemically defined flavourings, since specific toxicological data are not usually available, estimated exposure will be compared with thresholds for toxicological concern. In both cases the information of interest is usually that of long-term human dietary exposure to the substance.

Uncertainties affecting the estimation of additives and flavourings concentrations are summarised in Table A4. A feature specific to additives and flavourings is that they are intentionally added to food and that their presence in food is related to the product formulation, which may vary from brand to brand of every single food item. In some cases, e.g. sweeteners in sugar-free products, presence and concentration are closely controlled so the associated uncertainty is low. For many additives and flavourings, the food industry can choose among a variety of substances to impart a certain flavour, colour, texture or other technical function. When a substance has been chosen to enter in the formulation, variability and uncertainty on use level should not be very large since it is related to a technological need. However, in many cases these data are kept confidential and only Maximum Permitted Levels present in the legislation or Typical Use Levels or Upper Use Level reported by industry are available. The relationship between such levels and actual use levels is very uncertain. For some additives and/or in some categories of food no Maximum Permitted Levels have been set and the additive is permitted conditional on GMP (Good Manufacturing Practice). This is often the case for additives that have an ADI “not specified”. For new substances submitted for use as additives/flavourings, only intended use levels are available and can be used to assess anticipated human dietary exposure.

Few analytical data are currently available in relation to the concentration of additives/flavourings in foods and beverages ready to be consumed and little is known about the influence of storage and processing on the residues of these substances in food. Moreover, except for some flavourings, few data are available on the natural occurrence of these substances in foods and beverages; the concentration of these substances in natural foods is therefore often assumed to be zero in the dietary exposure assessment. The uncertainty related to such assumptions is difficult to quantify due to the lack of data.

The tendency of consumers to repeatedly purchase and consume the same food products, termed consumer loyalty, creates a dependency in the form of a positive correlation between the concentrations in different food items consumed by the same consumer. Thus, if a specific brand of processed food contains a high concentration of an additive or flavour, consumers of that brand would have higher dietary exposure of the substances than those consuming brands without, or with lesser amounts of the substance. In order to provide a conservative dietary exposure assessment, it may be assumed that consumers are loyal to the brands with the highest concentrations. This introduces uncertainty (rather, it introduces a bias, but provides a more accurate estimate for a consumer who is loyal, and also provides higher certainty that

the assessment is protective) in the dietary exposure assessment but takes into consideration the consumers who are potentially more exposed to the substance of interest.

Table A4. Uncertainties affecting the estimation of *additives and flavourings concentrations*, using different types of data.

Assessment input	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/ imprecise language
Direct measurement in foods/beverage ready for consumption	Analytical bias and variation. Treatment of non-detects. Validity of outlying values.	Importance depends on sample size and whether average or extreme values are required.	-	Extrapolation of data measured in one food to other foods of the same category may be difficult due to varying product formulation, storage time and processing, plus any regional or seasonal variation. Choice of percentile to assess high concentration.	Choice of distribution for concentrations (e.g. lognormal).	There may be a correlation between the concentration in different foods consumed by the same consumer (e.g. due to loyalty to a flavour in different foods)	May be uncertain which precise types of food were sampled, or what other conditions applied (if original records not available)
Reported Use Levels by industry	Reported use levels are usually based on quantities added to food, without considering the effect of storage, processing, etc.	Uncertain relationship between reported use level by petitioner and use level of other producers	-	If exposure is assessed only on the basis of concentration of the substance added as additive/flavouring, the relationship between this data and overall exposure (including natural content of food, other uses of the substance i.e. in pharmaceuticals and consumer products) is uncertain	idem	Idem	May be uncertain to which precise types of food the use levels refer
Maximum Permitted	Not applicable	Not applicable	-	Additives/flavourings could be used at levels	The use of Maximum	Idem	May be uncertain to which precise

Assessment input	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/ imprecise language
Level set in the legislation				higher than permitted in the legislation. There is therefore an uncertain relationship between Maximum Permitted Levels and levels in food/beverage available on the market. Data arising from surveillance activities can allow to quantify this uncertainty	Permitted Level tends to systematically overestimate current intakes. No exposure estimate can be performed if the substance is authorised at GMP		types of food the use levels refer

vi) Substances used in food contact materials

Exposure assessments for substances migrating into food from food contact materials (e.g. packaging) differ in a number of ways from other contaminants. The number of substances used just in plastics for packaging is considerable (over 1200 monomers and over 1000 additives). The contamination process depends on many factors including the duration of contact between food and packaging, and the temperature (during storage, during final preparation, etc.).

Instead of assessing dietary exposure through combination of concentration data in actual foods with consumption data, a model is used to calculate the maximum migration of the substance into food. In the model, it is assumed a person may consume daily 1 kg of non-fatty food that is in contact with a particular type of food contact material and that the kg of food is in the form of a cube of surface area 6 dm². For fatty foods it is assumed that a person may consume daily an amount of food containing 200 g of pure fat.

The level of migration may be obtained in three main ways (Table A5).

- Most commonly, concentrations in food are estimated from measurements of migration obtained in food simulants. Standard simulants are used (olive oil, water, 3% acetic acid, ethanolic solutions) to represent main categories of food with differing migration potential. Migration tests are generally performed at 40°C over 10 days and the results are expressed either as concentrations in food simulants or as mass of residues released per surface unit area. Because of the tendency of olive oil to overestimate migration into fatty foods, a “total reduction factor” between 1 and 5 may be used to extrapolate from olive oil to other fatty foods according to their fat content. The total reduction factor is the product of the “fat reduction factor” (to take account of the fat content of real foods), and the D reduction factor (to take into account the lower migration into fatty foods compared to olive oil, EFSA 2005c).
- In some rare cases, full dietary exposure assessment is performed based on concentrations measured in foods ready for consumption. It may be necessary to extrapolate these measurements from foods that are measured to other foods that are not, which can introduce some uncertainty. Further uncertainty arises because the contamination is generally tested on products sampled in the market, not on products sampled in households after storage time (from several days to several years according to the considered food product) and not after final preparation of food (e.g. microwave heating).
- A third approach is theoretical migration modelling with packaging-related rate constants and food-related uptake properties, intended to overestimate migration. Allowance can be made for many factors affecting migration, e.g. pack size (see below), food composition, temperature etc. Such models can also be used in conjunction with measured concentrations, e.g. to extrapolate to conditions other than those in which the measurements were made. However, each of the factors in the model is subject to its own set of uncertainties, depending on how it was derived.

One important source of uncertainty for packaging assessments arises because migration is positively correlated with the ratio of surface area to volume, which varies widely between individual products. For example, canned foods are often available in two or more different sizes of can, and cheese may be packaged either as large blocks or individual slices. In standard EU assessments, migration measurements are typically reported per unit surface area (e.g. mg/dm²) and then converted to concentrations using the default assumption of a cubic

1 kg pack of surface area 6 dm²/kg. This will underestimate dietary exposure for many packaged items, and overestimate it for others. A further complication arises if the migrant is associated with only part of the pack, e.g. a metal or plastic cap on a glass bottle; in such cases the standard assumption of 6 dm²/kg will overestimate dietary exposure. Improved estimates may be obtained if data are available on the actual surface area to volume ratios of relevant packaging, although this information may be incomplete or approximate, and the market shares of different pack sizes may also be uncertain.

There is a positive correlation (interdependency) between the concentrations in different food items consumed by the same consumer and his/her tendency, termed consumer loyalty, to repeatedly purchase and consume the same food products. Thus, if a specific brand of packaged food using a specific type of packaging contains a high concentration of a monomer or an additive, consumers of that brand would have higher dietary exposure of the substances than those consuming brands without, or with lesser amounts of the substance. In order to provide a conservative dietary exposure assessment, it may be assumed that consumers are loyal to the brands with the highest concentrations. This introduces uncertainty (rather, it introduces a bias, but provides a more accurate estimate for a consumer who is loyal, and also provides higher certainty that the assessment is protective) in the dietary exposure assessment but takes into consideration the consumers who are potentially more exposed to the substance of interest.

Table A5. Uncertainties affecting the estimation of *residues of food packaging materials*, using different types of data.

Assessment input	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/ imprecise language
Direct measurement in foods/beverage ready for consumption	Analytical bias and variation. Treatment of non-detects. Validity of outlying values.	Importance depends on sample size and whether average or extreme values are required.	-	Extrapolation of data measured in one food to other foods of the same category may be difficult due to varying ratio of packaging surface to the weight of the product, of the product formulation, storage time and processing, plus any regional or seasonal variation. Choice of percentile to assess high concentration	Choice of distribution for concentrations (e.g. lognormal).	Consumer loyalty to particular packaging types. Storage time and therefore contamination may be correlated with the frequency and volume of purchases by individual consumers.	May be uncertain which precise types of food were sampled, or what other conditions applied (if original records not available). Unidentified migrants (“forest of peaks”).
Estimated concentration of migrants in real foods from measurements in simulated foods	Analytical bias and variation. Treatment of non-detects. Validity of outlying values.	Sampling uncertainty due to limited number of migration tests performed	-	Extrapolation of migration data from the food stimulant (water, olive oil ,etc) to the food actually in contact with the material; extrapolation from experimental conditions (temperature, time, treatment of samples) to real conditions	Choice of distribution to represent variation between items of similar type.	Consumer loyalty to particular packaging types. Storage time and therefore contamination may be correlated with the frequency and volume of purchases by individual consumers.	May be uncertain which precise types of packaging were sampled, or what other conditions applied (if original records not available).
Estimated concentration	Measurement uncertainties in	Sampling uncertainty	-	Extrapolation from conditions of			Imprecise language could lead to

Assessment input	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/ imprecise language
from mathematical modelling of migration	experimental data used to develop models, e.g. diffusion and partition coefficients, activation energies	in experimental data used to develop models		experiments on which model was based to other conditions for which predictions are required			uncertainties about what problems the model is applicable to, precisely what inputs are required, and meaning of outputs.
Ratio of surface area to weight	Low unless estimated approximately.	Low variability and hence sampling uncertainty within pack types.	High uncertainty if a default value is used (e.g. 6 dm ² /kg)				
Market shares of different pack sizes, treatments etc.	Subjective uncertainty if estimated by expert judgement.	Sampling uncertainty if estimated from survey data.		Extrapolation between countries, over time.			Imprecise information about which packing is in contact with which foods.

vii) Chemical contaminants

Uncertainties affecting the estimation of contaminant concentrations are summarised in Table A6. The concentration of both natural (e.g. mycotoxins) and environmental (e.g. heavy metals) contaminants in food cannot be known indirectly because their level is not determined by a technical functionality in the food itself like food additives or in the raw commodity like pesticides or veterinary drugs. Furthermore, the concentration of chemical contaminant can decrease or increase during storage and processing. Therefore analytical measurements are necessary to establish the concentration level(s) to be combined with food consumption data in order to assess the dietary exposure. The results of analytical measurements will follow a distribution depending on the nature of the contaminant but also on where, when and how (e.g. targeted or random sampling) the samples were collected.

For a contaminant with a long-term toxicity, concentrations are generally estimated in 2 different ways:

- The **average** measured concentration can be used to represent the long-term dietary exposure, assuming that a consumer is unlikely to consume regularly highly contaminated food. The uncertainty attached to this mean is related to the way it was calculated. Available data can have been obtained both from single samples and from pooled samples and the mean can be weighted for pooled samples by the number of initial samples regrouped before the chemical analysis. In addition, uncertainty attached to the mean is also related to the sample size, and to the treatment of non-detect and unquantified results: these may be dealt with in various ways including assumed zero, assumed equal to the limit value or half the limit value, assumed to be distributed uniformly between zero and the limit value, or extrapolating a distribution from data above the limit value.
- The **full distribution** of contaminant concentrations can be used in a probabilistic modelling of the dietary exposure. In that case, the uncertainty is related to the treatment of non-detects and unquantifiable data and to the precision of the tails of the distribution.

For a contaminant with a short-term mechanism of toxicity (e.g. some marine toxins), the highest concentration recorded in a portion of foodstuff is often used to estimate the consumer exposure risk. These can be useful in some cases but are not the most adequate data as they may underestimate concentration peaks.

For contaminants controlled by Maximum Limits (ML) in regulations, in the absence of contamination data, the ML set for a contaminant in the regulation can be used. MLs are generally considered to represent a large overestimate of the concentration of contaminants actually present in foods and the resulting assessment is considered to be conservative. Nevertheless such an approach does not take account of any peaks of contamination over the MLs, related to poor practices.

Table A6. Uncertainties affecting the estimation of *residues of contaminants*, using different types of data.

Assessment input	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/ imprecise language
Direct measurement in foods/beverage ready for consumption or in raw commodities	Analytical bias and variation. Treatment of non-detects. Validity of outlying values.	Importance depends on sample size and whether average or extreme values are required.	-	Extrapolation of data measured in one food to other foods of the same category may be difficult due to varying production parameters, storage time and processing, plus any regional or seasonal variation. Choice of percentile to assess high concentration	Choice of distribution for concentrations (e.g. lognormal).	There may be a correlation between the concentration in different foods consumed by the same consumer (e.g. due to loyalty to a food produced in a specific area or under specific conditions)	May be uncertain which precise types of food were sampled, or what other conditions applied (if original records not available)
Maximum Level set in the legislation	Not applicable	Not applicable	-	Contaminants could be found at levels higher than permitted in the legislation, but are mostly lower. There is therefore an uncertain relationship between Maximum Levels and levels in food/beverage available on the market. Data arising from surveillance activities can allow to quantify this uncertainty		Idem	May be uncertain to which precise types of food the maximum levels refer

viii) Pesticide residues

Deterministic methods for dietary exposure assessment of acute and long-term hazards posed by pesticide residues have been summarised by WHO (1997). Methods are described for estimating residue levels and food consumption and using them to derive theoretical maximum daily intakes (TMDI) and international or national estimated daily intakes (IEDI or NEDI) for assessment of chronic exposures. International level methods include factors to allow for processing and inedible portions of commodities. Methods intended for national level assessments allow the use of more specific national data on residues and food consumption, and additional factors including the proportion of the crop or commodity treated with pesticide and the proportion imported. WHO (1997) also provides guidance on the treatment of values below the limit of determination (LOD). Both the underlying residue data and the various modifying factors are potentially subject to uncertainties.

There are significant differences between exposure assessments conducted for authorisation and those conducted for pesticides already on the market.

- Pre-authorisation assessments are based on a limited, standard dataset: 1 metabolism study to decide which substances are relevant for the risk assessment, 4 or 8 residue trials, 3 processing studies. The results of these studies are normally reliable as they are made under well defined protocols and strict conditions. Therefore the uncertainty related to their results is normally low. However, due to the low number of individual studies it is necessary to extrapolate to the real world situation with a wide range of environmental and agronomical conditions. These factors are reflected only to a limited extent in the pre-authorisation studies. Therefore conservative models and assumptions are used to avoid an underestimation of the risk.
- Post-authorisation assessments are based on monitoring data, and normally have more data points on the occurrence of residues in real commodities. However, substantial uncertainties may still arise, e.g. in extrapolating from monitored commodities to others.

The estimation of chronic exposure to pesticides is similar to the one for chemical contaminants regarding food consumption data. For pesticide residue exposure assessment, according to WHO methodology, the proposed MRL value is used for the calculation. For a refined assessment the median values from supervised field trials can be used.

Some uncertainties affecting the assessment of dietary exposure to pesticides are summarised in Table A7. They include measurement and other uncertainties affecting the analytical data, which generally comprise residues measured in pooled samples of commodity items (e.g. apples) derived from a single “supervised trial” in which a relevant crop is treated in a manner compatible with Good Agricultural Practice. If more than one such trial is available, the highest (most conservative) result is used. Where appropriate, this is multiplied by a factor to allow for effects of processing of the raw commodity.

For commodity items larger than 25g/piece, (e.g. apples), a meal-sized portion may contain only one or a few items and have concentrations substantially above the batch average, due to variation between items. Therefore, the pooled sample concentration is multiplied by a variability factor, which in effect extrapolates from the mean residue in the batch of commodity items to the expected residue for the 97.5th percentile of the distribution of residues between commodity items. The estimation of the variability factor is itself subject to

several types of uncertainty, and has been discussed elsewhere (Hamilton et al. 2004, EFSA 2005b).

In addition to the factors concerning pesticide concentration, the IESTI calculation uses a conservative (97.5th percentile) estimate for the size of a large food portion, the unit weight of the commodity, and a default body weight. One of the issues concerning the IESTI calculation is the overall degree of conservatism that is implied by combining conservative values for the average residue, the variability factor, and the large portion size, and whether this exceeds the degree of conservatism intended by risk managers.

Table A7. Uncertainties affecting the estimation of *residues of pesticides*, using different types of data.

Assessment input	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/imprecise language
Pesticide residue concentration (HR, STMR, MRL, OR)	Analytical bias and variation. Treatment of non-detects. Validity of outlying values.	Sampling uncertainty in estimation depending on supervised field trials or monitoring (number of independent observations).	Uncertainty when MRL is used to assess exposure, instead of measured residues.	Uncertainty about extrapolation from supervised residue trials in certain crop to other crop varieties (tomatoes – cherry tomatoes), from trials in one crop to other closely related crops (apples – pears), from trials with different formulations (EC-SC- formulation), from trials with different application equipment, weather/climatic conditions.	Choice of distribution for residue concentrations	Possible correlation between use patterns in MS and residue concentration in domestic food (no authorization of a pesticide in one country will result in less residues) or residue levels and occurrence of pests (e.g. dry weather conditions – low use rate of fungicides)	
Processing factor	Measurement uncertainty in data used to derive processing factor, or subjective uncertainty if estimated by expert judgement.	Sampling uncertainty in any data used to estimate processing factor.	-	Extrapolation from study conditions in which processing factor was measured to conditions of processing in commercial and home practice.	-	-	
Variability factor	Analytical bias and variation in data used to estimate variability factors. Treatment of non-detects. Validity of outlying values.	Sampling uncertainty due to limited number of trials in which individual residues were measured. Uncertainty due to the different choice	Different views (e.g. IUPAC, JMPR, EFSA and MS) on various aspects of variability factor estimation.	Extrapolation of variability between crops, between pesticides, between application methods and equipment.	Choice of distribution for between-trial variation in variability factors.	Possible correlation between mean and variance of individual item concentrations (i.e. between the average and variability factor for the batch).	-

Assessment input	Measurement uncertainty	Sampling uncertainty	Default value uncertainty	Extrapolation uncertainty	Distribution uncertainty	Correlations between inputs	Ambiguity/ imprecise language
		of market or filed trial commodities.					
Unit weight of single food commodities	Measurement uncertainty in data used to estimate unit weights.	Sampling uncertainty due to limited number of units and crop varieties	Uncertainty about representativeness of default unit weights.	Extrapolation from one crop variety to another variety (e.g. tomatoes/ cherry tomatoes)		Correlation between unit weight and surface of the commodity that is exposed to pesticide spraying	

ix) Microbial contamination

Microbiological exposure assessment describes the pathways through which a pathogen population is introduced, distributed and altered in the production, distribution and consumption of food. The result desired from the dietary exposure assessment is the prevalence, concentration and, if possible, virulence and toxin production of the pathogen in foods at the point that they are eaten and the level of consumption of the food by the population of interest. Uncertainties affecting such assessments are summarised in Table A8.

In many cases, there are no direct measurements for many elements of the assessment, in particular the frequency of contamination of foods and the total pathogen numbers ingested by consumers. However, estimates can be derived, based on data of contamination levels and prevalence at earlier points in the farm-to-fork chain, and the use of models of the effect of physical processes and conditions that the food undergoes from then until the point of consumption, i.e. final pathogen numbers ingested by consumers.

Figure A1 presents an example of the fresh meat chain from live animals to home preparation and consumption. The chain comprises many steps, and uncertainties arise at each step. Microbiological data are only available at certain points of the process and concerns generally presence/absence data. Data on microbiological contamination at time of consumption are very rare and difficult to assess. However, an exposure estimate can be derived, by using predictive exposure models. For this it is necessary to translate the qualitative data on microbial contamination into quantitative data by using mathematical approaches. For a complete dietary exposure assessment of the food chain illustrated in Figure A1, additional data is needed, especially regarding storage conditions during the several processes and the effects of home handling and preparation of fresh meat products on the final exposure. In addition, there is a potential for uncertainties to accumulate at successive steps when modelling the food chain, so it is desirable to check or validate the model if possible by measuring contamination at intermediate points along the chain.

The information on which the dietary exposure estimates are made is often limited. Many of these data are typically derived from studies intended for other purposes and are not ideally suited for the objectives of dietary exposure assessment. Often, they are published in the scientific literature, or appear in reports from regulatory authorities performing routine monitoring. Under the zero-tolerance regulatory approach used towards most infectious foodborne pathogens, concentration is not of particular interest so monitoring is mostly aimed at establishing the absence of a pathogen in a 25-g test sample in a ready to eat food. Data are also subjected to changes in production, processing, storage, etc. This also applies to home preparation practices and consumption habits. Data about consumption usually come from national or regional nutrition surveys. Many of these do not have the level of detail to assess the behaviour of micro-organism in the products during final consumer storage and preparation thus thwarting the assessment of growth, cross-contamination etc.

The assumptions on which the exposure estimates are based introduce uncertainty such as: simplification of complex processes into mathematical models for physical processes, inactivation and growth of micro-organisms introduce uncertainty; small sets of scenarios are generalized to all scenarios of importance; and assumptions are made about how recognizable components of processes operate. In addition, the limitations in testing methods for pathogens also introduce uncertainty in the levels of the pathogen in the food supply. A large range of

different methods for assessing micro-organisms (enrichment culturing are used; Most Probable Number method, plate counting) using a wide range of media, and different sample sizes.

Since models in general are simplified reflections of the reality, a large uncertainty might be expected. This especially applies both to range of growth of micro-organisms related for example to planktonic versus sessile growth conditions. There are few scientific data about the effect of processing conditions, types of foods, etc. on the virulence of pathogenic organisms. Also, dependencies between variables introduce uncertainty in the outcome of dietary exposure assessment. Some existing models (e.g. Combase and Sym'previus) describe the later steps of the food chain in a simplified way; this introduces model and scenario uncertainty, which needs to be considered.

Figure A1. An example of the fresh meat chain from life animals to home preparation and consumption. An estimate of human dietary exposure up to the retail can be derived using predictive models and on data available.

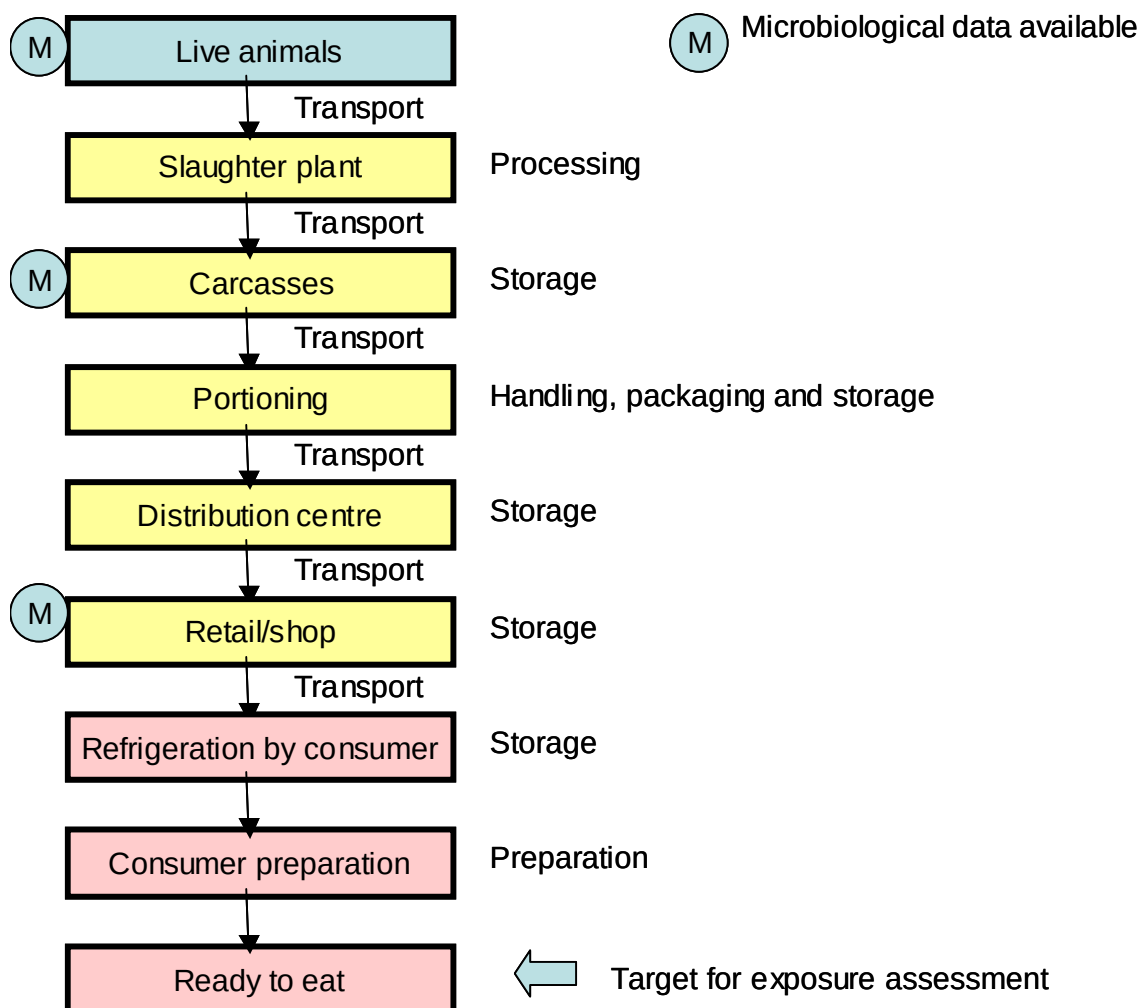


Table A8. Uncertainties affecting the estimation of exposure to *pathogenic (infectious) organisms*, using different types of data.

Assessment input	Measurement uncertainty	Sampling uncertainty	Extrapolation uncertainty	Model uncertainty	Correlations between inputs	Ambiguity/ imprecise language	Expert disagreement
Raw food materials							
Prevalence, concentration and variation in virulence of pathogens on raw (unprocessed) food materials.	Analytical variation; Use of different (not standardized) detection methods.	Selection may not be random; inhomogeneous distribution on batch	Extrapolation to other regions and seasons			Precise types of foods that are sampled, or what other conditions applied.	.-
Predictive models of storage and transport							
The effect of storage on virulence, resistance, etc of pathogenic organisms	Variation in analytical data used as initial contamination	Uneven temperature distribution in refrigerator, deep freezers, etc. Heating equipment	Extrapolation from planktonic growth to sessile growth of pathogens.	Use of a limited number of variables No reliable models for cross-contamination	Dependencies between storage time and storage temperature in exposure modelling;	Precise types of foods that are sampled, or what other conditions applied.	Types of models and simplification No standard modelling approach.
Predictive models of processing effects							
The effect of processing on virulence, resistance, etc of pathogenic organisms	Variation in analytical data used as initial contamination	Variation in processing conditions and product composition	Extrapolation from planktonic growth to sessile growth of pathogens.	Use of a limited number of variables by simplification	Dependencies between variables		Types of models and simplification. No standard modelling approach.
Predictive models of home preparation²⁾							
	No existing information how food is prepared in homes		Extrapolation from planktonic growth to sessile growth of pathogens	Use of a limited number of variables No reliable models for cross-contamination	Dependencies between variables		No standard modelling approach.

¹⁾ Batches are the units with acceptable uncertainties. Each batch, even produced by the same producer will not be completely, equal.

²⁾ So far no information collected on home preparation activities and their effects on exposure to pathogenic organisms