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Report Series

Exposure from Food Contact Materials

Summary Report of a Workshop held in October 2001

Organised by the
ILSI Europe Packaging Material Task Force
In Collaboration with the European Commission's
Joint Research Centre (JRC)

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EXPOSURE FROM FOOD CONTACT MATERIALS

By Kettil Svensson

SUMMARY REPORT OF A WORKSHOP HELD IN OCTOBER 2001 IN ISPRA, ITALY

ORGANISED BY THE ILSI EUROPE PACKAGING MATERIAL TASK FORCE IN COLLABORATION WITH THE EUROPEAN COMMISSION'S JOINT RESEARCH CENTRE (JRC)

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FOREWORD

Since the beginning of the harmonisation of legislation on food contact materials, a conservative approach with substantial built-in safety margins has been applied by the European Commission and the Scientific Committee for Food (SCF) for approval for use of substances in plastics packaging. This approach assumes that every European Union (EU) citizen consumes 1 kg of foodstuff each day over a lifetime, and that this is entirely packaged in the same plastics material. This potential "exposure" sets the maximum concentration permitted to migrate and is related to the toxicological tolerable daily intake (TDI) for the substance in question. In this way, substances are authorised for use subject to migration restrictions stipulated as specific migration limits (SMLs) or, in some cases, residual amounts of the substance in the material itself (QM).

In 1993, ILSI Europe, together with the Commission and scientific experts, started studies to support a more advanced exposure evaluation process. These new evaluation concepts are not limited to food consumption factors, packaging usage factors or thresholds of toxicological concern (or thresholds of regulatory concern) as shown during the workshop. Until the discovery in 1995 in Switzerland of high levels of bisphenol-A-diglycidyl-ether (BADGE) in canned fish products, the focus had been on migration into foods and migration limits in foods. Since then, studies of food consumption data have accelerated, in part to determine whether observed high levels are of concern from the health point of view (e.g. for BADGE) and in part to put migration into a wider perspective. Because daily ingestion of a specific food item containing a packaging substance over a lifetime may be decisive for adverse health effects, focus should be on long-time exposure. Scientists in the field of evaluating dietary exposure from food contact materials such as plastics and coatings were brought together with the purpose of capturing the latest scientific developments, drafting a refined exposure evaluation concept, developing guidelines, proposing tools and defining possible areas for further research. Presentations covered areas such as risk assessment, food consumption data, food packaging usage, migration aspects, probabilistic modelling and biomarkers.

These presentations were discussed in a 2-day workshop held jointly by the Joint Research Centre/ILSI Europe in Ispra, Italy (15–16 October 2001). During the workshop, a number of key themes were highlighted and formed the basis for further discussion. Among these themes were the need to define uncertainties in dietary exposure assessments (and risk assessment) and propose means to address them, including transparent risk communication, consumer protection, probabilistic modelling in exposure assessments, and the necessity for toxicity testing at threshold levels. The following sections summarise the presentations, key points from the discussions and conclusions from the workshop.

EXECUTIVE SUMMARY

To estimate dietary exposure to a substance migrating from a packaging material, information is needed first on the concentration of the substance in food products and then on the consumption level of those products as part of the diet.

Since the beginning of the harmonisation of legislation on food contact materials, a conservative approach has been applied by the European Commission and the SCF to approve and control the use of substances in packaging. This process has been based on potential dietary exposure from plastics materials and on assumptions about migration. This conservative approach assumes that every EU citizen consumes 1 kg of food each day over a lifetime and that this food is packaged in the same plastics containing the substance in question at the maximum concentration (migration level) permitted. A consequence of this assumption, generally speaking, is that the average consumer will be well protected. However, this approach contains several uncertainties. Thus, these uncertainties should be defined and means should be proposed to address them.

Under the present EU system for approval of packaging material substances, risk assessment would benefit from more accurate food consumption data when appropriate. An accurate estimate of the actual dietary exposure to a substance depends on knowledge about shortcomings in the food consumption data employed (24-hour recalls, food frequency questionnaires, dietary history, dietary records, etc.), each having its own advantages and disadvantages. It would be desirable to develop strategies to establish the most appropriate food consumption methodology to assess food contact materials and to create a decision-tree approach to provide an initial crude screening before proceeding to more accurate quantification of food intake. In some groups, such as children, vegetarians, or certain ethnic groups, better food consumption data is needed to reduce uncertainties and thereby refine exposure assessments. It may be possible to establish food consumption factors within the EU for three classes of food types – fatty, aqueous and alcoholic – to use as a basis for refining the exposure model.

One recurring theme in the workshop was probabilistic modelling, which may be a useful tool in the future for estimating dietary exposure from food contact materials in those situations in which basic information, such as food consumption data and migration data, is available and of good quality. The development of probabilistic models for assessing both chronic and short-term dietary exposure to pesticide residues might possibly serve as a way to similarly assess lifetime exposure from food contact materials. The conventional approach of using point estimates for pesticide residues frequently has yielded gross overestimates for several parameters. The probabilistic approach, therefore, was chosen to make better use of available data, replace single input values with probability distributions, refine point estimates and avoid giving the impression of absolute safety. The potential exposure to residual BADGE in can coatings from canned foods in Europe can be treated by a similar probabilistic approach. Modelling variables, such as the quantities of canned foods consumed, the variety of products, migration levels and body weight of individual consumers, leads to distributions of potential BADGE exposure.

Biomarkers can be used in some instances to verify and improve the probabilistic model used for exposure assessment. Exposure estimates for di-2-(ethylhexyl)adipate (DEHA) in the diet from various uses of plasticised film provide a case study. Data available on levels of DEHA in foods were compared with a study in humans in which a urinary metabolite (2-ethylhexanoic acid) was the biomarker used to assess exposure. Data on migration levels in foods were used to establish a probabilistic model of exposure to DEHA, and this was compared with the exposure distribution

from a urine biomarker study of 100 individuals. Preliminary results indicated a good correlation between the modelling data and the biomarker data, which will provide a basis for further refinement of the model.

Both for BADGE and styrenic polymers, it is particularly difficult to pinpoint factors that might affect the intake of a substance. One critical element is the definition of a "high consumer." Is the high consumer the individual eating an atypically high amount of the food in question, or is the extreme consumer the one exposed to unusual amounts of the contaminant through brand loyalty or other reasons?

Because regulations for food packaging materials should be proportionate to risk and ensure consumer safety, data should be provided to assist in refining current legislation. Thresholds of concern, such as the "threshold of regulatory concern for substances intended for use in food contact materials" introduced by the United States (US) Food and Drug Administration (FDA) in 1995, could help define the degree of refinement needed in intake estimates. A further development of thresholds of regulation to approve food packaging materials without the need for development of toxicological data should be considered.

OBJECTIVES

The goals of the workshop were:

- to establish the principles underpinning the estimation of dietary exposure to chemical substances originating from food packaging materials;
- to develop a refined dietary exposure evaluation process that could lead to a more realistic risk assessment of migrating substances; and
- to propose guidelines for predicting dietary intake of chemical substances from food packaging materials, information that will provide a solid basis for risk management.

PRESENTATIONS AND DISCUSSIONS

Introduction

Risk assessment of chemicals has been driven over the last few decades by a dramatic improvement in the achievable quantification limits for measuring substances in foods and other matrices, a level of analysis that is now down to parts per trillion. In addition, knowledge has developed about the toxicity of substances, the second important factor along with dose (exposure) in risk assessment. Toxicological effects, including hormonal, immunological and, to a larger extent, reproductive effects, that were not previously considered are now assessed.

Risk assessment is one of the important elements in risk analysis, the others being risk management and risk communication. The elements in risk assessment recognised by the Codex Alimentarius Commission can be summarised as:

- hazard identification;
- hazard characterisation;
- exposure assessment; and
- risk characterisation.

Several uncertainties are involved at each step of the risk assessment process, a few of which are mentioned below. The two major elements are the toxicity of a substance (hazard) and its dose (exposure). Exposure and ways to assess a more realistic dietary exposure are the key issues covered here.

Hazard identification is defined as identification of an agent with the potential of causing adverse effects/events to humans and/or the environment, together with a qualitative description of these effects/events. Several uncertainties can be recognised such as the extrapolations from animal data to possible human hazards? Are animals similar to humans? What criteria distinguish an effect from an adverse effect (no observed effect level [NOEL] or no observed adverse effect level [NOAEL])? Another tool for hazard identification may be epidemiological studies.

Hazard characterisation is centred on the quantification of the adverse effects, so that the dose–response relationships identified at this stage of the risk assessment can be compared subsequently with the potential for exposure (risk characterisation). Poor quality data can result in the identification of too low or too high a threshold value. Undue emphasis is often placed on a single data point in dose–response studies, forming the basis for the NOAEL. In addition, a consistent approach to the use of mathematical models for dose–response data is needed in extrapolating from animals to humans. A single hazard (chemical substance) can be characterised, but, because mixtures of chemicals are often used, the characterisation will be more complicated in practice.

Exposure assessment is concerned with the actual likely levels and duration of exposure of human and environmental species to the risk source. It characterises the nature and size of the human population and/or ecological communities exposed to an emission source and the magnitude, frequency and duration of that exposure. It is, therefore, important to have good knowledge about the kind of dose reported from a study. Is it the external dose, the internal dose, systemic concentration or target dose? Are data all available, or are there additional data and what about their quality? The EU population with its different cultures is not a homogeneous population, so

how does one obtain representative data for the entire population? Hence, there is a need for a common language and strategy and a common approach to define these uncertainties in exposure assessments. The development of modelling scenarios may be one tool in this effort.

Risk characterisation refers to the estimation of the probability of the occurrence and severity of adverse effects in a given human and/or environmental population by comparing the estimated exposure and hazard characterisation. One principal concern is to define the uncertainties in the identification of a risk in a clear and transparent manner and propose means of addressing them.

The importance of describing and explaining the entire risk assessment process in a better way should be emphasised. For example, when considering toxicity of food substances, chronic effects such as cancer are usually of greatest concern because of lifetime exposure (an exception is pesticides, for which acute effects are now also taken into account in foods). Therefore, occasionally exceeding a safety limit does not necessarily present a risk to health. The acceptable daily intake (ADI) for food additives, or the tolerable daily intake (TDI) set for contaminants in foods is based on the daily intake of a substance over a lifetime. The ADI/TDI is obtained from a NOAEL in experimental animals divided by a safety factor (uncertainty factor) of 100 or more to account for species and individual differences. An acute reference dose (acute RfD) is used for short-term assessments. This is very similar to the ADI/TDI but takes into account single or short-term exposures.

It is unlikely that a consumer will be exposed to the same substance from food packaging each day over an entire lifetime at levels equivalent to the maximum permitted limit. The average consumer, consequently, is overprotected by this conservative approach. However, because data are not available on each individual in a population, measures must be taken to protect the majority of individuals. In most cases, high percentage (percentile) values (97.5%) used by short-term surveys yield overestimates of chronic exposure. A refinement in the exposure assessment would lower the uncertainty, so that a more accurate risk assessment could be obtained. In a few cases, this may have implications for legislation, so that less restrictive limits could be set for chemical contaminants in foods. However, in cases in which it is not possible to refine dietary exposure assessments, uncertainties should be addressed. Better transparency is also needed when it is not possible to carry out a proper risk assessment because of insufficient or poor data. In this case, the precautionary principle should be applied.

Exposure elements

To estimate dietary exposure to a substance migrating from a food packaging material, information is needed on the types of foods packaged, the nature of the packaging material, migration data, packaging usage factors and food consumption.

Food consumption data

To a large extent food consumption data are available for EU consumers but are not accessible in a uniform way. Gaps, however, exist in knowledge about food consumption patterns in certain subpopulations, such as ethnic groups who for cultural or traditional reasons consume more of certain foods than other groups do. Food consumption data of better quality than that currently available are needed for vulnerable groups, such as children (who have higher consumption per unit of body weight than adults do) and extreme consumers (for example, populations with low incomes).

Food consumption data available for the European population suffer from some shortcomings, such as differing methods for collecting the data and differing time frames over which the data has been collected, with resulting variance in both quality and quantity of available data. Food surveys have been carried out for different purposes, often primarily to assess nutrient intake, or have been taken from export/import statistics, or collected to study acute or chronic health effects. When using data for purposes other than those originally intended, the methodological shortcomings should be taken into account. The application of the data may also differ, in that sometimes it is intended for making rough estimates (screening), whereas, sometimes, the aim is to obtain a precise quantitative assessment of the intake of a substance from a specific food item.

At present, several methods are used in Europe to assess food consumption. In addition to household surveys and total diet studies, four different classes of methods are recognised:

- twenty-four–hour recalls (retrospective);
- food frequency questionnaires (retrospective);
- dietary history (retrospective); and
- dietary records of 1, 2, 3, and 7 or more days (prospective).

All these methods are based on different time frames, ranging from 24 hours up to 1 year (for example, food frequency questionnaires). A short time frame usually tends to give an overestimation of the lifetime food intake. Other differences in these methods result from the varying aggregation level (national, household, and individual). To assess intake figures, various approximations and/or calculation methods can be used as cost-effective shortcuts. If the objective is to obtain only a rough estimate of the exposure, then screening is the most cost-effective approach. Screening involves the use of conservative decision trees and selection of (potential) risks, and most often will result in an overestimation of exposure. This is currently the case for exposure assessments relating to packaging materials for the EU population. However, if a rough estimate does not yield a figure that exceeds the relevant ADI, this may well fulfil the required purpose and more sophisticated tools may not be needed. For other reasons, such as the desire to raise limits or restrictions set in foods, the opposite approach is needed. If the objective is to get an accurate value of the exposure, quantifications must be made for each of the steps involved. Quantifications should be unbiased, consistent, and comparable with other results.

To refine chemical intake scenarios from packaged foods, total food consumption or a fraction of the total consumption can be used (food consumption factors). For the assessment of migrating substances from packaging materials, four broad food types are distinguished: aqueous, acidic, alcoholic and fatty foods. For all except acidic foods, food consumption surveys in combination with food composition tables can provide relevant data for a more accurate estimate of the intake of food packaging substances. Based on these considerations, more reliable and comparable data have been generated for the consumption of selected food groups and the intake of total fat, water

and alcohol across eight European countries as a whole. For the European countries, a food intake on average of not more than 200 grams of fat/person/day (95th percentile) has been assessed. Assuming a homogenous distribution of fat in foodstuffs, a consumption factor of 0.2 was proposed by industry. In comparison, food type distribution factors (called food consumption factors within the EU) for various packaging materials were established in the US in 1995. European results show that the variation in food consumption variables inside each individual European country is as large or larger than that between countries. Another conclusion from these studies of the European population is that for fat consumption, within-subject variation is larger than between-subject variation. Moreover, the time frame of the assessment method has a great impact on results and methods which overestimate intake levels for the lifetime exposure. However, it is possible to integrate a short time frame and life-stages to compare with lifetime exposure. For the future, improved assessment tools and better data sources must be developed to screen and quantify the exposure of priority food chemicals in a cost-effective way. Information available on brand names and market shares may also be an additional tool when collecting data. However, how reliable are market figures (overestimation?) and are there differences in food composition of a specific food item of the same brand? Especially for estimating accurate intake of food additives and contaminants, duplicate diet surveys or market basket surveys may be more valuable tools.

Food packaging usage

One of the key elements in the exposure assessment of food contact materials is to link the use of a specific food packaging to a specific food item. Some attempts have been made to establish what kind of foods are to be found in which packaging materials. In the 1990s, Maurice Palmer Associates (UK) collected data from several European countries. Today these data may have some drawbacks, such as being out-of-date because of changing trends, failing to include can lacquers, making some incorrect assumptions, not including in-store packaging, not including ready-meals and failing to correctly identify some materials. In the US, a system was introduced in the 1990s detailing food consumption factors for each material in contact with a specific kind of food, whether fatty, aqueous, acidic or alcoholic. Different types of packaging materials were considered, including paper, metals, glass and various kinds of polymers (plastics). In Europe, the American system has not been accepted, partly because some factors, such as consumption patterns, may be more heterogeneous in Europe than in the US. Fundamental differences are also apparent in the approval process. In the US, a substance is authorised only to be used in a specific polymer, whereas once authorised in Europe it can be used freely for any packaging application.

Researchers at Pira International (UK) are conducting an ongoing study on the use of packaging materials for dietary staples in the UK. This project, funded by the UK Food Standards Agency, aims to determine risks from food contact materials by quantifying how much of a dietary component is consumed and also what proportion of the diet is packaged in certain materials. The approach to the project is to identify and rank the 100 most important commodities and their market shares by brand and pack type. A qualitative risk assessment will be used to prioritise the commodities for further investigation.

For food packaging materials, numerous data of high quality are available when considering the total amount of packaging material used. Sources are well known, units are few and definitions are more consistent than those at the level of the individual packaged product. At the packaged product (consumer) level, data are few and of low quality, definitions are inconsistent, units are diverse and sources of information are disparate.

Changes in packaging trends, such as replacement of glass by polyethylene terephthalate (PET), replacement of polyvinyl chloride (PVC), emergence of active and intelligent packaging and replacement of rigid packs by flexible laminates, make an estimation of packaging use more difficult. Over time, however, trends are easily identified. The same is true for global packaging markets and global brands.

Because of varying legal requirements, significant differences exist between packaging use in different countries. For example, Denmark has banned aluminium cans for beverages. Cultural differences and varying food consumption patterns also affect packaging statistics. The differentiation at all levels of packaging products creates another obstacle to the collection of uniform information. This is exemplified by packaging for liquid soups, which is aggregated at a single level but, in reality, comprises a wide range of packaging materials, including cans, glass bottles, plastic tubs and jars, cartons and aluminium pouches. Packaging size also has an impact on exposure. More ready-made foods are now available, often in small packages, which implies a higher surface-area-to-volume exposure.

Migration aspects

Restrictions in EU legislation for food packaging substances in most cases are expressed as concentration in foods, more specifically as SML values or, in some cases, as compositional limits (maximum quantity) in a packaging material (QM). These limits are usually based on a TDI or ADI accounting for a lifetime exposure of a substance present in a foodstuff. However, the daily ingested amount of a specific food item will vary considerably during an approximate lifetime of 70 years. Food packaging will also vary, and the level of the substance will vary. The consumer's total food consumption will vary, depending on sex, age and other factors. However, legislative restrictions in foods presumably will never be expressed in exposure terms. Therefore, migration limits expressed as milligrams of substance per kilogram of food have been chosen as a model for the exposure, because of the lack of a better alternative. However, recent efforts have been made to make better use of available food consumption data to obtain estimates of intake of food packaging substances. These data could be used to set more scientifically based migration limits where appropriate.

Migration testing in contact with a food simulant is the normal procedure for checking a food packaging material (plastics) either for compliance testing or at the enforcement laboratories. Migration testing (methods and conditions) in response to restrictions put on packaging material or food for legislative purposes is being developed progressively. In some situations, migration results indicate that EU legislation should be better explained, and some revision may be needed in the future. Depending on the way in which the EU directive is interpreted, different results can be obtained that make it difficult to determine the compliance or noncompliance of certain food contact materials.

For example, a supplier of a packaging material may produce all the evidence requested to satisfy the relevant regulations (Directives 90/128/EEC, 82/711/EEC, and 85/572/EEC), with results that indicate that the food simulants are below specified limits. However, when tested by enforcement agencies, these limits may be exceeded for a specific food application. The manufacturer must comply with the legislation, which implies that the testing must be carried out on the empty package itself using a food simulant. For the enforcement laboratory, food samples in most cases are available by sampling from shops or from the food industry. Another possibility is to collect the packaging from the retailer and carry out the test using a food simulant, although this is less common.

The way in which migration results must be compared with SMLs depends on the application or the size of the packaging (or article). If two bottles of the same material are tested, for example, it may be that a bottle of 600 ml capacity with the lower migration (expressed as milligram per millilitre of simulant) into the simulant is not in compliance, whereas a 400 ml bottle with higher migration (expressed as milligram per millilitre of simulant) is in compliance. Hence, the size of the packaging article seems to matter. Packaging size may preferably be related to the area of the article or packaging.

In some cases, a product can be in compliance with 90/128/EEC in regard to the value for QM (residual amount expressed in milligrams per kilogram of plastics) but show migration into the food that is higher than the levels (SML) indicated as safe by the SCF. Hence, the correlation between QM and SML may not be satisfactory when testing thin layers and multilayer materials. By introducing QMA (mg/6 dm^2) in the relevant situations to replace QM, a conventional correction is made so that this food contact area is related to an extraction value taken as maximum possible migration value. In a few cases, QMA has already been introduced in the Directive 90/128/EEC. QMA is the maximum permitted quantity of the substance in the finished material or article expressed as mg per 6 dm^2 of the surface in contact with foodstuffs. The value is derived from the SML by assuming that a) the substance migrates completely (100% of migration) and b) surface/volume ratio equals 6 dm^2/1 litre.

A very modern tool to facilitate compliance testing of plastic materials is to take advantage of mathematical migration modelling using validated diffusion models for establishing the relationships between the quantity of a substance in the polymer and its specific migration value to be compared with the SML.

Future tools

Probabilistic modelling

Probabilistic modelling using Monte Carlo or Latin hypercube simulations is an empirical method to determine variation and/or uncertainty and a procedure that can examine a number of factors using individual distributions, such as food consumption, residue levels of a contaminant and body weight of the consumer. Single-point data are drawn from each distribution repeatedly, looking at numerous combinations of input data to give a frequency distribution of exposure over a specified time period. Some cases using probabilistic modelling are briefly outlined below and may serve as examples and models for the future in estimating exposure from food contact materials and, specifically, more realistic lifetime exposure assessments.

Probabilistic modelling such as Monte Carlo simulations has been used in the environmental field for quite some time (for example, to assess human exposure) and occasionally has been applied for food additives and pesticide residue levels in foods. The assessment of consumer exposure has been one of the fastest developing areas in pesticide residue regulation. There has been a move from development of deterministic models for assessing both chronic and short-term dietary exposure to pesticide residues to the approach of developing and using probabilistic models. In the past, the supervised trials median residue (STMR) level, highest residue (HR) level and maximum residue level (MRL) were established for specific crops treated with pesticides. In the 1990s, with increased awareness about cholinesterase-inhibiting pesticides, consumer exposure methodology moved from tolerable maximum daily intake (TMDI) to national estimated daily intake (NEDI) and national estimated short-term intake (NESTI) for acute effects such as

neurotoxic or behavioural effects. However, because point estimates gave results that were too conservative, because multifactorial submodels were used, because of a combination of these elements, and because results from one single event may differ from the general tendency, gross overestimates were obtained for several parameters. In addition, losses of pesticide residues when processing put pressure on to ensure that exposure calculations were as realistic as possible while still protecting the consumer. Probabilistic models, therefore, were developed tentatively to be able to take into account the interactions between the large number of variables that would be present in reality (Hamey and Harris, 1999).

A distribution characterises the range of values from a specific set of measures (for example, body weight) in the general population. It describes the most likely values and their variations, and provides a picture for a group of data. A Monte Carlo simulation works by assigning distributions to input parameters (e.g. body weight, food consumption or levels of a contaminant in food). The simulation randomly selects values from the distributions and calculates the exposure based on the selected values and an equation. It repeats the process thousands if not millions of times. The output is a plot with the calculated values in the form of a distribution of results (for example, intakes of pesticide residue). There are alternatives in the choice of the probabilistic model. For the presentation of distributions, a range (triangular, normal or log-normal functions) can be used and may or may not be truncated. Triangular distributions are limited at the upper end, normal distributions should be truncated to avoid unrealistic values and log-normal distributions should be truncated at the high end to avoid unrealistic values.

Probabilistic modelling has been employed to assess the potential exposure to residual BADGE in can coatings from canned foods in Europe. Potential variables modelled were food consumption quantities, variety of products, migration levels and individual consumer body weights. The Monte Carlo approach was used to model the consumption of a variety of canned food products and to model the migration levels of BADGE in the foods. Certain basic assumptions were made:

- the intake of BADGE was principally from canned foods with an approximate average consumption of 1 kg/day of canned food;
- the variety of food consumed was proportional to the production of canned foods; and
- migration levels measured by the Ministry of Agriculture, Fisheries and Food (now the Department of Environment, Food and Rural Affairs) in the UK for various food products were representative for all of Europe.

The basic equation used for exposure was the sum of the consumption for each food group multiplied by the migration level divided by the total consumption of canned food, assumed to be 1 kg. The minimum, average and maximum values for each food group for each country (seven countries = seven data points) were determined. From these statistics, a distribution was approximated. A log-normal distribution was selected based on professional judgement. An average consumption near 1 kg allows for very high end consumption levels beyond the available data. This appeared to represent the general public's use of canned foods. Most people are not expected to have a high proportion of their diets from canned foods every day. The number of simulations used in the model was specified as 5000. Outliers were identified. A sensitivity analysis for the average BADGE content for various food groups also was conducted based on the contribution to variance. Based on the available analytical data, the average food contamination appeared to be 0.245 µg BADGE/kg of food consumed (max 11.6 µg BADGE/kg), which is equivalent to 0.004 µg/kg of body weight/day for a 60-kg individual (max 0.19 µg/kg of body weight/day).

As a comparison, a single consumption of the contents of a 50-g can with a BADGE level of 1 mg/kg would give rise to a 50 µg intake (0.8 µg/kg of body weight). Because the Monte Carlo distribution is expressed per lifetime and includes several food items, a comparison is not possible. Nevertheless, the results obtained in this pilot study using Monte Carlo simulations presumably present a more realistic assessment of lifetime exposure from BADGE in canned foods. In addition to average values in this plot, various high percentiles for reported parameters selected by the programme (for example, grams of foods consumed per day and migration levels for these food groups) were obtained.

Because the Monte Carlo approach has been used in other fields for quite some time, considerable experience is available. The use of probabilistic modelling such as Monte Carlo conveys advantages, including the fact that such modelling:

- makes more use of data;
- replaces single input values with probability distributions; and
- refines point estimates and thus avoids the impression of absolute safety or absolute risk.

To make use of the probabilistic approach, food consumption data should be collected. Data should not be limited to that obtainable at a national level. The minimum set of data that would be needed for food contact materials should be adequately characterised. Moreover, knowledge is needed about the food consumption method used to collect the data. For food contact materials, it might be sensible to standardise (harmonise) the most appropriate food consumption method to use in constructing the model. Data on levels of food packaging substances could be added to the model one by one after the food consumption data are available.

Using probabilistic modelling should be the second or third option when estimating exposure from contaminants in food. A point estimate of food intake is a cheaper and simpler approach, whereas probabilistic modelling is costly. A decision tree for the entire approach of assessing exposure from food contact materials may be useful in avoiding unnecessary mistakes *(see section on Food Consumption Data on page 9)*. Traditionally, regulators have used point estimates. In order to get acceptance for probabilistic modelling when assessing exposure, it is necessary to have transparency and a clear explanation of uncertainties when putting data in the model.

Biomarkers

Biomarkers, such as urinary metabolites or hemoglobin adducts, that can give a more direct measure of exposure to a substance may be used either to assess that exposure or to validate and improve other indirect dietary exposure models such as probabilistic models. However, for biomarkers to be useful, the metabolite should be uniquely associated with the substance of interest, the relationship between dietary exposure and excretion should be established, any variation in excretion between individuals should be known and it should be clear that no other sources of the chemical in question (endogenous or exogenous) are present to contribute to that metabolite.

A case study for DEHA demonstrated the way in which biomarkers have been used in this area. DEHA has a long history of use as a plasticiser in PVC cling-film. Cling-film is employed both for wrapping foods at the retail level (for example, cheese, cooked meat, etc.) as well as for use in the home for a variety of applications (for example, covering cooked foods in the refrigerator, wrapping sandwiches, etc.). Over many years, exhaustive studies and numerous surveys have investigated DEHA migration into fatty foods to assess the levels of DEHA contamination in retail and home-wrapped foods. In 1986, and again in 1990, in the UK, this food data was used to make

crude calculations of likely human exposure to DEHA. Maximum estimates of 16.0 and 8.2 mg/person/day, respectively, were obtained in the two studies using a number of assumptions about food consumption and dietary behaviour. In 1994, a very different approach to assessing exposure was established using 2-ethylhexanoic acid as a urinary biomarker. For a UK population group of 100 volunteers, this biomarker study gave an average estimate of DEHA exposure at 2.7 mg/person/day, with a skewed distribution from 0.5 to 10.5 mg/person/day. This was believed to be in good agreement with exposure estimates obtained directly from the food data.

Subsequently, the original food contamination data was used to establish a probabilistic model of exposure to DEHA. Distributions for intake of PVC-wrapped food types (for example, cheese), migration levels of DEHA for those food types and body weights of individuals were used. Preliminary results indicated a good correlation between the exposure distribution obtained from the modelling data and the distribution indicated from the biomarker data. The biomarker data will be used in the future to provide a basis for further refining of the probabilistic model.

One important output from (probabilistic) modelling is the information it gives about the quality of the food contamination data required and its ability to indicate where the model is sensitive to patterns of food consumption. The probabilistic approach will have specific significance where data on extreme consumption are an important element in the exposure assessment.

Multiple-way data or extensive data allow for refinement in exposure assessments

Some chemical substances, such as styrene monomer, are widely used in a variety of food contact applications, which implies the potential for low-level exposure from many packaging sources. This is in contrast to DEHA, with which occasional high level migration occurs only into certain foods, such as cheese. The same applies to BADGE, which has been used in lacquers for cans. The discovery of high levels of BADGE in canned fish products in 1995 prompted the need to use food consumption data in a more structured way in this field. This can be seen as a milestone in the move towards estimation of real exposure compared with basing health risks on migration results. In this case, large amounts of migration data are available, and a solid picture of the average exposure for the general population can be made. However, the important question remains as to who is a high consumer and what constitutes individual exposure for high consumers.

Styrenic polymers and copolymers are used in a wide variety of food contact applications, both for single and repeated use. These applications encompass all food types (fatty, aqueous, acidic and alcohol) with contact at temperatures ranging from refrigerated storage to baking and for time periods from a few minutes to several months. Most styrenic plastics contain a fairly constant level of residual styrene monomer, typically 200–300 mg/kg, an amount that can be readily determined. Large amounts of data are available on the migration of styrene into food and food simulants. Generally, migration into olive oil is higher than migration into aqueous or alcoholic simulants. A worst-case estimate using migration data into olive oil of 300–600 µg styrene would give rise to an intake of 300–600 µg styrene/day if 1 kg of foodstuff in contact with 6 dm^2 material were ingested. On the other hand, a modified refined exposure assessment would give an intake of 15–30 µg styrene based on infrequent (more consistent with reality) contact with fatty food and a packaging use factor of 0.1 (taken from the American system for packaging usage for polystyrene). Estimates of average exposure range from 0.2 to 1.2 µg (literature search: ≥1.8–3.0 µg; total diet study: 9.0 µg/person/day using a migration model). Estimates of high exposure considering different food items packed in various packagings would give rise to an exposure of 22–32 µg/person/day of styrene.

Exposure to BADGE from canned fish in oil has been assessed from consumption data collected from each of the EU Member States and Switzerland, with migration data from a European survey of 382 samples in 1997. Trade figures were used when no food consumption data were available. The average consumption of canned fish in Europe was found to range from 2.3 kg/person/year in the UK to 5.1 kg/person/year in Denmark (compared with an estimated average per capita consumption of 2.65 kg/person/year as a whole for Europe). The exposure was calculated as micrograms per person per day. The data indicated that exposure to BADGE was in a range <4 mg/person/year or less than 9 µg/person/day, a fairly low exposure, in part resulting from the fact that canned fish is a relatively minor dietary item. An approximation assuming an average body weight of 60 kg for an adult would thus yield 0.15 µg/kg of body weight per day compared with the provisional limit of 1 mg/kg and an assumed 1 kg of food ingested.

Because consumption data on canned fish for Europe were not expressed in one uniform way, an estimation of the consumption had to be carried out. Some countries report import data, some balance-of-trade data and others provide estimated figures for canned fish consumption. However, in no instance is the question addressed as to whether some individuals are consuming canned fish in high amounts. An additional problem was that not all fish products reported were canned.

A migration study for BADGE covering the 15 EU Member States suffered from some shortcomings, such as a varying number of samples analysed. For example, one sample with a high level of BADGE (possibly an outlier) was found, resulting in a high average level of BADGE in canned fish for that specific country. High levels of BADGE, in particular, were associated with small cans, such as those used for anchovies, with high surface-area-to-volume ratios. In addition, the greater thickness of the can coating might have been an important factor. Another problem was the handling of results in which BADGE levels were below the detection limit. However, from the food consumption point of view, anchovies clearly are not a fish product consumed by everyone. Italy is a country with a high consumption of anchovies in general, but for the entire population probably only a small fraction of consumers could be regarded as high anchovy consumers.

These attempts to estimate exposure have raised fundamental questions about the definition of high consumers. Are they:

- consumers of large amounts of food in relation to body weight (for example, children);
- consumers of large amounts of specific food groups (with high levels of contaminants); or
- subgroups such as individuals with low incomes or ethnic groups?

This leads to questions about who is at risk. Are they:

- consumers of large amounts of specific types of food (for example, convenience food);
- consumers of small pack sizes;
- consumers showing brand loyalty; or
- consumers buying economy brands?

Exposure should be linked to the need for toxicity testing

Accurate and reliable methods of exposure assessment constitute a key component of the risk assessment process for packaging materials. Various approaches are available to estimate exposure, ranging from making the assumption of 100% migration to more refined methods taking account of quantitative measures of migration into food linked to survey data on intake of specific foods. However, using these methods to estimate exposure involves several conservative assumptions, such as:

- extent of use of a specific packaging material for food categories and share of market;
- migration under exaggerated or worst-case scenarios; and
- use of 3 kg food/person/day (in the US) or dietary survey data.

The link between an adverse effect level (toxic effect) and exposure (dose) is the critical point to remember. Toxicity testing required for approval of a food packaging substance should be proportionate to exposure. This leads to such questions as:

- when is exposure to a food contact substance so low that it presents, at most, a trivial risk; and
- what constitutes a potentially significant exposure, and how do we assess risk from such exposures?

A great deal is known about the relationship between chemical structure and potential for toxicity. The FDA has compiled a large database of substances with well-established toxicity/carcinogenicity. Using those data, the US agency predicts a risk for untested substances with a defined exposure. Human exposure thresholds can be defined below which it is possible to limit the need for any toxicological data.

In 1995, the FDA established a 0.5-ppb limit in the diet (corresponding to a dietary exposure of approximately 1.5 µg/person/day based on a total diet of 3 kg) as the "threshold of regulation for substances intended for use in food contact materials". The concept of a threshold of regulation (ToR) can be useful in determining the degree of rigour required in making intake estimates. This threshold represents the daily human exposure to a chemical below which there is no significant risk of adverse health effects from chronic exposure. Thresholds can be identified both for noncarcinogenic and possibly also for carcinogenic endpoints.

Databases are available to describe the quantitative relationship among exposure, chemical structure and toxicity for a wide variety of substances of different structure. These databases provide a reference point from which to judge the safety of chemical substances. Noncarcinogenic substances have been classified according to their toxicity, expressed by their NOELs. For structural class 3 substances (substances of a chemical structure that permit no strong initial presumption of safety or may even suggest significant toxicity; the "worst" class), taking into account 95% of the NOEL, a ToR intake of 1.5 µg/day still leaves a large safety margin. Migration below specified thresholds would limit the need for toxicological evaluation.

CONCLUSIONS AND NEXT STEPS/FUTURE REQUIREMENTS

Risk analysis with emphasis on risk assessment

Risk assessment should be science based and not mixed up with risk management. Risk assessments should be carried out in a transparent manner and followed by a thorough risk communication, because the risk assessment process involves several uncertainties for each step involved.

Considering the conservative approach applied by the European Commission and the SCF to evaluate potential dietary exposure to substances migrating from packagings (for example plastics and coatings), the average EU consumer seems, in general, to be well protected.

Until now the focus has been on migration and migration limits in the EU legislation on food contact materials. To develop a refined dietary exposure evaluation process and prevent unnecessary testing (and the accompanying commitment in related resources and test animals), there is a need to link to and make greater use of food consumption data.

Requirements

- Uncertainties in the risk assessment process should be defined and addressed in a clear and transparent manner. Research should be promoted in areas with gaps (for example, dietary exposure assessments).

Food consumption data

To a large extent, food consumption data are available for consumers in the EU, although these data are not accessible in a uniform way. Gaps exist in knowledge about food consumption in certain subpopulations, such as ethnic groups who for cultural or traditional reasons consume more of certain foods than do other groups. Food consumption data of high quality is needed for vulnerable groups, such as children or extreme consumers.

To make use of food consumption data, the objective of the food survey must be known. Generally, sufficient knowledge is not available about the food consumption methods (advantages and disadvantages) used. The food consumption method (time frame covered in data collection) is critical for results (especially for high and low intake levels). More refined and validated assumptions of food consumption are needed.

When carrying out a food survey to estimate the intake of a food packaging substance a top-down approach, beginning with the most "rough" method, is the most pragmatic and cost-efficient (screening <–> quantification) way.

Requirements

- Collect food consumption data for certain vulnerable groups such as children or extreme consumers; define needs.
- Increase knowledge about food consumption methods (advantages and disadvantages). A strategy to find the most appropriate food consumption method for food contact materials is desirable, including standardisation.

- The development of a decision tree for the choice of screening or quantification of food intake would be desirable.
- A tentative approach to establish food consumption factors for aqueous and alcoholic foods within the EU should be explored (food consumption factors for fatty foods have already been proposed).
- For the future, improved assessment tools and data sources should be developed to screen and quantify the exposure of priority food chemicals in a cost-effective way.

Food packaging usage

For food packaging materials, numerous data of high quality are available when considering the total amount of packaging material used. Sources are well known, units are few and definitions are more consistent than when assessing the packaged product. At the packaged product (consumer) level, data are few and of low or variable quality. Definitions are inconsistent, units are numerous and sources of information are disparate.

Packaging trends, differences among countries (legal requirements and cultural differences) and a high diversification of packaging materials may present problems when looking for uniformity.

Requirements

- Data from the Maurice Palmer Associates study should be investigated to see whether they are still usable; drawbacks should be addressed if these data are used.
- Packaging trends, differences among countries (legal requirements and cultural differences) and the way in which diversification of packaging materials affects packaging use should be investigated.
- Specific food items should be prioritised for further investigation.
- A step-wise procedure to estimate packaging use should be developed (for example, by developing packaging usage factors).

Migration aspects

Migration expressed as the concentration of a contaminant in foodstuffs should not be confused with exposure, which is the daily consumption of food containing the substance over a lifetime. Packaging size may matter when testing, and compliance or noncompliance may depend on how restrictions are expressed within EU legislation. Small packages tend to give rise to higher migration which seems to indicate higher exposure. Food simulants and real foods are both needed in migration testing. The choice is made as to whether compliance testing (food simulant) or a sample tested in the official control (real foods) is undertaken.

Requirements

- Revision and clarification of EU legislation are needed. Improvements and amendments are required for Directive 85/572/EEC (correlation between food simulants and foodstuffs) and Directive 90/128/EEC.
- Gaps concerning migration testing (in relation to restrictions in the legislation) should be defined.
- Protocols are needed to address how to handle false negative migration test results (depending on reaction with the food simulant or foodstuffs, etc.), how to handle outliers

when few samples are available or few tests have been carried out and how to handle samples with nondetectable levels in comparison with detectable levels of migrants.

- In addition, there is a need to develop migration modelling in the area of multilayer packaging materials to facilitate compliance testing.

Probabilistic modelling

Probabilistic modelling, such as Monte Carlo simulations, have been used successfully (for example, to assess human exposure) in the environmental field for quite some time and occasionally have been applied to food additives and pesticide residue levels in foods. A Monte Carlo simulation is an empirical method to incorporate more knowledge and determine variation and/or uncertainty. It is a procedure that can examine a number of factors using individual distributions, such as food consumption, residue levels of a contaminant, and body weight. Monte Carlo distributions present a more realistic assessment of lifetime exposure from food contact materials than conventional point estimates (worst-case estimates). Probabilistic modelling may be a useful tool to estimate exposure from food contact materials.

Requirements

- Criteria should be set on ways to best utilise probabilistic modelling for food contact materials. Harmonisation of a suitable food consumption method for food contact materials may be desirable.
- A decision tree for the most suitable approach to assess the exposure to substances in food contact materials might be useful. The purpose of the exposure assessment should be the guiding principle for which way to go, from point estimates (the inexpensive, rough alternative) to probabilistic modelling (the more costly method that yields refined assessments of lifetime exposure).
- Traditionally, point estimates have been used by regulators. To gain acceptance for probabilistic modelling when assessing exposure it is necessary to have transparency and a clear explanation of uncertainties when putting data in the model.

Biomarkers

Biomarkers, such as urinary metabolites or hemoglobin adducts in humans, may be used to verify an estimation of exposure from a food contaminant. The background level of the metabolite, stability, individual variation, and whether other sources (endogenous or exogenous) may contribute to the level, are essential factors to consider. Furthermore, biomarker studies are costly and should be only a second option. Biomarkers can be used to verify and improve a probabilistic model for exposure assessments.

Requirements

- For widely used food packaging substances giving rise to high migration, the possible use of biomarkers may need to be investigated.

Multiple data or extensive data allow for refinement of exposure assessments

The collection of multiple data or extensive data allows for a refinement of the exposure assessment. Collecting and comparing food consumption data and migration data (with undetectable levels, false-negative and false-positive results and outliers?) includes several uncertainties, including the identity of a typical high consumer. What is a high consumer? Do we mean consumers of large amounts of food in relation to body weight or consumers of large amounts of specific food groups (with high levels of contaminants)? This leads to questions about subgroups, such as individuals with low incomes, members of ethnic groups, consumers of large amounts of specific types of food (such as convenience food), consumers of exclusively small pack sizes, consumers showing brand loyalty and consumers buying economy brands.

Requirements

- The data set (raw data, including objective, origin, source, number of data points and quality) should be carefully checked when using food consumption data, packaging usage data and migration data (are standardisation and harmonisation of methods needed when collecting data?).
- Links between brands, packaging type and migration level should be identified, as should any links between food intake factors and packaging factors.
- Valid sampling procedures must be established for undertaking food surveys.
- A strategy is needed for handling survey data so that samples with undetectable levels, false-negative and false-positive results and outliers are included.

Exposure should be linked to the need for toxicity testing

Regulation of food packaging materials should be proportionate to risk and should ensure consumer safety. Reference databases used to describe the quantitative relationship among exposure, chemical structure and toxicity for a wide variety of substances of different structure are available. Threshold of regulation (US concept) offers an approach for approval of some substances for use in packaging materials without the need for toxicological data. Higher thresholds of regulation are feasible for noncancer endpoints. Thresholds can help to define the degree of refinement needed in intake estimates.

Requirements

- ToR should be developed to approve food packaging materials without the need for provision of extensive toxicological data.

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