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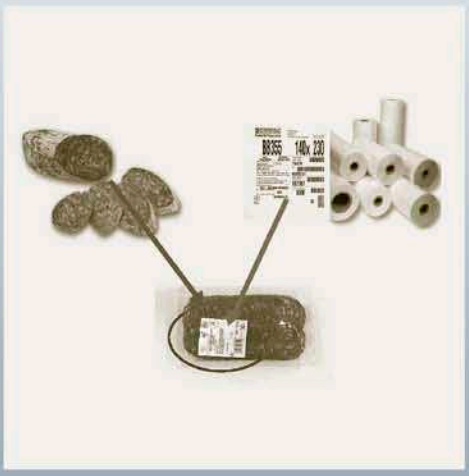

Chemical migration and food contact materials

Edited by Karen A. Barnes, C. Richard Sinclair and D. H. Watson

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Chemical migration and food contact materials

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CRC Press
Boca Raton Boston New York Washington, DC

WOODHEAD PUBLISHING LIMITED
Cambridge, England

Published by Woodhead Publishing Limited, Abington Hall, Abington
Cambridge CB21 6AH, England
www.woodheadpublishing.com

Published in North America by CRC Press LLC, 6000 Broken Sound Parkway, NW, Suite 300, Boca Raton, FL 33487, USA

First published 2007, Woodhead Publishing Limited and CRC Press LLC

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library.

Library of Congress Cataloging in Publication Data
A catalog record for this book is available from the Library of Congress.

Woodhead Publishing ISBN-13: 978-1-84569-029-8 (book)
Woodhead Publishing ISBN-10: 1-84569-029-X (book)
Woodhead Publishing ISBN-13: 978-1-84569-209-4 (e-book)
Woodhead Publishing ISBN-10: 1-84569-209-8 (e-book)
CRC Press ISBN-13: 978-0-8493-9130-9
CRC Press ISBN-10: 0-8493-9130-X
CRC Press order number: WP9130

The publishers' policy is to use permanent paper from mills that operate a sustainable forestry policy, and which has been manufactured from pulp which is processed using acid-free and elementary chlorine-free practices. Furthermore, the publishers ensure that the text paper and cover board used have met acceptable environmental accreditation standards.

Project managed by Macfarlane Production Services, Dunstable, Bedfordshire, England (e-mail: macfarl@aol.com)
Typeset by Replika Press Pvt Ltd, India
Printed by T J International Limited, Padstow, Cornwall, England

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1

Chemical migration into food: an overview

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1.1 Introduction

Packaging is beneficial. It protects the packaged foodstuff from spoilage by external agents such as pests, odours, micro-organisms, light and oxygen. However, the transfer of chemicals from packaging to food may have a negative impact on the quality and safety of food. This is why migration from packaging and other food contact materials merits study, consideration and control. Packaging is perhaps the most important, and certainly the most obvious, example of a material or article intended to come into contact with food. There are many other situations where materials are deliberately used in contact with food during its manufacture, transport, storage, preparation and consumption. These include the materials used to construct storage vessels, conveyor belts, tubing, food preparation surfaces, and cooking and eating utensils.

Food and beverages can be very aggressive products and may interact strongly with materials that they touch. Collectively, they are as good as many of the solvents used in a chemistry laboratory. For example, food acids can corrode metals, fats and oils can swell and leach plastics, and beverages can disintegrate unprotected paper and cartonboard. In fact, no food contact material is completely inert and so it is possible for their chemical constituents to 'migrate' into the packaged food. Metals, glass, ceramics, plastics, rubber and paper can all release minute amounts of their chemical constituents when they touch certain types of foods. This release of chemicals to the food is known technically as migration. This can be defined scientifically as 'the mass transfer from an external source into food by sub-microscopic processes'. More colloquial terms used are 'leaching', 'bleeding' or 'leaking' of substances

from the packaging into the food. In this chapter the term 'food' is used throughout to mean both food and beverages. Similarly, 'packaging' also denotes other food contact materials.

Any chemical migration into food is important because it can have two impacts on the food.

- Food safety – some substances used to manufacture packaging materials could be harmful if they migrated to the food and were ingested in large enough quantities.
- Food quality – migrating substances may impart taint or odour to the food and so reduce consumer appeal.

Chemical migration from packaging is not an inconsequential process. It has been estimated that the *per-capita* use of packaging materials for retail foodstuffs sold in the EU countries is about 1200 cm^2 per person per day. This is about the size of two A4 sheets of paper and is not an inconsiderable amount. It is also about the area of film used for just two 35 gram packets of potato crisps, for example. With the increasing consumption of snack and take-away foods (Chapter 19) and moves to smaller pack sizes (with higher surface area to mass ratio) to satisfy smaller households and convenience eating, it seems inevitable that the use of packaging materials in contact with our diet will continue to increase.

For some food–package combinations the concentration of chemical migrants in the food can approach that of substances used as direct food additives, at levels of tens of parts-per-million (mg substance per kg of food, mg/kg). Therefore, all parties involved in the production, transport, selling and consumption of foods need to be aware of the potential for chemical migration and ways of minimising it. Everyone involved needs to ensure that packaging materials are correctly specified and used for the intended application so that there is no excessive chemical migration. The chain of care involves:

- primary manufacturers of raw materials, e.g., polymer and paper manufacturers
- converters who turn the raw material into packaging for food use
- vendors of the materials, e.g., retailers of articles, supply companies
- users of the material – the food packer
- food retailers
- enforcement authorities
- consumers – with respect to the proper use both of pre-packaged foods and of materials and articles used in the home.

The correct specification and use of packaging materials requires effective exchange of information up and down this chain of use. It also requires an understanding of chemical migration and the main factors that control it.

1.2 Chemical migration and the main factors that control it

1.2.1 The mechanistic basis of migration

Migration of chemical substances is a diffusion process subject to both kinetic and thermodynamic control and can be described by diffusion mathematics derived from Fick's Law. The mathematics describe the diffusion process as a function of time, temperature, thickness of the material, amount of chemical in the material, partition coefficient and distribution coefficient. The kinetic dimension of migration dictates how fast the process of migration occurs. The thermodynamic dimension dictates how extensively the transfer of substances will be when migration is finished – when the system is at equilibrium. The kinetic and thermodynamic aspects should not be confused. For example, migration may proceed at a slow rate but, if the chemical migrant has a higher affinity for the food than for the packaging material, then given enough time (e.g. a long shelf life) it may still migrate extensively into the food. On the other hand, if a different food or beverage is packed and the chemical is only poorly soluble in that food or beverage, then migration could be low no matter how long the shelf life is.

Being a molecular diffusion process, chemical migration is subject to the normal laws of physics and chemistry. There are several determinants of chemical migration and exactly what migration occurs depends first on the identities and concentrations of the chemicals present in the packaging material. Other important parameters are the nature of the food along with the conditions of contact. Lastly, the intrinsic properties of the packaging material itself are important considerations. If a material interacts strongly with the food it could give high migration by leaching. Conversely, an inert material with low diffusivity is likely to give low migration values. It is important to understand the factors that control chemical migration because from this understanding springs the ability to prevent or limit any undesirable migration into foods.

1.2.2 Composition of the packaging material

The packaging material is the source of any chemical migration. The extent of any migration depends first on the concentration of the chemical in the packaging. If a substance is not present in a packaging material then it cannot migrate. This is self-evident but easily forgotten, and is important especially when considering models to assess consumer exposure (Chapter 6). If a substance is present in the packaging then, other things remaining equal, migration levels will be higher if the concentration in the packaging is increased and *vice versa*.

1.2.3 The nature and extent of contact

The nature and extent of any contact between the packaging and the food is the next important parameter to consider. This depends on the physical

properties of the food (solid foods make only limited contact whereas liquids make more extensive contact) and the size and shape of the pack. Consider an individual portion pack of margarine (say, 7 g in contact with 28 cm^2, or 4000 cm^2/kg) compared to a catering pack of the margarine (say, 2 kg in contact with 1050 cm^2 or 525 cm^2/kg). If the same plastic was used to make the two pack sizes (polystyrene or polypropylene would be candidates) then the same migration on a unit area basis would give rise to an eight-fold higher exposure per portion eaten for the individual portion pack, compared with the catering pack. The most extreme examples of this mass ratio of surface area to food are to be found outside the area of general packaging materials, for example, the relatively limited contact made by small gaskets used in a large food processing plant, gloves or conveyor belts used to handle tonnes of food in a packing plant, or tubing used to pipe tens or hundreds of thousands of litres of liquid during its service life.

Another factor that determines the nature and extent of any contact with the food is the presence of a barrier layer. If the chemical that may migrate is located in one layer of the packaging material but this is separated from the food by an intervening layer, then this barrier layer – between food and chemical migrant – may retard or prevent migration from occurring. This is quite a common situation with modern multi-laminate packaging materials where inks, adhesives, or one or more of the laminate plies do not touch the food directly. The packaging industry has long exploited barrier layers to protect food products from air, light and moisture, in controlling the inner atmosphere of the pack (MAP and CAP, modified and controlled atmosphere packs), and in retaining desirable aromas whilst protecting the packed food from undesirable odour pick-up. The same physico-chemical laws on barrier properties that endow these quality benefits can also be used to prevent or limit chemical migration.

1.2.4 The nature of the food

The nature of the food that touches the packaging is important for two reasons:

Incompatibility

If the packaging is not compatible with a given type of food then there can be a strong interaction leading to an accelerated release of chemical substances. Examples are the interaction of fats and oils with certain plastics that leads to swelling of the plastic and leaching of substances from that plastic. Leaching, formally known as Class III migration, occurs because the diffusivity of the plastic increases with any swelling. This means that with swelling, the plastic starts to behave more like a fluid. An even more extreme example of an undesirable interaction between packaging and food is the corrosion of uncoated metal surfaces leading to high metal release into certain acidic foods, or the leaching of heavy metals from ceramic glazes. It is important to avoid such

obvious mismatches and ensure that packaging materials are compatible with the food that it is intended to pack.

Solubility
The nature of a food has a pronounced influence on chemical migration because it determines the solubility of any packaging chemical in that food. This influences the amount of migration that may occur. Foods are conventionally classified into five categories: aqueous, acidic, alcoholic, fatty, and dry. The three main drivers of migration with respect to these different food categories can be characterised by the type of substances that have a high affinity for them and so tend to migrate more readily (Table 1.1).

1.2.5 The temperature of contact

The migration of chemicals is like virtually all chemical and physical processes in that it is accelerated by heat. So migration will occur faster if the temperature is raised. Packaging materials are increasingly used under a very wide range of temperature conditions, ranging from storage deep frozen, refrigerated and at ambient temperature, to boiling, sterilisation, microwaving and even baking in the pack. Clearly, a material suitable for one particular application may not necessarily be suitable for another.

1.2.6 The duration of contact

Materials suitable for short duration contact may not be suitable for longer service times. The kinetics of migration are, to a first approximation, first-order in that the extent of migration increases according to the square-root of the time of contact: $M \propto t^{1/2}$. The time (duration) of contact for common packaging can vary enormously:

- minutes (e.g. take-away foods)
- hours (e.g. fresh bakery, sandwiches)
- days (e.g. fresh milk, meat, fruit and vegetables)
- weeks (e.g. butter, cheese)
- months and years (e.g. frozen foods, dry goods, canned foods, drinks).

The performance requirements of the material must be specified accordingly.

Table 1.1 Classification of foods and the types of chemical migration that they are likely to elicit

Nature of the food in contact	Nature of chemicals most likely to migrate
Acidic foods, aqueous foods and low alcohol beverages	Polar organic chemicals, salts, metals
Fatty foods, distilled spirits	Non-polar, lipophilic ('fat-loving') organic substances
Dry foods	Low molecular weight, volatile substances

1.2.7 Mobility of the chemicals in the packaging

The mobility of a chemical in the packaging material depends on the size and shape of the molecule, any interaction it experiences with the material, and the intrinsic resistance to mass transfer that the material presents. It is assumed that the chemical is compatible with the material. If the chemical is not compatible with the material then it could 'bloom' to the surface and give enhanced migration. The exact mechanisms of migration and its mathematical modelling are considered in depth in Chapter 8. To provide a general understanding, it is helpful to consider three general cases: impermeable materials, permeable materials and porous materials. These are depicted in Figs 1.1–1.3 and described below.

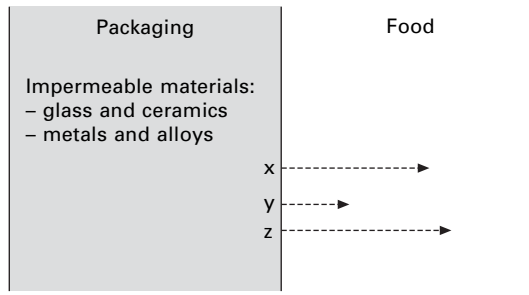

Fig. 1.1 Depiction of chemical migration from an impermeable material.

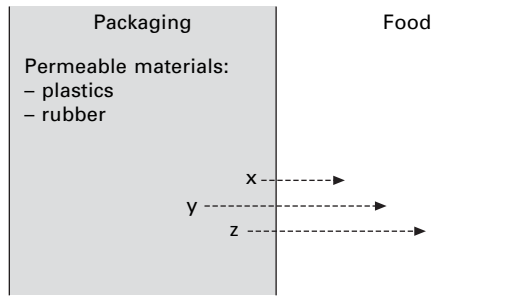

Fig. 1.2 Depiction of chemical migration from a permeable material.

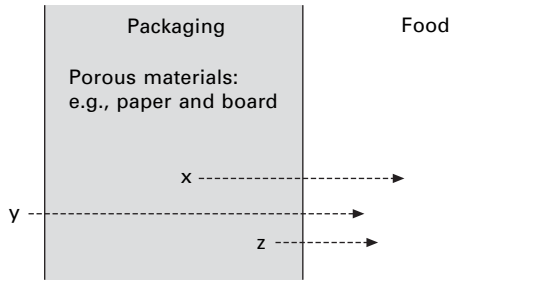

Fig. 1.3 Depiction of chemical migration from and through a porous material.

Impermeable materials
These are exemplified by 'hard' materials such as metals, glass and ceramics. The material is an absolute barrier and there is no migration from the interior. Migration is confined to a surface phenomenon only.

Permeable materials
These are exemplified by 'plastic' materials such as plastics, rubbers and elastomers. The material offers some limited resistance to migration but this can occur not only from the surface but also from the interior of the material. The resistance to mass transfer depends on the structure, density, crystallinity, etc., of the material.

Porous materials
Exemplified by paper and board materials with a heterogeneous, open network of fibres with large air spaces or channels. Low molecular weight substances in particular can migrate rather rapidly with little hindrance offered.

1.2.8 Summary of factors that control the migration process

Migration from packaging materials is a diffusion process that is subject to the normal laws of chemistry and physics.
Migration increases with

- increased duration of contact
- increased temperature of contact
- higher levels of the chemical in the packaging material
- surface area of the contact
- aggressive foodstuffs.

Migration decreases with

- higher molecular weight substances in the packaging material
- only dry or indirect contact
- low diffusivity ('inert') packaging materials
- presence of a barrier layer.

1.3 The range and sources of chemicals in food packaging that pose a potential risk

1.3.1 The range of materials used in contact with foods

Food contact materials are generally classified into ten main categories. As even a cursory glance around any supermarket will confirm, the first four categories in the following list dominate the packaging of food in the developed world:

1. plastics, including varnishes and coatings
2. paper and board

3. metals and alloys
4. glass
5. regenerated cellulose
6. ceramics
7. elastomers and rubbers
8. paraffin waxes and micro-crystalline waxes
9. wood, including cork
10. textile products.

Plastics in particular have a dominant position, especially considering that many paper and board packages are laminated to plastics as the food contact surface and most metal cans are lacquered inside with polymeric coatings to protect the metal from the food.

1.3.2 The chemicals in these food contact materials

Substances present in these materials may originate from a number of sources:

- known ingredients used to make the basic packaging materials of plastics, paper, coated and uncoated metals, and glass, for example, monomers and additives in plastics, chemicals used in paper-making, pigments used on ceramics
- chemicals used to convert or fabricate the basic packaging material into its finished form, for example, inks and adhesives
- known or unknown isomers, impurities and transformation products of these known ingredients
- unknown contaminants in the raw materials used, and especially those in the feedstock if materials are recycled.

Unexpected or unknown substances originating from the last two categories in this list are what have become known as NIAS (Not Intentionally Added Substances). These can be a particular challenge to industry and enforcement authorities alike.

1.4 Health issues

There can be absolutely no doubt that food packaging has greatly improved human health both now and through the ages by helping to provide regular and reliable supplies of safe, wholesome and nutritious foods. But chemical migration is always undesirable and if not controlled it could be hazardous to the health of consumers. The exception is for ‘active packaging’ which may be intended to release substances into the food with beneficial effects, such as antioxidants or preservatives. Active packaging is described in detail in Chapter 17.

The main health concerns are for possible effects from chronic (i.e. long-term) exposure to migrating substances. There are two specific exceptions to

this, where an acute effect may arise. One is migration of tin from tinplated steel into (especially) canned tomato products where high tin concentrations in food may cause short-term stomach upsets in some people but without any lasting harm. The other concerns latex allergen transfer which could have serious implications for some individuals. Recent research sponsored by the UK Food Standards Agency has shown that latex allergens may be present in some food packaging materials and that there is a theoretical possibility of transfer from the material to the food. The materials include cold seal adhesives based on latex and latex food-handling gloves. Further work is being done to improve methods to detect and quantify latex allergens in packaging and foods, to see if these allergens do migrate into food.

To address possible long-term health concerns, the risk assessment process involves describing the toxicological hazard profile of the chemical substance, using qualitative and quantitative data, and coupling this to an estimate of exposure to a chemical migrant, to assess any risk. Consequently, the information that is required on packaging chemicals comprises data on (i) toxicity, and (ii) dietary exposure. As a general principle, the higher the exposure the more toxicological information is required. The toxicological data required and how exposure may be estimated from migration concentrations are described in detail in Chapters 7 and 6 respectively.

1.5 Key scientific advances – achieved and needed

In outlining recent key scientific advances, it is in fact sobering to realise just how slow and hard-won some scientific advances have been. Looking back more than 25 years ago to a seminal meeting, the papers presented at the International Symposium on Migration held in Hamburg in 1980 are listed in Table 1.2. The chapters of this book reveal that many of the topics

Table 1.2 Topics covered in the 1980 Hamburg symposium

Topic	Papers
The diffusion mechanism of migration of low molecular weight components out of plastics	3
Mathematical modelling of migration	2
Migration studies and their relationship to dietary intake	1
The low molecular weight fraction of polyvinylchloride – a potential source for migration	1
Better food simulants – are they needed, are they possible?	1
Regulatory aspects of chemical migration	2
Migration experiments using simulants	3
Chemical analysis of foods and simulants	3
Sensory analysis of polyethylene	1

* Proceedings of the Third International Symposium on Migration, 22–24 October 1980, Hamburg (D). Unilever Forschungsgesellschaft mbH.

discussed in 1980 are still a matter of live debate now. These examples serve to illustrate that there can be a long gestation period for the development and general acceptance of ideas. For example, the very substantial investment made over the long term into the development of mathematical models of migration does appear to be bearing fruit at last.

1.5.1 Advances in analytical chemistry

With the almost universal uptake of GC-MS (gas chromatography coupled to mass spectroscopy) into analytical laboratories and with LC-MS (liquid chromatography coupled to mass spectroscopy) fast becoming commonplace too, analysis of foods for chemical migration in the ppm and ppb range (parts-per-million and parts-per-billion, milligrams and micrograms per kilogram, 1E-6 and 1E-9 respectively) is within the reach of most laboratories nowadays.

As analytical capabilities have evolved, there has been a swing away from a preponderance of migration measurements made using simulants (model foods, see Chapters 3 and 5), towards testing foods. This trend has coincided with a move in most European countries towards a more overt consumer protection stance and the establishment of Food Safety/Standards Agencies, with their attendant surveillance and research programmes, testing foods from border controls and the marketplace. The resulting concentration data are needed to allow estimates of exposure of consumers to chemical migrants.

With this increased emphasis on testing foods, activity in searching for alternative simulants has diminished. This is to be welcomed. The use of food simulants in compliance testing for the general case (see Chapter 15) is still important. But the quest for alternatives that mimic simulants that in turn are intended to mimic foodstuffs represents a cul-de-sac. A simulant has to resemble a food in its interaction with the food contact material. It is clearly the case that different simulants are needed for different foods and for different materials, paper versus ceramics versus plastics for example. And maybe even different simulants could be needed for different classes of plastics and different types of substances. But if simulants have to be fine-tuned and tailored for individual applications then they lose much of their utility.

1.5.2 Chemical assessment of the overall migrate

Of the overall migrate from plastics, rubber, paper, coatings, etc., we know the starting substances that are used to make the materials because these normally appear in compositional lists of monomers, additives, solvents and so forth. But relatively little detailed compositional information is known beyond this. Packaging materials may contain many substances that are not used intentionally and do not appear in lists of permitted ingredients.

Nevertheless, they may be present as impurities in the substances used, as reaction intermediates formed during polymerisation processes or as decomposition or reaction products. As stated before, these NIAS (Not Intentionally Added Substances) can be a particular challenge to the industry and authorities alike.

Mass spectroscopy (MS) is now an almost obligatory requirement for the task of migrate identification. It is the only technique that provides the standards of evidence that are required today. As described above, the techniques of GC-MS and LC-MS have reached a highly advanced state for the analysis of targeted ('known') substances. But their capabilities for detection and identification of unexpected or unknown chemicals (NIAS) are more limited. Advances to meet this requirement are desirable.

1.5.3 Estimation of migration levels by modelling

Since chemical migration follows basic chemical and physical laws it can be modelled using mathematics and computation. Empirical composition–migration relationships have been established for certain well defined plastics. There have been significant advances in mathematical modelling of migration into food simulants. One limitation is that existing computational programs are designed to overestimate migration compared to simulants, and simulants are in turn designed to overestimate migration to be expected into foods so the models have limited usefulness. There are interesting developments of modelling procedures for migration into foods and, if successful, these would be of great utility in providing migration concentration data for exposure estimates as part of general risk assessment procedures.

1.5.4 Hazard assessment of the overall migrate

Comprehensive chemical analysis of the total migrate is a challenging task. It would also go only part way towards a risk assessment of the food contact material. The substances detected would still have to be subjected to a hazard assessment, individually or collectively as a mixture. Procedures being developed that might help in this include testing the total migrate using one or more *in vitro* toxicity assays. The aim of this approach must be to use *in vitro* assays that are relevant to human health. To gain wide acceptance, it seems likely that any such *in vitro* assessment of the total migrate would need to be standardised and adopted by bodies such as ECVAM – the European Centre for the Validation of Alternative Methods.

There is a clear distinction between the aims of full chemical analysis and *in vitro* bioassay of the total migrate. The first attempts a full identification of all individual substances but gives no information on any hazard that the substances may pose. Hazard assessment must follow. In contrast, bioassay of the total migrate should give information directly on the hazard, if any, but cannot reveal any information on the identity and concentration of the

chemical substance(s) responsible. Chemical analysis would have to be applied if this information was required, perhaps using bioassay-directed fractionation, isolation and identification of the causative agent(s).

1.5.5 Quantitative hazard assessment

As described above, measuring chemicals in foods to parts-per-billion concentrations is rather routine nowadays. These capabilities in analytical chemistry have far outstripped the capabilities and capacity of risk assessors to evaluate the significance, if any, of the analytical findings. What is urgently needed are ways to accelerate the hazard assessment process. Writing as a non-specialist, it seems it would be useful to have scientifically justified, generally accepted procedures for using structure–activity relationships, structural alert databases and expert systems coupled with threshold(s) of toxicological concern or threshold(s) of regulation. These are described in Chapter 7.

1.6 Future trends

Technological advances accompanying the use of materials for food packaging have brought many benefits. Without wishing to appear complacent, it does seem that present-day food packaging materials are clearly fulfilling their primary rôle of protecting the microbiological safety of our packaged food, its quality and nutritional value. Consequently, the technological push is towards materials that have even better properties. These include the re-use and recycling of packaging materials, development of active and intelligent packaging, packaging with higher barrier properties, packaging derived from biobased source materials and biodegradable materials, and the use of nanomaterials.

Accompanying this technological push, there is a regulatory brake. Legitimate questions have been raised about the available evidence supporting the safety and desirability of new and existing packaging materials. That is to say, not that there is necessarily evidence of harm, but that the available chemical and toxicological evidence may not in some cases meet modern standards. These questions on safety arise mostly from the issue of chemical migration. How these questions are addressed in detail is described by the individual experts who have contributed chapters to this book.

1.7 Sources of further information and advice

FDA webpage on indirect food additives at http://vm.cfsan.fda.gov/~lrd/foodadd.html

Community Reference Laboratory for Food Contact Materials. Website at http://crl-fcm.jrc.it

Food Chemical Safety. *Volume 1: Contaminants*. D. H. Watson (editor), Woodhead Publishing Ltd, Cambridge, UK and CRC Press, Boca Raton, USA, 2001. ISBN 1-85573-462-1.

Migration from Food Contact Materials. L. L. Katan (editor), Blackie Academic and Professional, Glasgow, UK, 1996. ISBN 0-7514-0237-0.

Food Packaging: Ensuring the safety, quality and traceability of foods. Proceedings of the 3rd International Symposium organised by ILSI Europe. J. Gilbert and A. Theobald (editors). *Food Additives & Contaminants*, 2005, volume 22, issue 10.

Part I

Regulation and quality control of chemical migration into food

2

Regulation of food contact materials in the USA

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2.1 Introduction

In the United States (US), terminology and regulatory processes have changed dramatically in the past decade with regard to components of food contact articles, often referred to as indirect food additives. A thorough understanding of the US regulatory processes for these substances allows the regulated industry to determine the regulatory status of a substance and understand the available regulatory options. In this chapter, we discuss the past and present regulatory approaches for obtaining legal approval for use, interpretation of the regulatory status of the various components of a food contact article, and the administrative and technical reviews of a food contact notification (FCN).

2.2 Regulatory authority

Two acts are pertinent to any discussion regarding the regulation of food contact materials in the US. These are the 1958 Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act (FFDCA) and the National Environmental Policy Act (NEPA) of 1969. A brief discussion of the authority granted the Food and Drug Administration (FDA) under each follows.

2.2.1 FFDCA

The US Congress granted authority to the FDA to regulate food additives in the 1958 Food Additives Amendment to the FFDCA. A food additive is

defined as '…any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food.' (FFDCA, Section 201(s)). The food additive definition contains certain exclusions, such as for color additives, substances whose use is generally recognized as safe, and substances approved for their intended use prior to September 6, 1958.

As detailed in the FFDCA, a food additive shall be deemed unsafe unless it conforms to an exemption (for investigational use), a regulation listing or, as explained below, an effective food contact notification (FCN) (FFDCA, Section 409(a)). Moreover, in the US food additives require pre-market evaluation before introduction into interstate commerce. As originally established in Section 409(a)(3)(A), such an evaluation of a food additive can lead to an approval through a food additive petition resulting in the publication of a regulation authorizing its intended use. The food additive petition ('petition') process is codified in Title 21, Part 171, of the Code of Federal Regulations (denoted as 21 CFR 171.1 through 171.130). The general and specific regulations for all food ingredients and packaging materials, as per 21 CFR 170 through 189, are shown in Table 2.1. Experience has shown that the promulgation of a regulation for the food additive has often proved to be a lengthy and resource-intensive process. A thorough assessment of the cost (time)/benefit (safety) analysis of the administrative aspects of the petition process was a major factor leading to the development of two additional processes that have supplanted the petition process with regard to pre-market approval of components of food contact articles, these being the Threshold of Regulation (TOR) exemption process and the FCN process.

Table 2.1 General and specific listing regulations for food ingredients and packaging: Title 21 of the Code of Federal Regulations

Regulation	Description
25	Environmental impact considerations
170	General information on food additives
171	General information on food additive petitions
172	Direct food additive regulations
173	Secondary direct food additive regulations
174–178	Indirect food additive regulations
175	• Adhesives and coatings
176	• Paper and paperboard
177	• Polymers
178	• Adjuvants and production aids
179	Irradiation of foods
180	Substances permitted on an interim basis
181	Prior-sanctioned food ingredients
182	Generally recognized as safe (GRAS) substances
184	Direct substances affirmed GRAS
186	Indirect substances affirmed GRAS
189	Prohibited substances

In 1995, the FDA established the TOR exemption process (codified in 21 CFR 170.39) (U.S. Food and Drug Administration, 1995), exempting certain substances used in food contact articles from the requirement for an authorizing regulation prior to use in contact with food. To obtain an exemption, the following criteria must be met and reviewed and confirmed by FDA: the estimated daily intake from the proposed use of the substance must be less than or equal to 1.5 micrograms per person per day (equivalent to a dietary concentration of less than or equal to 0.5 micrograms per kilogram of food consumed) and the substance must not be known to be a carcinogen in man or animals. FDA may decline to grant an exemption if the substance is a potent toxin or if there is a reason, based on the chemical structure of the substance, to suspect that the substance is a carcinogen. In addition, the substance must not contain a carcinogenic impurity with a tumor dose 50 (TD_{50})[1] value of less than 6.25 milligrams per kilogram body weight per day. (A TD_{50} value of greater than or equal to 6.25 milligrams per kilogram body weight per day represents a lifetime cancer risk of less than or equal to 1×10^{-6} for a 60 kilogram person consuming 1500 milligrams of solid food per day.) Alternatively, if the substance is currently regulated for direct addition to food and the exposure from the proposed use is less than or equal to 1% of the acceptable daily intake value, a TOR exemption from the need for a regulation may also be granted.

In 1997, the FDA Modernization Act amended Section 409 of the FFDCA to establish a new process whereby food additives that are food contact substances (FCS) can be deemed safe for their intended use, referred to as the FCN process (U.S. Food and Drug Administration, 2002). The FFDCA defines an FCS as '…any substance intended for use as a component of materials used in the manufacturing, packing, packaging, transporting or holding food if such use in not intended to have any technical effect in such food.' (FFDCA, Section 409(h)(6)). The new FCN process (described in 21 CFR 170.100 through 170.106) is intended as the primary method of authorizing new uses of an FCS; however, the petition process is still available. As codified in 21 CFR 170.100(c), a petition must be submitted to FDA for an FCS (unless FDA agrees to accept an FCN) in cases where the cumulative estimated daily intake is greater than 3 mg per person per day (or 0.6 mg per person per day for biocidal compounds) or where there exists a bioassay[2] on the FCS that FDA has not reviewed and which is not clearly negative for carcinogenic effects. FDA has generally agreed to accept an FCN rather than a petition if the sponsor submits a draft FCN and consults with FDA (termed 'prenotification consultation') prior to submission of an FCN, such that there is adequate time for a thorough review of the safety information.

1. For the purpose of this chapter, the TD_{50} is the feeding dose that causes cancer in 50% of the test animals when corrected for tumors found in control animals.

2. Bioassay herein describes a chronic feeding study for the assessment of the potential of a chemical to produce carcinogenic effects.

A listing of the current regulatory options available for an FCS is shown in Table 2.2. Of particular note is the applicability of an FCN with regard to both the range of allowable exposures and substances. In contrast to the food additive definition, the definition of an FCS encompasses a broad range of substances used in contact with food, including constituents of food additives such as monomers and those substances that are generally recognized as safe and prior-sanctioned for the intended use. Thus, the FCN process permits notifications for FCSs that do not meet the definition of a food additive. This concept is important, as it extends the applicability of an FCN beyond the food additive definition and allows manufacturers/suppliers to obtain clarification with regard to the notified use of the FCS.

In regard to these options, stakeholders should examine the comparisons outlined in Table 2.2. In contrast to the TOR exemption and the petition processes, the FCN process results in an authorization for only the notifier and manufacturer/supplier listed in the FCN as opposed to the 'generic' listing in the CFR that results from a petition approval. A TOR exemption is effective for any manufacturer/supplier of the FCS; however, unlike a petition, a CFR listing is not generated as a result of the safety review. Instead, FDA maintains a list of effective FCNs and TOR exemptions on its website (a list of current website addresses is contained in Table 2.3). Furthermore, unless the FDA objects, an FCN becomes effective 120 days after the acceptance date and the FCS may be legally marketed for the proposed use. In contrast, TOR exemption requests and petitions do not have a statutory time frame default approval like FCNs and, unlike petitions, FCN submissions are confidential until the 120 day effective date or the date the Agency objects to the submission.

Under all three processes, the submitter bears the burden of demonstrating that the intended use of the FCS is safe. In reviewing the submitter's determination of safety, FDA uses the 'reasonable certainty of no harm' safety standard (codified in 21 CFR 170.3(i)). Thus, the data and information in all three processes are generally comparable for a given level of exposure and, internally, FDA's safety review and standard are equivalent for the three options. To date, the FDA has received and processed hundreds of TOR exemption requests and FCNs for food contact articles.

2.2.2 NEPA

The FDA has environmental responsibilities under the NEPA of 1969. NEPA requires Federal agencies to take, to the fullest extent possible, environmental considerations into account in the planning and making of their major (subject to judicial review) and final Agency decisions. To implement NEPA, the regulations of the Council on Environmental Quality require Federal agencies to develop their own regulations to comply with the procedures and achieve the goals of the Act (codified in 40 CFR 1500–1508). FDA's Implementing Procedures are set forth to supplement the regulations of the Council on Environmental Quality (codified in 21 CFR Part 25).

Table 2.2 Regulatory options relevant to food contact materials with regard to the food additive petition (petition), food contact notification (FCN) and threshold of regulation (TOR) exemption processes

Factor	Petition process	FCN process	TOR process
Requirements	Data requirements specified in 21 CFR 171.1; environmental requirements are specified in 21 CFR 25.15 and 40	Data requirements specified in 21 CFR 170.101; environmental requirements same as petitions	Data requirements specified in 21 CFR 170.39; environmental requirements same as petitions
Review period	180 day review period after filing that can be 'reset' with a new filing date as a result of substantive amendment	120 day review period after acceptance that cannot be reset	Review period is variable, averages 45 days
Review outcome	Federal Register (FR) publications; Regulation listing in 21 CFR 170–199	Notification letters; listing on CFSAN website	Letter to submitter; listing on CFSAN website
Legality	Not legal until a regulation is published	Legal if the Agency has no objections after the 120 day review period	Not legal until letter is received
Ownership	Generic to all manufacturers	Exclusive to the supplier or manufacturer named in the FCN	Same as petitions
Confidentiality	Disclosure of submission and data during review; automatic disclosure of environmental assessments at the time of filing	Disclosure after 120 day review period, including disclosure of environmental assessments	Same as petitions; automatic disclosure of environmental assessments at the time of receipt of submission
Qualifying exposure	None	Cumulative dietary concentration of less than 1000 µg/kg food consumed	Dietary concentration of less than or equal to 0.5 µg/kg consumed

NEPA is a declaration of the nation's environmental policy and goals. It supplements FDA's authority under the FFDCA and other public health statutes but it does not supersede these statutes. It does not require substantive FDA decisions to favor environmental protection over other considerations mandated by other statutes the FDA administers. NEPA is a full disclosure statute that requires public involvement and it is a broad statute that considers all aspects of the human environment. In addition, NEPA applies abroad and requires Federal agencies to identify those actions that may have trans-boundary environmental effects. The FDA considers allowing an FCN to become effective

Table 2.3 Useful links on the 'Food Ingredients and Packaging: Food Contact Substance Notification Program' section of the CFSAN website (http://www.cfsan.fda.gov/~lrd/foodadd.html)

Contents	Location (URL)
Inventory of effective FCNs	http://www.cfsan.fda.gov/~dms/opa-fcn.html
Inventory of environmental records for effective FCNs	http://www.cfsan.fda.gov/~rdb/opa-envt.html
Administrative guidance	http://www.cfsan.fda.gov/~dms/opa2pmna.html
Chemistry guidance	http://www.cfsan.fda.gov/~dms/opa2pmnc.html
Toxicology guidance	http://www.cfsan.fda.gov/~dms/opa2pmnt.html
Environmental guidance	http://www.cfsan.fda.gov/~dms/opa-guid.html#
FDA Form 3480	http://www.cfsan.fda.gov/~dms/pmnforms.html
CEDI/ADI database	http://www.cfsan.fda.gov/~dms/opa-edi.html
Threshold of Regulation (TOR) guidance	http://www.cfsan.fda.gov/~dms/torguid.html
Inventory of TOR exemption requests	http://www.cfsan.fda.gov/~dms/opa-torx.html
CFR listing through GPO	http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfrv3_01.html
List of indirect additives used in packaging	http://www.cfsan.fda.gov/~dms/opa-indt.html
Redbook 2000	http://www.cfsan.fda.gov/~redbook/red-toca.html
Toxicology templates	http://www.cfsan.fda.gov/~dms/opatoxtm.html

to be both a major and a final Agency action and, thus, the FCN process is subject to NEPA considerations.

2.3 Regulatory considerations

Pre-market submissions often concern the use of a food contact article that may be composed of a base polymer used in conjunction with several adjuvants, such as fillers, antioxidants, processing aids, or blended with other polymers. It is important to understand what previous regulatory authorizations can be relied upon, when a new submission is required, and when multiple submissions are necessary.

The most fundamental consideration with regard to the overall regulatory status of a food contact article is the consideration of the regulatory status of each individual component that comprises the article. The overall regulatory status is important, since it dictates the regulatory options available to industry; either all components are regulated and the article can be used under the most restrictive conditions of use, or one or more components are not authorized and either reformulation of the article or a submission to FDA is in order. One approach to determining the overall regulatory status involves obtaining the regulatory status of each component from the various suppliers. Alternatively, the regulations in Table 2.1 and the lists of effective FCNs and

TOR exemption requests may be consulted to determine the regulatory status of each component. The regulations pertaining to FCSs principally include substances in 21 CFR 175 through 178 and fall into three different types: those that list specific polymers or classes of polymers (e.g., §177.1520 Olefin polymers; §177.1315 Ethylene-1,4-cyclohexylene dimethylene terephthalate copolymers), those that list FCSs by use or function (e.g., §176.300, Slimicides; §178.2010, Antioxidants, and/or stabilizers for polymers), and those that list FCSs based on the type of packaging they may be used in or on (e.g., §175.300, Resinous and polymeric coatings).

The language found in a regulation and in TOR exemption and FCN Agency letters generally includes a unique chemical descriptor, specifications for the FCS and limitations on its use in food contact articles. As shown in Table 2.3, the 'Food Ingredients and Packaging – Food Contact Substance Notification Program' section of the Agency's website contains several tools that may be used to assist in this determination. One tool is a link to the U.S. Government Printing Office for online searching of 21 CFR. As the regulations generally include specific polymers, substances by use or function, and substances based on the type of packaging or processing that they may be used in, the identity and function of each component, e.g., base polymer or antioxidant, along with the proposed use can be used to determine the regulatory status in 21 CFR. The FDA has also developed an electronic list of permitted additives arranged in alphabetical order, the 'Indirect Additives' database. This database has thousands of individual substances, unique identifier codes and regulation citations, and serves as another useful resource for determining compliance.

Even if the component is neither regulated in 21 CFR nor the subject of a TOR exemption request, it may be the subject of an effective FCN submitted by the supplier/manufacturer of the component and allowed for use as described in the FCN. An important regulatory difference is that while the food additive regulations and TOR exemptions are generic, the effective FCNs are exclusive to the notifier and manufacturer/supplier identified in the FCN; i.e., only the notifier and manufacturer/supplier identified in the FCN may rely on an effective notification for an FCS. If a substance is permitted for the use, the next step in ensuring compliance involves understanding any limitations or specifications with regard to use conditions.

Specifications for an FCS are typically minimum and/or maximum values that are considered acceptable for one or more physical or chemical properties. For FCSs that are the subject of petitions, which result in generic regulations in 21 CFR, specifications serve to ensure that the FCS marketed by a manufacturer is equivalent to that subjected to the safety evaluation when the regulation was initially promulgated. Historically, regulations have generally included a limited number of specifications, typically, molecular weight, intrinsic viscosity, residual monomer levels, or 'end-tests' for maximum extractable fractions, as was deemed appropriate when regulated. Specifications are generally set for polymeric FCSs since they are less well-defined than their non-polymeric counterparts.

For FCNs, specifications serve to ensure that the substance marketed by the manufacturer/supplier identified in the notification is the same as that subjected to the safety evaluation when the FCN became effective. Several specifications may be given in an FCN. Specifications are applicable only to the manufacturer/supplier identified in the FCN and are well known to them. Thus, they are generally not included in FCN letters. As noted above, the notifier is held to the specifications and use conditions identified in the FCN. Accordingly, changes in the manufacturing process that result in new impurity profiles may require communication with the FDA and, if warranted, new FCN submissions.

Use limitations may include limits on the level of the FCS in the manufacture of the food contact article, as well as 'food types' and time–temperature conditions under which articles manufactured from the substances may be used. As given in Table 2.1 of 21 CFR 176.170(c) and used in regulatory and notification language, 'food types' are designations (Roman numerals I–IX) that classify types of raw and processed foods as aqueous, acidic, alcoholic or fatty (see Table 2.4). Also defined in Table 2.2 of that section are the 'conditions of use' which are time–temperature conditions for thermal treatment and extended storage of food contact articles intended for single-use (see Table 2.5). It is important to determine the food types and conditions of use prior to the initiation of migration studies or any other studies to determine migrant levels in food, as both are intimately linked to the appropriate testing protocol and are essential for estimating consumer exposure. The relevance of food types (Table 2.4) and conditions of use (Table 2.5) with regard to migration testing are discussed in more detail below.

2.4 Food contact notifications

2.4.1 Administrative overview

FDA has several options following receipt of an FCN, all linked to the internal review processes. The FDA uses a two-phase approach in the administrative and technical review of FCNs. Phase 1 review, conducted during the first three weeks of initial receipt of the FCN, consists of an administrative review to ensure that the basic data and informational elements are present and that the submission meets the requirements set forth in the applicable statute and regulations. During this process, the reviewers assigned to the FCN examine it for regulatory, environmental, chemical, and toxicological completeness. This includes conducting literature searches and a preliminary assessment, including structure–activity relationship analysis, of the data to identify potential concerns.

A formal meeting is conducted 20–30 days after receipt of the FCN to discuss the submission, identify deficiencies that inhibit going forward with the review, and discuss potential concerns that may arise during phase 2 review (discussed in more detail below). If deficiencies are noted, the FCN

Table 2.4 Classification of food types and recommended food simulants for food contact articles

Type	Description	Classification
I	Nonacid, aqueous products; may contain salt, sugar or both (pH > 5)	Aqueous
II	Acid, aqueous products; may contain salt, sugar or both, and including oil-in-water emulsions of low- or high-fat content	Acidic
III	Aqueous, acid or nonacid products containing free oil or fat; may contain salt, and including water-in-oil emulsions of low- or high-fat content	Fatty
IV	Dairy products and modifications	
	A. Water-in-oil emulsions, high- or low-fat	Fatty
	B. Oil-in-water emulsions, high- or low-fat	Aqueous
V	Low moisture fats and oils	Fatty
VI	Beverages	
	A. Containing up to 8% alcohol	Low-alcohol
	B. Nonalcoholic	Aqueous
	C. Containing more than 8% alcohol	High-alcohol
VII	Bakery products (other than those under types VIII or IX)	
	A. Moist bakery products with surface containing free fat or oil	Fatty
	B. Moist bakery products with surface containing no free fat or oil	Aqueous
VIII	Dry solids with the surface containing no free fat or oil	Dry
IX	Dry solids with the surface containing free fat or oil	Fatty

Recommended food simulants (a more detail discussion is in the chemistry guidance document):
aqueous/acidic/low-alcohol foods – 10% ethanol
high-alcohol foods – 50% ethanol
fatty foods – aqueous ethanol solutions or food oil

is considered incomplete and the notifier is asked by letter to address the deficiencies in a timely manner. If the notifier adequately addresses all deficiencies in a timely manner, usually within ten working days from the date of the deficiency letter, the FCN is considered complete. Conversely, if the deficiencies are not adequately addressed, the notifier is informed that the FCN is not acceptable in its present form and is encouraged to withdraw the FCN without prejudice to future submission; alternatively, the FDA may issue a non-acceptance letter. The 120-day review period begins on the day the complete FCN is received by FDA. The review process enters phase 2 once the FCN has been 'accepted' for review. Phase 2 review involves a detailed analysis of the safety data and other information contained in the FCN or otherwise obtained by FDA. Once accepted for review, FDA may still object to the FCN due to safety concerns. If no safety issues arise during the phase 2 review, the FCN becomes effective and the FCS may legally be marketed for the proposed use at the end of the 120-day review period.

Table 2.5 Time–temperature conditions of use for single- and repeat-use

Designation	Name or description	Protocol
Single use		
A	High temperature, heat sterilized or retorted above 100 °C	120 °C/2 h, 40 °C/238 h
B	Boiling water sterilized	100 °C/2 h, 40 °C/238 h
C	Hot-filled or pasteurized above 66 °C	100 °C/0.5 h, 40 °C/239.5 h or 66 °C/2 h,40 °C/238 h
D	Hot-filled or pasteurized below 66 °C	66 °C/0.5 h, 40 °C/239.5 h
E	Room temperature filled and stored (no thermal treatment in the container)	40 °C/240 h
F	Refrigerated storage (no thermal treatment in the container)	20 °C/240 h
G	Frozen storage (no thermal treatment in the container)	20 °C/120 h
H	Frozen or refrigerated storage; ready-prepared food intended to be reheated in container at time of use	100 °C/2 h
Repeat use		
	Repeated use in contact with food	Highest intended use temperature for the longest time
High temperature use		
	Dual-ovenable trays	Highest intended conventional oven temperature for the longest time
	Microwavable containers	See guidance document
	Microwave heat-susceptor applications	See guidance document

2.4.2 Safety assessment

FDA's safety assessment relies on evaluating probable consumer exposure to an FCS, including all constituents or impurities, as a result of the proposed use and other authorized uses, and ensuring that probable consumer exposures are supported by the available toxicological information. It is important to understand that the safety assessment focuses on those substances that would be expected to become components of food from the proposed use of the FCS. A general discussion of the recommended chemistry, toxicology, and environmental information for an FCN follows below.

As discussed in the chemistry guidance document for FCSs (Table 2.3), the recommended chemistry information includes discussions and data on the identity, manufacture, stability, technical effect and proposed use of the FCS, all of which are used to identify and estimate consumer exposure to the various substances originating from the FCS. Exposure estimates, expressed as dietary concentration (DC) and estimated daily intake (EDI) values, usually involve combining migrant levels in food with parameters based on information

on the use of articles that might contain the FCS. Cumulative exposure estimates, expressed as cumulative EDI (CEDI) or a cumulative DC (CDC), are the sum of the exposure estimates from the proposed use and other permitted uses. Noteworthy, unless there is reason to believe the substance may be carcinogenic or overtly toxic, current guidance does not suggest examination of cumulative exposures for DC values which are less than or equal to 0.5 micrograms per kilogram food consumed.

As discussed in the toxicology guidance document for FCSs (Table 2.3), the recommended toxicology information includes both an overall safety narrative and a comprehensive toxicological profile for the FCS and each of its constituents. The safety narrative summarizes all the information relevant to a conclusion that the intended use of the FCS is safe. The comprehensive toxicological profile consists of summaries and critical evaluations of all the available toxicological information pertinent to the safety evaluation for each substance. This information includes reviews and conclusions of toxicity studies on the FCS and other relevant substances that are either published in the literature or available elsewhere.

In summary, FDA combines the regulatory, chemistry, toxicology, and environmental information on a new FCS or new use of an FCS for its pre-market safety assessment for the intended conditions of use. Pivotal aspects of the chemistry, toxicology, and environmental reviews are elaborated upon in the next three sections.

Chemistry information

As noted above, exposure estimates for FCSs and their constituents usually involve combining migrant levels in food with parameters based on information on the use of articles that might contain the FCS. FDA classifies food contact articles as single-use or repeat-use articles. Single-use describes an article that will be used one time, such as a plastic bottle for holding beverages, whereas repeat-use articles will be used over an extended period and will contact food repeatedly, such as an o-ring or conveyor belt used in a food processing plant, or a food tray. The following discussion will focus on estimating consumer exposure.

In general, migrant levels in food are determined by one or more of the following methods: (i) accelerated migration studies conducted with food simulants under the most severe anticipated conditions of use; (ii) the assumption of 100% migration to food using actual use or residue levels; or (iii) mathematical modeling of migration in polymers based on a thermal processing-extended storage scenario using actual use or residue levels. The general protocols for single-use and repeat-use articles are discussed in Parts 1 and 4, respectively, in Appendix II of the chemistry guidance document and summarized in Table 2.5. These protocols are generally intended to model the thermal treatment and extended storage (or contact) of the article containing the FCS. The intended use conditions of the FCS (i.e., use level and article(s), food types and time/temperature conditions) are crucial in

determining test parameters (i.e., test sample(s), food simulants, and accelerated time/temperature protocols) and applicable packaging factors, at least for single-use applications. In other words, the intended use of articles containing the FCS determines the appropriate food types and classifications (Table 2.4) as well as the accelerated time/temperature conditions (Table 2.5) that should be used to determine migrant levels in food. It is important to note that these migration protocols for a new FCS or use bear no relation to the 'end-test' specifications listed in the CFR for compliance evaluation.

In some cases where the use level of the FCS or residue level of a migrant is low, it may be possible to dispense with migration studies altogether by assuming 100% migration of the substance to food. Although migration studies might result in a lower migration to food, hence a lower EDI, such studies would be unnecessary if the resulting EDI is sufficiently low or otherwise supported by the available toxicological information. Alternatively, mathematical modeling of migration based on the principles of diffusion in polymers, an approach also recognized by the European Food Safety Authority, can be used (Begley *et al*., 2005). Migration modeling is discussed in Section II, Part D.5, of the chemistry guidance document.

For single-use articles, information on the uses of food contact articles that may contain the FCS is captured by packaging factors which include both consumption factors (CF) and food-type distribution factors (f_T). The CF describes the fraction of the daily diet expected to contact specific packaging materials and represents the ratio of the weight of all food contacting a specific packaging material to the weight of all packaged food. CF values for select packaging categories (e.g., polymer and paper), specific food-contact polymers (e.g., low density polyethylene), and applications (e.g., microwave susceptors) are summarized in the chemistry guidance document and presented here in Table 2.6. FDA will modify these values as new information on the use of packaging materials in the marketplace becomes available. In fact, the more information a notifier can provide on the specific scenarios of use, such as subdividing packaging or resin categories with marketing information, the more accurately FDA can estimate exposure. The use of packaging factors for determining consumer exposure contrasts with the approach utilized by other regulatory bodies (Heckman, 2005).

The f_T describes the fraction of all food contacting each material that is aqueous (aq), acidic (ac), alcoholic (al) and fatty (fat). The f_Ts account for the variable nature of foods contacting each packaging material. The use of these factors in calculating exposure is critical, as migration is dependent on several factors, including the nature of the food matrix, i.e., the food type. Although migration might be highest in fatty foods for a particular FCS, use of the article containing the FCS might also be extremely limited in its application to fatty foods. Applying the f_Ts to the migrant levels in food allows for a 'weighted average' migration to food, denoted as <M>, to be used in generating an exposure estimate.

The expression relating migrant levels in food and packaging factors to

Table 2.6 Select packaging factors for several packaging categories (a complete list may be found in Appendix IV of the chemistry guidance document)

Category	Packaging factors				
	CF	f(aqueous)	f(acid)	f(alcohol)	f(fat)
Metal – uncoated	0.03	0.54	0.25	0.01	0.20
Metal – polymer coated	0.17	0.16	0.35	0.40	0.09
Paper – uncoated and clay coated	0.1	0.57	0.01	0.01	0.41
Paper – polymer coated	0.2	0.55	0.04	0.01	0.40
Low density polyethylene (LDPE)	0.12	0.67	0.01	0.01	0.31
Linear LDPE (LLDPE)	0.06	0.67	0.01	0.01	0.31
High density polyethylene (HDPE)	0.13	0.67	0.01	0.01	0.31
Polypropylene (PP)	0.04	0.67	0.01	0.01	0.31
Polyethylene terephthalate (PET)	0.16	0.01	0.97	0.01	0.01
Nylons	0.02	0.10	0.10	0.05	0.75
Adhesives (consistent with §175.105)	0.14				
Retort pouch	0.0004				
Microwave susceptor	0.001				

DC (units of mass of migrant per mass food consumed) for the purpose of estimating exposure for single-use articles is:

$$DC = CF \times \langle M \rangle = CF \times [(M_{aq})(f_{aq}) + (M_{ac})(f_{ac}) + (M_{al})(f_{al}) + (M_{fat})(f_{fat})] \quad 2.1$$

The expression relating DC and EDI, assuming a consumption of 3 kilograms (1.5 kilograms liquid and 1.5 kilograms solid) food per person per day, is:

$$EDI = DC \times 3 \text{ kilograms food per person per day} \quad 2.2$$

For repeat-use articles, FDA takes into account information on the uses of articles that may contain the FCS such as the weight of food contacting a known area of a representative repeat-use article, contact time of food with the repeat-use article, and the average lifetime of the article. This allows the calculation of a representative food mass-to-surface area ratio for the use and extrapolation of the representative migrant levels in food over the entire service lifetime of the article. In general, exposure estimates for repeat-use applications are lower than those for single-use, primarily because of the large food mass-to-surface area ratio used in the calculations.

Historically, FDA has implicitly considered exposure to repeat-use applications when evaluating single-use applications during the safety assessment, unless the requestor specifically states otherwise or the article is not stable for repeat-use. As single-use exposures are generally orders of magnitude above most repeat-use exposures, this approach is sufficiently conservative from a safety standpoint and more efficient from an administrative standpoint; however, this is something notifiers should keep in mind with regard to environmental requirements (discussed in detail below). As an

example, a requested use of an FCS qualifying for a categorical exclusion under 21 CFR 25.32(i) may also need to claim the exclusion under 21 CFR 25.32(j) if articles containing the FCS could also be used in repeat-use applications. Alternatively, use conditions may be interpreted differently with regard to environmental impact versus exposure assessment, as is the case with latex gloves whose use is repeated but their disposal is in a pattern of hours or days. Historically, the environmental review has considered gloves used in food preparation, for example, to be single-use articles even though for human safety evaluation they are considered repeat-use articles; this is because the disposal pattern of such gloves, for the purpose of estimating environmental introductions and, hence, environmental impact, does not meet the definition of long service-time as defined in the preamble to the FDA NEPA-implementing regulations.

Toxicology information

FDA's toxicological assessment is based on a tiered approach and is consistent with the general principle that increased exposure leads to increased potential health risks; however, the inherent toxicity of a structural/functional class of compounds is also considered, as demonstrated by the separate requirements for biocides. This approach to defining the endpoints of concern at exposure thresholds is the cornerstone of FDA's TOR exemption process and the tiered testing scheme used to analyze the safety of FCSs (Table 2.7). FDA has provided detailed guidance on the toxicology recommendations for submission of an FCN as referenced in Table 2.3. The following section discusses FDA's approach to the evaluation of toxicological information in the overall safety assessment of a FCS.

As depicted in Table 2.7, FDA does not ordinarily suggest conducting toxicity tests at DCs less than or equal to 0.5 micrograms per kilogram food consumed; rather, a literature search and a structural comparison to known carcinogens are requested. This approach and the safety information requested are equivalent for FCNs and TOR exemptions on an FCS. It is noteworthy that the tiered approach in Table 2.7 expands the test requirements with increasing exposure. Accordingly, the information needed to support safety at these low doses is required for any level of exposure. The use of structural comparisons or structure activity relationship analysis has long been important in prioritizing toxicity concerns. With the development of the TOR and FCN processes, an FDA review group now reviews every submission explicitly from this perspective. The tools and applications used in this analysis were recently elaborated on by Bailey *et al*. (2005) and are the focus of Chapter 7.

At the next tier of exposure, between 0.5 and 50 micrograms per kilogram food consumed, FDA recommends assessing the genetic toxicity of the substance using *in vitro* assays.[3] These assays are less expensive and time

3. For the purposes of this text, *in vitro* refers to experiments performed in an artificial environment, such as a test tube or glass vessel.

Table 2.7 Toxicology testing recommendations for food contact substances based on dietary concentration (DC) and corresponding estimated daily intake (EDI) values. Note that the cumulative exposures are based on non-biocidal chemicals; biocidal tiers are one-fifth the cumulative dietary concentration (CDC) and cumulative estimated daily intake (CEDI) values expressed. DC and CDC values are in units of mass of migrant per mass food consumed. EDI and CEDI values are in units of mass of migrant per person per day. Abbreviations are as follows: μg (microgram), kg (kilogram), mg (milligram), ≤ (less than or equal to), < (less than), > (greater than), and ≥ (greater than or equal to)

Exposure	Recommendation
DC of ≤ 0.5 μg/kg (EDI of ≤ 1.5 μg/person/day)	• No toxicity testing recommended • Available information on potential mutagenicity and carcinogenicity, published and unpublished, should be submitted and discussed • Structural similarity of the substance to known carcinogens or genotoxic chemicals should be discussed, if appropriate
CDC of > 0.5 μg/kg but ≤ 50 μg/kg (CEDI of > 1.5 μg/person/day but ≤ 150 μg/person/day)	Recommendations for DC of ≤ 0.5 μg/kg and: • Genetic toxicity tests on the substance (i) A test for gene mutations in bacteria (ii) An *in vitro* cytogenetic test in mammalian cells or an *in vitro* mouse lymphoma tk± assay
CDC of > 50 μg/kg but < 1000 μg/kg (CEDI of > 150 μg/person/day but < 3 mg/person/day)	Recommendations for DC of ≤ 0.5 μg/kg and: • Genetic toxicity tests on the substance (i) A test for gene mutations in bacteria (ii) An *in vitro* cytogenetic test in mammalian cells or *in vitro* mouse lymphoma tk± assay (iii) An *in vivo* test for chromosomal damage using rodent hematopoietic cells • Potential toxicity of the substance should be evaluated by two subchronic (90-day) oral toxicity tests, one in a rodent species and the other in a non-rodent species • Results from these studies or other available information may trigger the need for longer term (1-year or 2-year) or specialized (e.g. reproductive/developmental toxicity, neurotoxicity, etc.) tests
CDC of ≥ 1000 μg/kg (EDI of ≥ 3 mg/person/day)	Recommend Food Additive Petition containing the data listed above for lower exposures and: • Two-year carcinogenicity bioassays in two rodent species (one study should include *in utero* phase) • A two-generation reproductive study in rats with a teratology phase • Other specialized studies, as appropriate

consuming than a bioassay and they provide information on the ability of the substance to cause genetic damage, a key event in the development of cancer (Pitot III and Dragan, 2001). As many of the chemicals involved in the production of FCSs are likely to be of wide interest, based on other uses and/or subject to another regulatory authority, these studies are often available in the open literature. These assays have varying specificities and sensitivities, as recently evaluated by Kirkland *et al.* (2005), and measure different endpoints. Therefore, when differences in individual test results arise, the collective data may be difficult to interpret with regard to the overall carcinogenic potential of the substance. Accordingly, by examining multiple endpoints of genetic toxicity, a broad assessment of the substance's ability to cause genetic damage is obtainable. Pairing these data with structure–activity relationship analysis allows for a more comprehensive review of a chemical's potential to be mutagenic and/or carcinogenic.

At exposures of greater than 50 micrograms per kilogram food consumed, in addition to the data requested at less than or equal to 50 micrograms per kilogram food consumed, FDA recommends the completion of an *in vivo*[4] test for chromosomal damage using rodent hematopoietic cells (i.e., mouse micronucleus assay) and two subchronic studies, one rodent and one non-rodent. Additional studies may be suggested based on the results of the subchronic studies and/or structure–activity relationship analysis. FDA uses this information to determine an acceptable daily intake (ADI) value for the substance from the most sensitive species (hence the need for both rodent and non-rodent data). In determining an ADI value, FDA uses the no observed effect level or the no observed adverse effect level, if appropriate, and uncertainty (or safety) factors. Table 2.8 details the determination of an ADI value and the applicable uncertainty factors used by the FDA. Once an ADI value is determined, this value is compared to the CEDI. If the ADI value is greater than the CEDI, the substance is considered safe for the proposed use. If the ADI value is less than the CEDI, the substance is not considered safe for its proposed use and more information, either toxicological or exposure, may be used to establish safety. In general, ADI values are not calculated for substances with positive genotoxic or neoplastic findings.

At exposures of greater than 1000 micrograms per kilogram food consumed, FDA recommends the completion of two two-year carcinogenic bioassays in rodents (one with an *in utero* phase) to determine the carcinogenic potential of the substance, a reproductive/developmental study, and other specialized studies as warranted by the data. Again, substances with DCs greater than or equal to 1000 micrograms per kilogram food consumed are not acceptable for submission of an FCN without previous agreement with FDA.

With regard to a food additive, which may be the FCS or manufactured from the FCS, Section 409(c)(3)(a) of the FFDCA states that 'no additive

4. For the purpose of this text, *in vivo* refers to experiments performed in a living organism.

Table 2.8 Examples of FDA's approach to toxicity safety assessment depending on endpoint of concern

Endpoint	Example of assessment approach
Non-neoplastic endpoint	Derivation of an acceptable daily intake (ADI) value using the no observed effect level (NOEL): $\text{ADI (mg/kg bw/day)} = \frac{\text{NOEL (mg/kg bw/day)}}{\text{UF1} \times \text{UF2} \times \text{UF3}\ldots)}$ ADI (mg/person/day) = ADI (mg/kg bw/day) × 60 (kg/person) Uncertainty factors (UF): • 10 extrapolation from animals to humans • 10 intraspecies variability • 10 for less than chronic exposure Typical FDA Uncertainty Factors: • 100–200 for chronic toxicity studies • 1000–2000 for subchronic toxicity studies • 1000 where reproductive and developmental effects are severe and/or irreversible • 100 where reproductive and developmental effects are not severe or are reversible
Neoplastic endpoints	
Food additive	Delaney clause applies – assessment is qualitative (positive or negative)
Constituent – genotoxic	Multiply unit cancer risk by EDI to obtain worst case upper bound lifetime cancer risk • Unit cancer risk (UCR) is defined as the sum of the slopes of lines drawn from the lowest apparent effective dose of the chemical through zero for each tumor site • Tumors arising from multiple sites are assumed to be independent and are added to obtain the overall UCR • Lowest dose at which significant neoplastic findings are reported is used to calculate UCR
Constituent – non-genotoxic	• Evaluate using threshold approach applying applicable uncertainty factors detailed above

shall be deemed safe if it is found to induce cancer when ingested by man or animal…' This is the so-called food additive or anti-cancer Delaney clause. The Delaney clause applies to the additive itself, not to constituents of the additive or impurities that may be present (Scott v. FDA, 728 F. 2d 322 (6th Cir. 1984)). Accordingly, individual constituents of the food additive may be evaluated under the general safety standard using applicable risk assessment procedures. This regulatory interpretation is often referred to as the Constituents Policy (U.S. Food and Drug Administration, 1982). In the case of a polymer manufactured from one or more monomers, the polymer that is intended to contact food is considered the food additive. However, a notifier may identify

the polymer or one or more of the individual monomers as the FCS, depending on the approach taken in the notification.

In numerous cases, considering the regulatory authority/requirements of other regulatory bodies, both in the U.S. and other countries, some FCSs or their constituents have been subject to carcinogenicity studies, such as two-year bioassays. Although the level of exposure from an FCS may not necessarily require such studies for FDA approval, these data are considered pivotal regardless of the level of exposure expected. In the safety assessment of the FCS, neoplastic data on constituents of an additive are reviewed to determine whether or not the constituent is a carcinogen. If there are no positive carcinogenic findings, this resolves any cancer issues and other toxicity data are considered in the safety assessment of the constituent. On the other hand, if the constituent is determined to be a carcinogen, risk assessment procedures are used to determine whether or not the proposed use would present more than a negligible risk. The unit cancer risk derived from the linear, low-dose extrapolation is used in combination with the exposure estimate to determine the upper-bound lifetime cancer risk. Details of this approach for constituents are provided in Table 2.8, have been elaborated upon by Lorentzen (1984), and are the subject of Chapter 7. It is important to note that this approach is applicable only to constituents of food additives and not to food additives themselves, which are subject to the Delaney prohibition.

There are several important considerations to keep in mind with regard to toxicity data. First, although FDA has established a tiered approach to testing, these are not rigid criteria but points that trigger examination of additional endpoints. As the safety standard is 'a reasonable certainty of no harm', it is important to consider a comprehensive approach to the data and how the structure of the substance relates to its potential toxicity. As an example, though toxicological testing is not ordinarily requested for exposures less than or equal to 0.5 micrograms per kilogram food consumed, it may be requested for a substance that contains biophores indicating mutagenic activity. The same can be said for reproductive structure–activity relationship analysis at exposures of less than or equal to 50 micrograms per kilogram food consumed. In addition, notifiers are required to submit and discuss all available, relevant data regardless of the level of exposure. For this reason, the FDA receives numerous studies that would not be required based on the estimated exposure. Some of these studies, such as 28-day studies, are not considered appropriate for setting ADI values; rather they are used to assess toxicity which may be the basis for requesting a subchronic study to ensure safety.

Notifiers should thoroughly search all publicly available databases, including those of international and foreign regulatory agencies, for applicable information with regard to their safety analysis. A thorough review of available information often avoids questions and requests for additional information during the phase 1 review in which FDA does its own literature searches. Additionally, correspondence between FDA and notifiers regarding available, previously determined safety analyses conducted by FDA is often time saving

and can assist in the safety assessment of a new FCN. This is important if exposure is expected to a substance that was evaluated prior to the inception of the FCN process, because the substance may not have been evaluated for mutagenicity when it was evaluated for general toxicity. In such cases, the notifier proposing a new use may be requested to submit genetic toxicity studies to supplement the available data.

Over the last several years, the FDA has developed several toxicology assessment tools to aid in the submission process. The *Redbook 2000 Toxicological Principles for the Safety Assessment of Food Ingredients* (U.S. Food and Drug Administration, 2004) details testing guidelines for commonly requested toxicology tests. Additionally, the FDA has developed toxicology templates to aid in the review and evaluation of commonly requested tests. Lastly, FDA-developed ADI and unit cancer risk values are available either on FDA's website or through correspondence with the Agency.

Environmental information

The Agency will not accept an FCN, a TOR exemption submission, or a petition for review if the environmental component is missing or deficient (21 CFR 25.15); thus, every FCN, petition, and TOR exemption submission must contain either an environmental assessment or a claim of categorical exclusion from the need to prepare an environmental assessment. The discussion below on FCNs is also applicable to TOR exemption submissions and petitions.

A claim of categorical exclusion applies to Agency actions that do not individually or cumulatively affect the quality of the human environment. An adequate claim of categorical exclusion (definition codified in 21 CFR 25.15) must include a citation of the CFR section under which the exclusion is warranted (Table 2.9), a statement of compliance with the categorical

Table 2.9 Claims of categorical exclusions applicable to food-contact materials: Title 21, Parts 25, Section 32 of the Code of Federal Regulations (denoted as 21 CFR 25.32)

21 CFR 25.32 Subsection	Category of substances
i	Substance is present in the finished food-packaging material at not greater than 5% by weight (wt.-%) and is expected to remain with finished food-packaging material through use by consumers or when the substance is a component of a coating of a finished food-packaging material
j	Substance is to be used as a component of a food-contact surface of permanent or semipermanent equipment or of another article intended for repeated use
q	Substance that is registered by the U.S. Environmental Protection Agency (U.S. EPA) under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) for the same use requested in the FCN
r	Substance that occurs naturally in the environment when the action does not alter significantly the concentration or distribution of the substance, its metabolites, or degradation products in the environment

exclusion criteria, and a statement that, to the notifier's knowledge, there are no extraordinary circumstances that will require the submission of an environmental assessment.

The Council on Environmental Quality's view is that the information submitted in a request for categorical exclusion is usually sufficient to determine that the exclusion is applicable to the requested action. Therefore, FDA has formulated its categorical exclusions to include specific criteria so that, in most instances, a categorical exclusion can be determined simply by citing the exclusion listed in 25 CFR 25.32 or confirmed by review of other information submitted as part of the FCN, available in the Agency's files, or published in the open literature. However, in limited instances, it may be necessary to submit additional information to establish that the criteria for a categorical exclusion have been met, particularly for exclusions claimed under §25.32(i), §25.32(q), and §25.32(r). Guidance on when and what additional information is needed to support a claim of categorical exclusion is available on the Agency's web site (Table 2.3).

When a proposed use in an FCN does not qualify for a claim of categorical exclusion or when extraordinary circumstances exist, as determined by the notifier or the Agency, the FCN must contain an adequate environmental assessment as defined under 21 CFR 25.40. An adequate environmental assessment is one that addresses the relevant environmental issues and contains sufficient information to enable the Agency to determine whether the proposed action may significantly affect the quality of the human environment. It must contain a brief discussion for the need for the proposed action, of introductions, fate, and effects of the substances in the environment, of alternatives to the proposed action, and the environmental impact of the proposed use as a result of use and disposal of the substance. The environmental guidance on FDA's web site contains additional recommendations for inclusion in an environmental assessment.

The majority of proposed uses of FCSs qualify for categorical exclusion under 21 CFR 25.32 (i), (j), (q), or (r); those that do not qualify for categorical exclusion require an environmental assessment. Examples include secondary direct food additives and FCSs used in the production of food and are not intended to remain with food, processing aids used in the production of food-packaging material that are not intended to remain as components of finished food-packaging material, and components of finished food-packaging material present at greater than 5% by weight (wt.-%) of the finished packaging. For example, if the FCS is for use in all polymers, the proposed use would qualify for categorical exclusion under 21 CFR 25.32(i) if it is present at not greater than 5 wt.-% of the finished food-packaging material. However, if the FCS is a chemically bound component of a polymer (such as a monomer) used to make finished food-packaging material, then the FCN must contain an environmental assessment even if the FCS is present at not greater than 5 wt.-% of a polymer that is used at levels greater than 5 wt.-% of the food-packaging material. In these cases, the substance that is the subject of FDA's

review under NEPA regulations is the material that will be introduced into the environment; specifically, the polymer containing the FCS. For an FCS used in polymeric finished food-packaging material, FDA believes that, in general, little or no introduction of the FCS into the environment will result from its use because it is almost completely incorporated into food-packaging material and essentially all of it is expected to remain with this packaging throughout use of the product. The environmental impacts of polymeric food-packaging material may result from disposal of the food-packaging material.

NEPA Section 102 (b)(6) states that one goal of NEPA is to 'enhance the quality of renewable resources and approach the maximum attainable recycling of depletable resources'. A polymeric FCS/food additive, or a polymer that contains the FCS in a chemically bound state, may impact the environment as a result of disposal by affecting solid waste management practices such as recycling (resources and energy use), landfilling (groundwater contamination), and incineration (acid gas emissions). Therefore, an environmental assessment for a polymeric food additive/FCS should discuss the environmental impacts of the proposed use as a result of the disposal of the polymeric packaging. In general, unlike for human safety determinations, FDA does not review the environmental impact of contaminants present in polymeric materials.

The Agency's NEPA-implementing regulations do not specify what data the environmental assessment must include to demonstrate that the proposed use in the FCN is not expected to cause a significant impact on the environment. It is the notifier's responsibility to demonstrate no significant impact on the environment as a result of the proposed use of the FCS using either actual data or prediction models such as the U.S. Environmental Protection Agency's ECOSAR and EPIWIN (U.S. Environmental Protection Agency, 2004). FDA will accept data obtained from testing either under its own testing methods or those of any other entities such as the U.S. EPA, the Organisation for Economic Co-operation and Development, or other international regulatory bodies. Regardless of the method used to determine no significant impact on the environment, the notifier should consider the physical/chemical properties of the FCS (water solubility, dissociation constants in water, *n*-octanol/water partition coefficient (Kow), and vapor pressure or Henry's Law constant), environmental depletion mechanisms (adsorption coefficient (Koc), aerobic and anaerobic biodegradation, hydrolysis, and photolysis), and fate data (aquatic toxicity mostly).

FDA's assessment of the environmental impact of FCSs is the same under the FCN and petition review processes; however, there is a major difference in the availability of the environmental record. NEPA is a full disclosure statute and Sec. 1506.6(a) (Public Involvement) of the Council on Environmental Quality regulations implementing NEPA states that Federal agencies shall make diligent efforts to involve the public in preparing and implementing their NEPA procedures. As a result, the environmental record for a petition is made publicly available at FDA's Dockets at the time a filing

notice is published in the Federal Register. However, the FFDCA requires that the FCN remain confidential during the 120-day review period (FFDCA section 409(h)). Because NEPA does not supersede the main statute under which the Agency functions, the environmental record for an FCN is not made publicly available until FFDCA permits its availability.

2.5 Pivotal and emerging issues in FDA's approach to safety assessment

2.5.1 Consumer exposure

Exposure estimates, developed from migrant levels in food and information on food contact uses, determine the amount of toxicological information needed to support the proposed use of an FCS. Limitations on use conditions may be imposed by the notifier, possibly at the suggestion of FDA, to reduce exposure to either the FCS or to a constituent due to safety concerns identified during the review. This approach can be advantageous to the notifier. For example, if the available toxicological information is limited and, thus, supports only a low exposure in accord with the tiered testing scheme, a notifier may submit an FCN for a narrow or limited use. As additional chemistry or toxicological data become available, the notifier may submit another FCN for expanded use of the FCS. As another example, consider two monomers used in the manufacture of polymeric food contact articles, one of which is commonly used as a 'base' monomer and the other used as a minor monomer. Through its evaluation of numerous submissions that the FDA has processed, FDA has determined that some polymeric articles, manufactured from certain monomers, are used only in such niche or specialty applications that they are not expected to see wide use in food packaging. As such, they usually require minimal data to ensure safety at their respective exposures. This approach to safety assessment allows the FDA not only to fine tune the safety assessment for the particular notification in question, but also to reassess the safety assessment of FCSs and their constituents on a continuing basis. If concerns are raised in the reassessment, they may result in post-market action on any permitted uses of the FCS.

Exposure estimates derived from packaging factors are 'averages' across the U.S. population and may be thought of as 'per capita' estimates. FDA believes that this 'per capita'-based approach to estimating exposure to food packaging components is appropriate because consumer selection of food is not generally dependent on the type of packaging; rather, it is dependent on the eating habits and spending preferences of the consumer. In fact, one criticism of FDA's approach to consumer exposure for packaging materials is the assumption that a food(s) eaten by a given consumer will have been packaged with the same material 100% of the time. For example, if a notifier proposes use of an antioxidant in high-density polyethylene, the consumer is assumed to ingest the selected food(s) only if it is packaged in the high-

density polyethylene with the antioxidant, even though the food(s) may be packaged in other materials as well. With regard to selecting or developing an appropriate CF for a FCS for use in refining an exposure estimate, the FDA encourages the submission of marketing or other information that may be used to subdivide packaging markets. Given the exclusive nature of the FCN process, FDA continues to explore new methods to utilize marketing information in exposure refinement. On occasion, exposure estimates for packaging components may be derived based on the intake of a particular food, with focus on the 'mean' intake of the particular food rather than the 90-plus percentiles. This approach can be used when an FCN identifies use only with specific foods, such as for polymeric absorbent pads used only for raw chicken or fruit.

2.5.2 Dose related toxicity

In applying the hazard information gained in toxicology testing to a safety evaluation, it is essential to assess the hazard based on the exposure resulting from the use(s) of a substance in food contact articles. In many cases, only limited information may be available on a substance; however, if the substance has a large toxicological data base of information, the safety assessment may be made using the data deemed most relevant to the exposure level being evaluated. As an example, consider the proposed use of a substance with a dietary concentration of one microgram per kilogram food consumed and supporting data consisting of genetic toxicity tests and a subchronic study. At one microgram per kilogram food consumed, the genetic toxicity studies would be thoroughly reviewed because they can provide information relevant at such a low level while the subchronic study would be subjected to a preliminary review. If the preliminary review of the subchronic study indicates a safety concern based on the margin of exposure, the study would be thoroughly reviewed to establish an acceptable daily intake value. An acceptable daily intake value need not be calculated if the exposure and preliminary review do not warrant an extensive evaluation of the additional data to ensure safety.

2.5.3 Continuous monitoring

The exclusive nature of the FCN process allows for a safety assessment for the FCS and its constituents in each and every FCN submitted by each and every notifier. The safety assessment may be for a new FCS or constituent or may be an updated assessment for a FCS or constituent that the FDA has evaluated previously. Thus, the FDA can monitor all safety information on FCSs and their constituents on a continuing basis and quickly address any safety concerns in the process. Moreover, as noted above, this process allows the FDA to acquire and maintain knowledge of the manufacturers/suppliers of the FCS or articles manufactured from the FCS. In addition, because the

notifier/supplier is bound by the limitations and specifications of the FCS as submitted in the effective FCN, including the manufacturing process, any substantive changes in the manufacturing process should be assessed by FDA to determine compliance. Notifiers must contact FDA regarding details as to the manufacturing changes for review and determination of whether the resultant changes require the submission of a new FCN. These correspondences are usually handled in a prenotification consultation, allowing FDA to provide detailed guidance on compliance or future submissions. This knowledge base contrasts the previous 'generic' food additive petition process and affords FDA the ability to more quickly respond when post-market issues arise, have a more detailed knowledge of the regulated industry and its practices, and allows FDA to continually evaluate the key steps used in its approach to the safety assessment of food contact articles.

2.5.4 Constituents

Another important aspect of the safety assessment is the evaluation of constituents of food additives, which include impurities and byproducts, as well as the low molecular weight oligomeric fraction of polymeric substances. For example, the safety evaluation for every FCN encompasses all components that would be expected to migrate to food, including the FCS, the food additive, and constituents of the food additive. This assessment is complex and the lack of proper evaluation and supporting documentation on all substances is the most common deficiency.

Polymerization aids constitute one specific class of substances that is frequently the subject of a constituent safety evaluation. Polymer manufacture necessarily requires the use of various substances, such as catalysts, initiators, and chain transfer agents, to aid in the polymerization process but that are not essential in the final polymer. These substances are used at low levels and are typically incorporated into the polymer during polymerization or are removed during the final manufacturing steps. Solvents are also generally used in the manufacturing process and are removed during the final steps.

Under the food additive petition process, polymers were either generically listed as unique entities e.g., 21 CFR 177, or by way of the monomer building blocks used in the manufacture of certain polymers, such as polyester container coatings under §175.300. The FDA could not anticipate every polymerization aid that might be used by manufacturers as a result of a generic regulation listing. Polymerization aids were considered to be part of the base polymer and were, in most cases, not subjected to an independent regulation. This concept, often referred to by the regulated industry as the 'basic resin doctrine', does not apply to substances that are not essential to the polymerization reaction. In any case, safety assessments are conducted on all substances that might become components of food, including polymerization aids, monomers and oligomers.

Under the FCN process, polymerization aids and solvents are also subjected to an independent safety assessment along with the monomers and polymer and are also typically not included in the language in the notification letters. However, as the FCN is exclusive to the notifier, the identity and manufacturing information contained in the FCN apply to the FCS whether or not such information is included in the language in the notification letter or website listing of effective notifications. FCNs have been submitted for catalysts as an FCS.

2.5.5 Polymeric FCSs

A challenging issue with regard to the safety assessment of food contact articles is the safety evaluation of the low molecular weight oligomeric fraction of polymeric FCSs. For most polymeric FCSs, the primary focus is on the low molecular weight oligomeric fraction that might become a component of food, primarily due to the expected low solubility (in food or food simulants) and/or the low diffusivity (in the polymer matrix) of higher molecular weight oligomers. Toxicological evaluation of the low molecular weight oligomeric fraction of a polymeric FCS can be problematic due to the additional cost of fractionation and concentration of sample and/or the development of facsimiles for testing. Currently, FDA evaluates representative structures based on structure activity relationship analysis and the available data on the monomeric components, with consideration given to the oligomers that are unique to the specific FCS and the molecular linkages and steric changes that may have occurred during polymerization. This information and the assumptions used to generate the conclusions of the toxicology review are weighted with the exposure estimate to determine if additional data are necessary to ensure safety.

2.6 Conclusions

In summary, the last decade has witnessed a change in the U.S. with regard to regulatory processes for components of food contact articles, though the safety standard has remained unchanged since the Food Additives Amendment of 1958. FDA's approach to the safety assessment of these substances is exposure driven, in that it is specific to the intended use and the resultant dietary exposure, which determines the amount of toxicological data consistent with the tiered requirements. Structure activity relationship analysis or the pairing of structure activity relationship analysis with short-term genetic toxicology data can be used to determine the carcinogenic potential of a substance in lieu of available data. Potentially carcinogenic constituents with bioassay or analog data are evaluated using quantitative risk assessment principles and, when data are available and exposure warrants review,

acceptable daily intake values are established for comparison to cumulative exposure values.

Currently, FDA is exploring the development of refined tiers for multiple endpoints of genetic and reproductive toxicity, the safety evaluation of low molecular weight oligomeric fractions of polymeric substances, and the use of market share in the refinement of packaging factors. FDA's goal has been, and will continue to be, the use of all available information and the identification of the accompanying uncertainties in the safety analysis to develop better guidance and thorough, efficient safety evaluations.

2.7 Acknowledgements

The authors wish to thank Drs Mitchell Cheeseman, George Pauli and Paul Kuznesof for insightful comments and suggestions used in this chapter.

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3

Regulation of food contact materials in the EU

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3.1 Introduction

In the European Union two types of legislation exist for food contact materials: Community legislation which is adopted by the EU and national legislation adopted by the Member States. The European Union aims, amongst other things, at establishing an internal market and an economic union. This should be achieved while attaining a high level of health protection. Measures are taken to remove barriers to trade between the Member States. In the area of food contact materials the first Community legislation was adopted in 1976 laying down the general principles in a Framework Directive. At that time national legislation on food contact materials and articles existed in the Member States but provisions were divergent and thus were posing a barrier to trade. The adoption of the Framework Directive was a first step in harmonisation of the food contact materials legislation. In the meantime specific Community legislation on food contact materials has been adopted but not in all areas.

National provisions on specific materials still exist in areas where Community legislation is not adopted. The rule of mutual recognition applies to this national legislation. Any product lawfully produced and marketed in one Member State must, in principle, be admitted to the market of any other Member State. The only reason a Member State can reject a product is on the basis of protection of human health. Even under mutual recognition, national legislation may foresee that the use of a substance lawfully manufactured and/or marketed in another Member State is subject to prior authorisation provided certain requirements are fulfilled such as a simplified procedure for having the substance included on a national list.[1] In non-harmonised areas

Member States may even adopt new national legislation. This has to be notified to the Commission and must not introduce a new unjustified barrier to trade.

3.2 Community legislation

The Community legislation comprises general rules applicable to all materials and articles laid down in the Framework Regulation and specific rules only applying to certain materials or certain substances. The two general principles on which legislation on food contact materials is based are the principles of inertness and safety of the material. A general overview is presented in Fig. 3.1.

Since 2005, Community legislation can be adopted in the form of a Directive, a Regulation or a Decision. While a Regulation is directly applicable in each Member State, Directives have to be transposed into national law with transposition times of up to 18 months. In the past the 1976 and 1989 Framework Directives required a Directive as the legal instrument to adopt the specific implementing measures, but with the new Framework Regulation the favourite implementing measure has become the Regulation.

The Framework Regulation is adopted by the European Parliament and the Council while specific Directives and Regulations are adopted by the Commission after consultation with Member States in the Standing Committee of the food chain and animal health. The Commission can adopt only those proposals that gain a qualified majority of Member States in the Standing Committee.

3.3 Framework regulation

The Framework Regulation (EC) No 1935/2004[2] is the basic Community legislation that covers all food contact materials and articles. As a basic framework it defines what is meant by the term 'food contact materials and articles' and then sets the basic requirements for these materials. In Community legislation food contact materials include the following products: materials that are already in contact with food such as the packaging of pre-packaged food; materials that are intended to come into contact with food, such as cups, dishes, cutlery, food packaging not yet in use; materials that can reasonably be expected to be brought into contact with food such as table surfaces in food preparation areas or the inner walls and shelves of a refrigerator; and materials that can reasonably be expected to transfer their constituents to food such as a cardboard box around a plastic bag of cereals.

Basic requirements are set to ensure safe food and protect consumer interests. Three basic requirements are set to ensure safe food: food contact materials

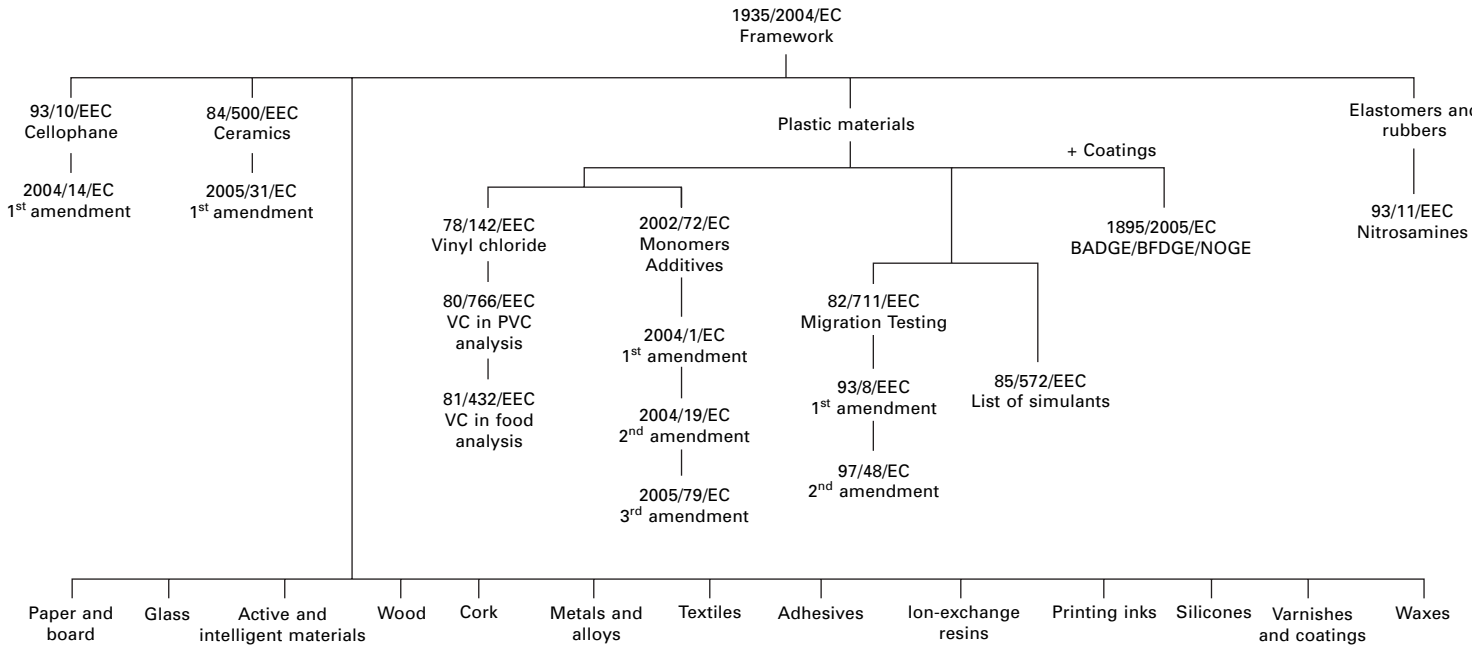

Fig. 3.1 Overview of community legislation.

shall not endanger human health; they shall not change the composition of the food in an unacceptable way; they shall not change taste, odour or texture of the food. Exemptions from the last two requirements are made for active materials (see section 3.5.5). Labelling of food contact materials is required to ensure both safety and protection of consumer interests. The consumers should be informed on: (i) the suitability of the product for food contact (to this purpose a symbol representing a glass and fork can be used); (ii) the person responsible for manufacture or placing on the market of the product; (iii) instructions for the safe use of the product; (iv) means of identification of the product for traceability.

Traceability is a general obligation derived from the general food law to ensure, e.g., retrieval of batches in case of need. Different ways of labelling are possible: on the product itself, on accompanying documents or at the retailer on a sign near the product. The information that is provided in the labelling shall not mislead the consumer. If the food contact material is also covered by Community specific legislation the producer has the obligation to declare that his food contact material is compliant with these specific requirements (see sections 3.4 and 3.5). The declaration of compliance of a packaging material for example has to contain all information on the product that is necessary for the food industry to comply with migration limits (see section 3.4).

The Framework Regulation empowers the European Commission to set requirements for specific materials. These requirements are specifications of the general rules of the Framework Regulation. These specific requirements can be set for certain types of materials, such as plastic or ceramic, or they cover only the use of certain substances. Specific requirements can comprise authorisation of substances used in food contact materials, limits on substances used, authorisation of manufacturing processes or certain materials, rules on labelling and compliance testing. The authorisation of substances is divided in a risk assessment procedure performed by the European Food Safety Authority (EFSA) followed by a risk management decision by the Commission. A person interested in the authorisation of a substance has to submit via a Member State a dossier for evaluation to EFSA. EFSA will evaluate the substance following a conventional risk assessment procedure. After consultation of the Member States the European Commission will, based on EFSA's toxicological evaluation take a decision on authorisation or not of the substance. Authorisations given until now are for substances used in plastic (see section 3.4) and regenerated cellulose film (see section 3.5.2).

All authorisations granted are general authorisations. This means everybody may use a substance authorised. There exists also the possibility to authorise the use of substances, materials or processes only for the individual petitioner. Authorised substances are listed in specific Community legislation. The Framework Regulation contains a list of materials for which specific legislation may be adopted. This list comprises 17 different materials. Only a few are yet covered by specific Community legislation (see sections 3.4 and 3.5).

3.4 Plastics

The Framework Regulation sets out the general principles that apply to materials in contact with food. Details for implementing these general rules taking account of the specific risks of the individual material is given in the specific legislation. Plastic materials and articles were the first materials to be covered by Community harmonisation. The harmonisation of the sector is not yet finished, therefore, provisions applicable to plastic materials and articles exist at Community level as well as at national level. Not all Member States have national legislation on plastics. An overview can be found in section 3.7.

The plastics Directive 2002/72/EC[3] covers plastic monolayer and multilayer structures that purely consist of plastic. A monolayer structure may be a polyethylene (PE) bag, a multilayer structure a plastic tray for pre-packaged food consisting of different plastic layers, e.g., ethylene vinyl alcohol copolymer/polyethylene (EVOH/PE). Multilayers that consist of plastic and other materials such as plastic covered paper board, as in beverage cartons, do not fall under the specific Community legislation on plastics. In this case national legislation applies. Usually Member States require that each layer has to comply with the requirements set for the respective material, while the finished article has to comply with the overall requirement of the Framework Regulation. For these multilayers compliance with the Framework Regulation is usually interpreted by most Member States as complying with the migration limits set down in the plastics Directive.

Plastic coatings, adhesives and epoxy resins are only covered in part by specific Community legislation on plastics. Usually they are used on other substrates than plastic and thus do not fall under the plastics legislation. In addition, monomers and additives used only in plastic coatings, adhesives or epoxy resins are not listed in Community lists. Plastic coatings and adhesives are covered by national legislation in some Member States. Plastic coatings containing epoxy derivatives are regulated by Regulation (EC) No 1895/2005[4] (3.5.4) Biobased polymers and biodegradable polymers such as poly-lactic acid (PLA), poly-hydroxybuteric acid (PHB), poly-caprolactone (PCL) or starch based polymers are covered by Community legislation on plastic.

The general principles set down in the Framework Regulation are the principles of inertness and safety of the material. These are interpreted in the specific legislation on plastic food contact materials as follows. The principle of inertness is translated into an 'overall migration limit' (OML). The overall migration comprises the total amount of all substances transferred from the plastic food contact material to the food. The OML is set to 60 milligrams per kilogram of food (mg/kg/food). In addition it has to be ensured that a substance migrating from the food contact material does not exhibit a technological function into the food (unless it is an active packaging: see section 3.5.5). This may occur if the substance used in food contact materials is at the same time an authorised food additive, e.g., antioxidant or preservative.

In this case the migration limit is defined by the amount of substance that does not exhibit a technological function in the food providing any limit on the amount of the food additive permitted in the food is not exceeded.

The principle of safety is translated into specific authorisation of substances which are used for the manufacture of plastic materials after their favourable toxicological evaluation by the European Food Safety Authority (http://www.efsa.europa.eu). A general authorisation for the use of the substances is given. Everybody may use the substances respecting the restrictions and specifications given in the authorisation, not only the applicant who provided the data for the evaluation. Authorised substances and their restrictions and specifications are published in Community lists annexed to the plastics Directive 2002/72/EC. The list is regularly and routinely modified through amendments to the plastics Directive. If necessary for the safety of a material 'specific migration limits' (SML) are laid down. The specific migration is the amount of a single substance that may be transferred from the plastic food contact material to the food. The SML is set individually and is based on the toxicological evaluation of the substance. A tolerable daily intake (TDI) is translated into a SML based on a conventional system. This system assumes that 1 kg of food is consumed daily by a 60 kg person. This 1 kg of food is packaged in a plastic material releasing the substance at the level of the TDI. The SML can vary from non-detectable (allowing for analytical tolerances) up to several mg/kg/food. The migration of a single substance may not exceed the overall migration limit of 60 mg/kg/food nor may it cause the total amount of migrating substances to exceed this total.

Harmonisation of national legislation on the substances used in food contact plastics was started with monomers as these are reactive substances and thus of primary importance as regards any potential health risk. Monomers and other starting substances are fully harmonised at Community level. This means that only the monomers listed in the specific Community legislation can be used in food contact plastics. An exemption exists for plastic coatings, adhesives and epoxy resins. Monomers which are used only in their manufacture are not listed in the Community lists.

In a second step, the harmonisation of additives used in plastic food contact materials was started. However, this step is not yet finished. Therefore, additives listed both in the Community legislation and in national legislation can be used in food contact plastics (for national lists see section 3.7). It is foreseen that harmonisation on additives will be finalised by 2007. Until 31 December 2006 all parties interested in additives authorised at national level have to supply EFSA with a valid application for evaluation of this additive. Only additives for which a valid application has been supplied may continue to be used according to national authorisation until evaluation is finalised by EFSA and a decision on authorisation is taken by the European Commission. The Community list on additives contains those additives that are used solely in plastics and those used both in plastics and coatings. However, it does not contain additives used only in plastic coatings, adhesives and epoxy resins.

The list does not contain solvents and aids to polymerisation, which are not intended to remain in the final product and colorants.

Impurities, reaction and degradation products of the authorised substances are usually not evaluated unless listed in restrictions and specifications for the authorised substance. They remain the responsibility of the producer of the material and article who has to take care that they do not migrate in quantities that pose a health risk.

3.4.1 Verification of migration limits

Analysis of migration from food contact materials can be performed according to different protocols. Verification of the migration limit can be performed in the foodstuff itself, in case the food is already in contact with the food packaging. Verification of migration limits may also be performed in food simulants, usually in the case of packaging which is not yet in contact with food. The legislation foresees four food simulants representing the different possible extraction properties of food (Directive 82/711/EEC)[5]. These four simulants are water for aqueous food, 3% acetic acid for acidic food, 10% ethanol for alcoholic food and olive oil for fatty food. A correlation list is laid down in legislation that indicates which food is represented by which food simulant (Directive 85/572/EEC)[6]. Verification can also be performed by extracting the residual amount of a substance in the food contact material. The residual amount can then either be directly compared with the SML or be subject to mathematical migration modelling giving the migration potential of the application. For proof of non-compliance with SML values only the migration testing of food and food simulants can be accepted.

Migration testing has to be performed under worst foreseeable contact time and temperature for the envisaged application. A long-term storage at room temperature is, for example, represented by storage for ten days at 40 °C. A correlation table with migration test conditions is laid down in the legislation (Directive 82/711/EEC). Analytical methods for migration testing of overall migration and specific migration have been standardised at European level by the European standardisation body CEN (http://www.cennorm.be).

3.5 Other materials

Not only for plastics but also for some other materials specific Community legislation exists, namely Ceramics and Regenerated Cellulose Film (Cellophane, RCF). For rubber teats and soothers migration of nitrosamines is regulated. For coated materials, plastics and adhesives the substances BADGE, BFDGE and NOGE are regulated. No specific Community legislation exists yet for active and intelligent materials but some general rules for those materials are laid down in the Framework Regulation.

3.5.1 Ceramic articles

Ceramic articles may pose a risk to the consumer through heavy metals used in the glazing and colouring. Substances of major concern in the past have been lead and cadmium. Community legislation (Directive 84/500/EEC[7] amended by Directive 2005/31/EC[8]) therefore imposes limits for lead and cadmium leaching from ceramic articles into a 4% (v/v) acetic acid solution. Rules for migration testing and performance criteria of the analytical method are set out in the legislation. For other heavy metals the general rules of Article 3 of the Framework Regulation applies. Some Member States have national restrictions for some of the other heavy metals and separate limits for migration from the mouth rim of cups and beakers (see national legislation).

3.5.2 Regenerated cellulose film (cellophane)

At Community level specific rules for materials and articles made of cellophane exist (Directive 93/10/EEC[9] as amended by Directive 93/111/EC[10] and Directive 2004/14/EC[11]. Exempted are synthetic casings such as those used for sausages. In these exempted cases national legislation applies. The legislation contains a positive list of substances that can be used in the manufacturing of cellophane. The restrictions in the positive list are usually expressed as residual content in the film because migration testing with pure cellophane film into a liquid simulant is in general not feasible due to the absorption of water by the film. The positive list does not include dyes, pigments and adhesives. Substances used for these purposes shall not migrate into food in detectable amounts. As from 29 July 2005 the legislation also covers plastic coated cellophane. For the plastic coating, only substances in the lists of authorised substances in the plastics Directive (Directive 2002/72/EC as amended) shall be used. The whole film has to comply with overall migration and specific migration limits in the plastics Directive. Analytical methods for compliance testing are published electronically on the internet at http://crl-fcm.jrc.it.

3.5.3 Rubber teats and soothers

In the 1980s it became evident that rubber teats and soothers may release carcinogenic nitrosamines, which are reaction and degradation products from accelerators and stabilisers used in the rubber. Legislation contained in Directive 93/11/EEC[12] prescribes that nitrosamines and nitrosatable substances that can be transformed into nitrosamines in the stomach shall not be released from the teats and soothers in detectable quantities. Methods for the analysis are proposed with the detection limit set to 0.01 mg/kg rubber for nitrosamines and 0.1 mg/kg rubber for nitrosatable substances.

3.5.4 BADGE, BFDGE and NOGE in coated materials, plastics and adhesives

In the 1990s high amounts of BADGE (Bisphenol A diglycidyl ether) were discovered in fish in oil in tins. The source of the contamination was the coating where BADGE was added as an additive. As the substance contains epoxy groups it was a suspected carcinogen although it was not considered to be genotoxic. Measures were taken to reduce the migration of BADGE from the coating, the plastic and any adhesive. The measures also covered the replacement products BFDGE (Bisphenol F diglycidyl ethers) and NOGE (Novolac glycidyl ethers) which are similar in structure to BADGE. The toxicity of BADGE has now been more thoroughly investigated and studies have clarified that BADGE is not carcinogenic in humans. Toxicity of BFDGE and NOGE, however, is still not clear. The Community legislation takes account of the new toxicological results (Regulation 1895/2005/EC) and sets a new, higher migration limit for BADGE and its hydrolysis products at 9 mg/kg/food, but for BADGE chlorohydrins it maintains a limit of 1 mg/kg/food. The use of BFDGE and NOGE was prohibited as from 1 January 2005 and 1 March 2003 respectively. Exempted from this ban are heavy-duty coatings in tanks of a capacity greater than 10,000 litres and attached tubing. Analytical methods have been developed by CEN.

Although it is specific to these substances, this legislation has been the first to explicitly set out any rules for coatings and adhesives and those plastics not within scope of the rules on food contact plastics. This last point arises from the fact that the legislation covers all plastic materials and articles, not just those within the scope of Directive 2002/72/EC, as amended.

3.5.5 Active and intelligent materials and articles

The main functions of packaging were regarded in the past as protecting the food from contamination and spoilage and enabling transport of the food. From this concept the basic principles of food contact materials legislation are derived: packaging should be inert; it should not release substances into food that pose a risk to human health; it should not release substances into food that change the taste and composition of the food. Recent technological developments have made it possible to assign new functions to the packaging; it could inform the consumer about the condition of its content and may even interact with the food by releasing or absorbing substances. In view of these additional functions food contact material legislation was revised in 2004. Two new concepts – apart from inert packaging – have therefore been introduced in the legislation, intelligent food contact materials and active food contact materials. The basic principles of food contact materials have been adjusted in the Framework Regulation to take account of these new features.

Intelligent food contact materials are those that provide the consumer with information on the status of the packaged food or the atmosphere in the

packaging. This information may, for example, indicate storage conditions the food has undergone using time/temperature indicators that turn from green to red when the food has been stored for a certain time at elevated temperatures. Other examples are indicators for oxygen level in the food or for the presence of microorganisms that spoil the food. The general principle of inertness and the requirements that control substance migration continue to apply to this type of food contact material. However, given the extra function of the packaging, it has to be ensured that the information provided to the consumer is not misleading. A freshness indicator, for example, should not misleadingly indicate freshness when the food is already spoiled.

Active food contact materials are those that actively change the composition of the food or its surrounding atmosphere. Two functions have been distinguished, those of absorbers and releasers. Absorbers are those that work by absorbing substances from around the food or the atmosphere inside the packaging, e.g., oxygen scavengers that reduce the oxygen level around and in the food and thus prevent microbiological growth and reduce oxidation of the food. Releasers are the converse: they release substances into the food to improve the food or its condition, e.g., packaging that releases preservatives into the food. The new characteristic of the packaging now permitted is that the active substance is added to the material to be intentionally released into the food. However, traditional packaging that releases its natural constituent into the food such as wooden barrels used in wine and whiskey production are not covered by the definition of active packaging. Neither are materials to which an antimicrobial substance is added to keep the surface of the material free of microbiological growth. The function in this latter case is exhibited on the material itself and not on the food. Examples are antimicrobials in chopping boards or conveyer belts.

Thus, in contrast to the traditional concept that food contact materials are inert and perform no intended function on the food, active materials may change the composition of the food, e.g., by releasing preservatives, and may change the environment around the food by the absorption of oxygen; they may also change the taste of the food, e.g., by releasing flavours and may change the colour of the food by releasing colorants. To take account of this and to ensure safe application of the material the principle of inertness was modified in the Framework Regulation. Active materials may release substances into food but only under certain specified conditions. The substance released has to be a substance that is authorised in the context of food legislation,[13] e.g., an authorised food additive, or an authorised flavouring. The substance may only be released into the foods in which its presence is authorised for release by food legislation, e.g., sorbic acid may be added to pre-packed sliced bread but not to whole bread. The substance may only be released in quantities authorised in food legislation, e.g., sorbic acid 2000 mg/kg pre-packed sliced bread. The change in the composition or taste of the food shall not mislead the consumer about the quality of the food, e.g., an absorber may not mask food spoilage, a colorant may not mask low food quality.

Information has to be provided to all operators in the food chain and to the final consumer to ensure the correct application of, and compliance with, food legislation. Therefore strict labelling rules have been established. The producer of the material has to provide to the food packer information on the identity of the substance used and levels released. The food packer has to list the released substance in the table of ingredients. Labelling also has to clearly show when active or intelligent materials are used. Non-edible parts of the packaging, e.g., absorbing sachets in food packaging, have to be clearly labelled as non-edible. Only the basic requirements are laid down in the Framework Regulation; additional requirements may be necessary (see section 3.9.2).

3.6 Control of food contact materials in the EU

The basic rule in the Community food legislation specifies that only safe food shall be placed on the market (General Food Law[14] Art. 14). Consequently food contact materials shall not transfer their substance into the food in concentrations that can endanger human health (Art. 3 Framework Regulation). The main players to ensure safety as regards food contact materials are the packaging industry, the food industry, competent authorities in the Member States, and the European Commission.

3.6.1 The role of the business operators: food industry and packaging/contact material industry

Both the food industry and the food contact material industry have a shared responsibility for the material in contact with the food and, as a consequence, for the food itself. In the case of food packaging the food packer has to ensure that he uses only packaging that is suitable for the packaging of the food and that it conforms to the Community and/or national legislation on food contact materials. The packaging industry has to supply packaging that is suitable for food contact. This means they have to make sure that substances they use in the food contact material are authorised (if positive lists exist) and/or are not transferred into food in concentrations that pose a danger to human health. They have to confirm this in a declaration of compliance. An intensive dialogue between the two parties is therefore essential for compliance with the legislation to be achieved. The food business operator has an obligation to withdraw unsafe food from the market and to collaborate with the national control authorities on that (Regulation (EC) 178/2002 – the general food law). The European Commission has published guidelines to help business operators to comply with this obligation.[15]

3.6.2 The role of the Member States

Member States have the responsibility for enforcing the Community and their own national legislation and must monitor that the requirements of the legislation are fulfilled by the business operators (general food law). Inspection and control measures on food contact materials shall be carried out according to the Regulation (EC) No 882/2004 on official feed and food control[16] (OFFC). In the OFFC it is specified that control of the application of the rules on materials and articles in contact with food are within its scope. Member States are required to carry out official controls regularly and with appropriate frequency that should be based on the level of assessed risk. The controls shall include those on materials and substances including those covering food contact materials. They shall treat equally products for the EU and the local market as well as imports and exports. Official control can cover the following actions: monitoring, surveillance, verification, audit, inspection, sampling and analysis. The text explicitly mentions inspections on materials and articles in contact with food. Member States have to lay down a catalogue of sanctions and measures including dissuasive penalties for non-conformity with the food legislation. The measures taken by Member States may include prohibiting placement on the market; they may order and monitor withdrawal of goods from the market, recall and destruction. Furthermore they have the right to detain consignments from third countries.

When Member States take measures that affect other Member States, such as withdrawal from the market when the article originates from, or is distributed to, another Member State, they should inform the Commission and the other Member States via the electronic Rapid Alert System for feed and food (RASFF). Other Member States affected by their action are then also able to act. Member States have to lay down their control activities in multi-annual control plans as from 2007.

3.6.3 The role of the European Commission

The European Commission's Food and Veterinary Office carries out Community controls in the Member States and in third countries in order to check their national control systems. On food contact materials, until now, desk studies on the systems in place have been performed.

3.6.4 Methods for sampling and analysis in the official control

The OFFC Regulation establishes a hierarchy of methods used for sampling and analysis in applying official controls. First priority is given to methods laid down in Community legislation. If these do not exist, methods according to internationally established rules such as those of CEN or those in national legislation should be applied. In the absence of these methods other methods fit for the purpose or developed in accordance with scientific protocols shall be used. In the area of food contact materials analytical methods are laid

down in Community legislation for vinyl chloride in PVC and food, lead and cadmium leaching from ceramic ware, nitrosamines and nitrosable substances in rubber and food as well as rules for migration testing. The majority of methods in the area are standardised CEN methods covering migration testing procedures (series EN1186) and the analysis of specific migrating substances (series EN13130).[17] Examples for methods laid down in national legislation are the methods according to §64 of the German Lebensmittel-, Bedarfsgegenstände- und Futtermittelgesetzbuch.[18]

Other methods used in the context of official controls such as those used for in-house control purposes may be single laboratory validated according to internationally accepted protocols (e.g. IUPAC harmonised guidelines). General criteria for the characterisation of methods of analysis exist.

A system of Community Reference Laboratory (CRL) and National Reference Laboratories (NRLs) is being established to achieve uniformity in the application and the performance of laboratories in the official control. This system has become fully functional in 2006 with the contact materials laboratory at the Joint Research Centre IHCP in Ispra acting as CRL (http://www.crl-fcm.jrc.it).

3.7 Specific national legislation

Community legislation was introduced to harmonise national legislation and to remove barriers to trade. Member States legislation is based on different principles and this can still be observed in those areas which are not yet covered by Community legislation. Four main legal systems can be distinguished.

1. Pre-market approval system: this system was applied by some new Member States. All materials and articles had to be approved by a central authority before they could be placed on the market. This system no longer exists.
2. System of authorised substances and migration limits comparable to the Community system: this system was applied in the Netherlands (*warenwet*) and to some extent in France and Italy. It still exists for those specific areas where no Community legislation is yet in place.
3. System of recommendations and quantities of substances recommended to be used in the final material or article: this system is applied in Germany (BfR recommendations).
4. System of no specific legislation but industry code of practice defining due diligence of the business operators: this system is applied in the UK.

Most of the 25 Member States do not have specific national rules. Newer EU Member States replaced their national legislation with Community legislation before accession to the EU.

Member States that do not have specific national legislation on food contact materials will sometimes refer to other Member States' legislation, such as Dutch *warenwet* or the German recommendations, when testing for

safety compliance. Some Member States may also refer to the application of the general safety clause included in the new Framework Regulation to the resolutions and policy statements of the Council of Europe. In the area of food contact materials the Council of Europe (CoE) (http://www.coe.int) can take initiatives in those sectors which are not yet harmonised at Community level.

Table 3.1 gives an overview of the Member States in which national legislation exists and in which sectors national legislation is applicable. Links to national legislation are provided in section 3.10. Norway, Iceland and Liechtenstein, as part of the European Economic Area (EEA), also apply the Community legislation while keeping additional national legislation. Switzerland has adopted regulations corresponding to the Community legislation.

3.8 Strengths and drawbacks of EU legislation

The general rules are applicable to all materials and articles manufactured in the internal market and to all imports. Specific rules are adopted only when necessary from a risk point of view keeping legislation to a minimum. Through the concept of mutual recognition, materials and articles manufactured according to the rules of one Member State can be traded also in other Member States. Following the concept of subsidiarity, control is within the responsibility of Member States but according to harmonised rules and principles. Through this concept the requirements that food contact materials have to fulfil are harmonised but a certain freedom is left to Member States to ensure that they are implemented in the least burdersome manner and in line with existing national legislation.

Rules and limits apply to all materials and articles; no individual authorisations are given. The limits are set based on a conventional system after toxicological evaluation of the substances. This system allows for all producers to use the substances within the limits set while ensuring a high level of consumer protection. The rules are thus transparent and equal for all producers. The system does not require that every new user files its own application, thus new uses are legitimate whenever they are compliant with the limits and specifications set in the legislation. This reduces administrative work for manufacturers and the authorities. Risk assessment and risk management are separated between two organisations, ensuring the independence of both.

The division of EU legislation into Community and national rules leads to a complex system which may lack clarity. In areas where no harmonised specific Community legislation exists, different interpretations of general rules by Member States and industry may lead to legal uncertainty. The procedure for adoption of new Community rules is time consuming as a fixed procedure and agreement of Member States has to be gained, making

Table 3.1 Summary of national legislation

Member State	Other	Adhesives	Ceramics	Glass	Enamel	Metals alloys	Cork	Wood	Textile
Austria	–	–	+	–	+	–	–	–	–
Belgium	–	–	–	–	–	–	–	–	–
Cyprus	–	–	–	–	–	–	–	–	–
Czech Republic	–	–	+	+	+	+	+	+	–
Denmark	Mandatory registration[1]	–	+[2]	–	–	–	–	–	–
Estonia	–	–	–	–	–	–	–	–	–
Finland	–	–	–	–	–	+	–	–	–
France	–	–	+	+	+	+	–	+	–
Germany	–	+[3]	+[4]	+[4]	+[4]	–	–	–	–
Greece	–	–	–	–	–	+	–	–	–
Hungary	–	–	+	–	+	+[5]	–	+	–
Ireland	–	–	–	–	–	–	–	–	–
Italy	–	–	+	+	+[6]	+[7]	–	–	–
Latvia	–	–	–	–	–	–	–	–	–
Lithuania	–	–	–	–	–	–	–	–	–
Luxembourg	–	–	–	–	–	–	–	–	–
Malta	–	–	–	–	–	–	–	–	–
Netherlands	–	–	+	+	+	+	+	+	+

Table 3.1 Continued

Member State	Other	Adhesives	Ceramics	Glass	Enamel	Metals alloys	Cork	Wood	Textile
Poland	–	–	+[8]	–	+[8]	–	–	–	–
Portugal	–	–	–	+[8]	+[8]	–	–	–	–
Slovakia	–	–	–	+	–	+	+	+	+
Slovenia	Yes: colours[9]	+	–	+	+	+	–	+	+
Spain	Yes[10]	–	–	–	–	–	–	–	–
Sweden	–	–	–	–	–	+	–	–	–
UK	–	–	–	–	–	–	–	–	–

+ : National legislation applies; – : no national specific legislation

1. Mandatory registration for producers and importers of plastics, ceramics, glass and regenerated cellulose
2. Also for glass and ceramic products
3. BfR recommendation
4. DIN standard
5. National legislation and standards
6. Limitation on lead
7. Specific measures for stainless steel, tin-free steel, tin containers
8. National standards
9. Rules on the requirements concerning the hygiene suitability of consumer goods
10. Plastic materials legislation, prohibition of recyled plastics, register on substances and manufacturers

Table 3.1 Continued

Member State	Paper board	RCF	Plastics	Varnish coating	Printing inks	Silicone	Wax	Rubber	Ion-exchange resin
Austria	–	–	–	–	–	–	–	–	–
Belgium	–	–	–	+[11]	–	+[11]	–	–	+[11]
Cyprus	–	–	–	–	–	–	–	–	–
Czech Republic	+	–	–	+	+	+	–	+	–
Denmark	–	–	–	–	–	–	–	–	–
Estonia	–	–	–	–	–	–	–	–	–
Finland	+	–	–	–	–	–	–	–	–
France	+	–	+	+	–	–	–	+	–
Germany	+[3]	–	+[3]	–	–	+[3]	+[3]	+[3]	–
Greece	+	–	+	+	–	–	–	–	–
Hungary	–	–	–	–	–	+[12]	–	+[12]	–
Ireland	–	–	–	–	–	–	–	–	–
Italy	+	+	+	+	–	+	–	+	–
Latvia	+[13]	–	–	–	–	–	–	–	–
Lithuania	–	–	–	–	–	–	–	–	–
Luxembourg	–	–	–	–	–	–	–	–	–
Malta	–	–	–	–	–	–	–	–	–
Netherlands	+	+	+	+	+	+	+	+	–
Poland	+[8]	–	–	–	–	–	–	–	–
Portugal	–	–	–	–	–	–	–	–	–
Slovakia	+	–	–	+	–	–	–	+	–
Slovenia	+	–	–	+	–	–	–	+	–
Spain	–	–	+	–	–	–	–	–	–
Sweden	–	–	–	–	–	–	–	–	–
UK	–	–	–	–	–	–	–	–	–

11. Resolutions (adoption pending)
12. For teats
13. Paper and cardboard materials and articles cannot release more than 0.5 mg cadmium from 1 kg of paper and not more than 3 mg of lead from 1 kg of paper

quick reactions to innovations impossible. Long transposition times of Community Directives into national legislation add to this. However, more recently, the framework for EU legislation on food contact materials and articles has changed to permit EU harmonisation and consumer protection through the adoption of European Regulations that apply directly in all 25 EU Member States. This avoids all 25 Member States having to go through sometimes lengthy processes to transpose EU rules into national legislation. It also reduces ambiguity in the rules that can arise from such widespread transposition work. The harmonised rules are therefore in place much quicker than in the past.

General authorisation asks for a greater margin of safety when setting limits than authorisations given only for specific applications. In an exposure-based system, in cases of very limited individual applications, higher limits could be set.

3.9 Future trends

3.9.1 Plastic

The completion of harmonisation of rules for plastic food contact materials and articles is within sight. The finalisation of the positive list for authorised additives is likely to happen in 2008. In 2007 the Commission will, besides the Community list of authorised additives, publish a list of additives authorised at national level for which a valid application for EU authorisation has been made to EFSA. Only these substances may be used until evaluation is finalised by EFSA and a decision on authorisation is taken by the European Commission. Another project in the plastics sector is the extension of the rules to multimaterial multilayer structures where the plastic layer is in contact with the food. At this moment only plastic materials which consist entirely of plastic are covered by the plastics Directive. These materials, when they are made up from layers of plastic, constitute only about 15% of the mutilayer market. Other multilayer materials such as beverage cartons, which consist of a food contact layer of plastic and aluminium and/or paper, are not yet covered by specific legislation. Extension of the plastics rules to these materials will have to take into consideration requirements for the non-plastic layers and establish rules for migration testing of these materials.

When migration limits for substances are set a conventional system is applied to calculate exposure. It is assumed that a 60 kg person will consume 1 kg of packaged food per day. However, a different convention is sometimes necessary for some circumstances. One such arises in the case of lipophilic substances. Lipophilic substances migrate readily into fatty foods. The consumption of fatty foods is usually only 200 g or less per day. For these substances a reduction factor is therefore planned for use in compliance testing, taking into account the lower consumption of fat.

In multilayer materials a layer can function as a barrier to migration of

substances into food. When such a functional barrier layer is applied that ensures no migration into food it may not be necessary to authorise the substances behind that layer if the substance is not carcinogenic, genotoxic or toxic for reproduction. Recycling of plastic materials has come into focus as sustainability of production and environmental issues become more important. Recycling of used PET beverage bottles into new beverage bottles is increasingly common in Member States. Requirements on the use of recycled plastic for use in contact with food vary between EU Member States from a ban to authorisation schemes to no requirements at all. Some Member States, such as the UK, apply the rules for virgin plastics to recycled plastics. EU harmonisation of the rules is necessary to ensure the equal treatment of recycled plastics in all Member States. Critical points in the recycling for food contact are the quality of the material that is being recycled and the ability of the recycling process to reduce contamination. These points will have to be addressed when regulating these materials.

3.9.2 Active and intelligent materials

Basic requirements for active and intelligent materials have been set in the Framework Regulation. However, some issues need further clarification. The main issues are the applicability of the requirements of the plastics directive to active and intelligent plastic materials, especially compliance with overall and specific migration limits, rules for non-plastic active and intelligent materials, risk assessment of active ingredients and if necessary conditions/restriction of their use, and rules on the efficacy of the materials in relation to instructions for their use and protection of the consumer.

3.9.3 Nanomaterials

In food contact materials, as in other areas, substances may be used in manufacturing materials and articles and added in the form of nanoparticles to increase the functionality of the material. The use of this technology is developing. The challenge for the industry and European authorities is to assess if the migration behaviour from the nanomaterial is different from that of traditional materials and whether substances migrating are more reactive and have a different toxicological profile from regular substances. The answers to these questions will determine if specific requirements are necessary for nanomaterials and if there is a need for a specific implementing measure. At this moment the EU is developing general strategies for policies on nanomaterials, nanoparticles and nanotechnology on a horizontal level.

3.9.4 Risk assessment

For the majority of materials and articles specific Community legislation is not yet in place. In the area of plastic materials and articles, monomers and

additives are toxicologically evaluated but possible impurities, reaction and degradation products are not taken into consideration in the authorisation unless they have been evaluated in the risk assessment. Therefore it is the manufacturer's responsibility to assess and ensure the safety of such substances that migrate from their products. To ensure the safety of the product the manufacturer should apply scientifically based risk analysis including exposure assessment in those instances where an established migrant into the food is not specifically regulated in law.

3.9.5 Other materials

For materials not yet harmonised at Community level the Council of Europe resolutions could be taken as a basis for discussion on new rules. Paper and board, coatings and adhesives are the sectors most likely to follow after the work on the harmonisation of plastics is complete.

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4

Traceability and food contact materials

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4.1 Introduction

Traceability has become an integral requirement of modern quality management systems: tools to address recall of defective products have been put in place by food contact materials and articles manufacturers, either as part of Good Manufacturing Practice (GMP)[1] or within the ISO 9000 certification.[2] Tracing all elements that contribute to a finished product is mainly needed to address quality defects, i.e., traceability has been primarily conceived as a tool to remedy failures of quality control. The good quality of food contact materials and articles is not only a legal requirement but is also an obvious competitive advantage. It is in the industry's interest to maintain a high level of control over its production and this can be achieved through suitable traceability systems.

Another driver for the implementation of traceability systems is that the food market does not accept food contact materials and articles of uncertain origin. In the early 1990s systems for controlling hygiene of products became common practice in the food contact manufacturing industry. As a consequence of the adoption of HACCP[3] by food industries and the entering into force in Europe of Directive 93/43/EC,[4] procedures for traceability of products became used to address possible recalls related to hazards transferred to food from food contact materials. Hazards from adventitious contamination (chemical, physical or microbiological) have been managed through these traceability procedures, but there is little evidence of food recalls triggered by contamination due to the intrinsic chemical nature of the food contact materials. In fact, although several scares have been reported in relation to the chemical composition of food contact materials, in particular plastics, all of them were

eventually demonstrated to be 'perceived risks' rather then 'real risks', since consumers' exposure to chemicals from these materials is low enough to hardly cause any effect on human health. Consequently there are no examples of recalls of products related to the field of application of Regulation 1935/2004/EC (or the former Directive 89/109/EC).

Nevertheless, the European Commission, while revising Directive 89/109/EC, took the decision to introduce a clause of mandatory traceability for food contact materials and articles. This was requested by some Member States that were claiming a lack of control tools for determining responsibilities in the value chain. Another reason for the introduction of mandatory traceability for food contact materials and articles was found in Article 18 of Regulation 178/2002/EC.[5] That established the same requirement for traceability of food, feed, food-producing animals and any other substance intended to be, or expected to be incorporated into a food or feed at all stages of production, processing and distribution. Although substances migrating from food contact materials and articles are not intentionally added to the food, they may be seen as substances expected to be incorporated in the food, therefore the new provisions on traceability of food contact materials and articles fill the gap that article 18 of Regulation 178/2002/EC may have created.

4.2 Regulation of traceability of food contact materials

4.2.1 Field of application

Framework Regulation 1935/2004/EC[6] covers all materials and articles that '(a) are intended to be brought into contact with food or (b) are already in contact with food and were intended for that purpose or (c) can reasonably be expected to be brought into contact with food or to transfer their constituents to food under normal or foreseeable conditions of use' (Article 1.2). In Annex I of the Regulation are listed the materials and articles that shall be covered by specific measures, i.e.,

- active and intelligent materials and articles
- adhesives
- ceramics
- cork
- rubbers
- glass
- ion-exchange resins
- metals and alloys
- paper and board
- plastics
- printing inks
- regenerated cellulose
- silicones

- textile
- varnishes and coatings
- waxes
- wood.

The field of application, however, is not limited to the above-mentioned materials and articles but would include other products provided that they fulfil the requirements of Article 1.2. In the field of plastic materials, for example, not only plastics for wrapping foodstuffs are covered, but also plastic laminates used as inner parts of furniture or fridges with which food may be put in contact.

4.2.2 Definitions of traceability

There are numerous definitions of traceability, applicable to different environments. For example, definitions can be found in Article 18 of Regulation 178/2002/EC for food and feedstuffs, in Regulation 1830/2003/EC on Genetically Modified Organisms[7] and in the Codex Alimentarius.[8] From these sources the following definition of traceability can be derived: 'the ability to go back in the history of a food contact material or article, from the retail stage back to the point of its manufacturing, identifying all appropriate information.'

There are two levels of traceability, i.e.,

- Level 1 – traceability within the operation of each stakeholder: this level concerns the systems that each stakeholder has in place to link a lot of his products to the starting materials used to produce them.
- Level 2 – traceability between different stakeholders: this level is concerned with the transmission of information along the chain. It should be possible from any point downstream, and in particular at the retailing point, to go back in the chain and identify by whom the material or article has been manufactured.

This also implies that, in the opposite direction, the material or article can be traced from any point in the chain down to the retailing point. In other words, if traceability can be described as the possibility to trace back from finished goods shipments to raw material lots, this should not neglect that there is a need to trace forward from raw material lots to identify all finished goods shipped. In fact traceability was introduced primarily for ensuring that defective food contact materials are identified and withdrawn from the market, in particular as far as compliance with the applicable legislation is concerned. If a given raw material is found in violation of the law, or such as to impair safety of the finished product, traceability systems shall be such as to allow withdrawal of all other finished product in which the concerned raw material has been used. To achieve this objective both levels must function properly.

4.2.3 Article 17 of Regulation 1935/2004/EC

Traceability is addressed in Article 17 of this Regulation, which reads as follows:

> 1. The traceability of materials and articles shall be ensured at all stages in order to facilitate control, the recall of defective products, consumer information and the attribution of responsibility.
> 2. With due regard to technological feasibility, business operators shall have in place systems and procedures to allow identification of the businesses from which and to which materials or articles and, where appropriate, substances or products covered by this Regulation and its implementing measures used in their manufacture are supplied. That information shall be made available to the competent authorities on demand.
> 3. The materials and articles, which are placed on the market in the Community, shall be identifiable by an appropriate system, which allows their traceability by means of labeling or relevant documentation or information.

Paragraph 1 explains the rationale under which traceability is established. It should be noted here that all the stakeholders are expected to benefit from the introduction of the Article: public authorities, because of facilitation of control, manufacturers and users of food contact products, who will benefit from recall and easier attribution of responsibility, and finally a stricter regulation of traceability would give additional reassurance to consumers. As stated above, the main reason for traceability procedures having been introduced by food contact materials producers was related to defective product recall, i.e., linked to potential technical failure of them, rather than health hazards (that are extremely unlikely). Therefore such a paragraph can be interpreted as a measure of prevention that is not deemed to bring extra safety factors to the final consumers.

Paragraph 2 is very important and worth a closer examination. First of all we notice that while traceability shall encompass identification of the companies from which a given raw material is purchased and to which a finished product is shipped, nothing is said about internal traceability, meaning that according to this article it is not strictly mandatory. In other words, paragraph 2 does not require that manufacturers of food contact materials are able to relate the batch identification of their finished products with the batch identification of the raw materials used for the production of the said finished products. The choice of not requiring internal traceability has been determined by the necessity of not exceeding the requirements placed on food and feedstuffs and relevant components by article 18 of Directive 178/2002/EC. However, since internal traceability is felt to be an important issue, the food contact materials industry has been successively requested by the Commission (DG SANCO) to develop guidelines addressing internal traceability. These would in principle be used, especially by small and medium-size enterprises, to harmonise the procedures adopted. Such a request was formalised by a specific

letter sent by the European Commission, Health and Consumer Protection Directorate-General to the European Plastics Converters Association.[9]

As we will show later in this chapter, the processes that raw materials undergo, e.g., in the plastics industry, are often very complex and internal traceability entails the use of sophisticated tools of control. In some cases a one-to-one correspondence between an incoming lot of a raw material and a specific lot number of a finished product is not technically achievable, therefore a certain degree of uncertainty has to be accepted. The Legislator, introducing the clause dealing with 'technological feasibility' in Paragraph 2, implicitly recognises the need for some approximation. The extent of precision in traceability depends on type of food contact material, component and process; the more complex they are the less is the degree of precision that has to be accepted.

Paragraph 3 deals with methods for the identification of food contact materials and articles. While identification tools are necessary for allowing traceability, the use of appropriate tools is left to the industrial operators. These tools may be different in relation to the process, e.g., labelling each item that goes into retail stores may be easy and appropriate for simple processes, involving only one step of manufacturing done by one single operator. But it may be less appropriate for those processes that are carried out by more than one operator, where labelling of pallets or boxes containing items of a single production lot may better serve the purpose. The information may be conveyed via alphanumeric codes or via bar codes. The latter are largely used, and some of them such as EAN 128 are becoming a standard requirement of the food industry. Some companies have adopted radio frequency indicators (RFID), which allow the storage of a large amount of information, thus serving other purposes than merely identifying the products. The food contact materials manufacturers consider flexibility in the choice of the most appropriate tool very important, as this has a direct influence on cost.

4.3 Industrial guidelines for traceability of materials and articles for food contact

4.3.1 Objectives and contributors to the guidelines

As already highlighted in the previous section, the associations representing the food contact materials and articles industries have been requested by the Commission to develop guidelines that would help the industry to harmonise the procedures adopted to achieve the objective set forth by Article 17 of Regulation 1935/2004/EC. These Guidelines have been prepared by a team representing virtually all the food contact materials industries; the team was led by EuPC, the European Association of Plastics Converters (see Fig. 4.1). The Guidelines are published in the form of a Code of Practice. This Code

- **APEAL**, Association of European Producers of Steel for Packaging
- **BLIC**, European Association of the Rubber Industry
- **CEFIC FCA**, European Council of Chemistry, Food Contact Additives
- **CEI-Bois**, European Confederation of Woodworking Industries
- **CEPE**, European Council of Paint, Printing Inks and Artists' Colors Industry
- **CEPI**, Confederation of European Paper Industries
- **CIAA**, Confederation of the food and drink industries of the EU
- **CIPCE**, Comité International de la Pellicule Cellulosique
- **CPIV**, Standing Committee of the European Glass Industries
- **EAA**, European Aluminium Association
- **ETS**, European Tissue Symposium
- **EuPC**, European Plastics Converters Association
- **EuroCommerce**, the retail, wholesale and international trade representation to the EU
- **FEFCO/ProBox**, European Federation of Corrugated Board Manufacturers
- **FEVE**, European Container Glass Federation
- **FPE**, Flexible Packaging Europe
- **PLASTIC EUROPE**, Association of Plastics manufacturers in Europe
- **SEFEL**, European Secretariat of Manufacturers of Light Metal Packaging

Fig. 4.1 Contributors to Industrial Guidelines on Traceability of Materials and Articles for Food Contact (also referred as 'the Code').

is available in the Community Joint Research Center website[10] and it was submitted to the European Commission for comments in January 2006. Converters and raw materials producers were the main contributors to the Guidelines although representatives of the food industry and retailing industry provided their view, especially in the preparatory phase. It was recognised, however, that their needs in terms of traceability for food contact materials and articles are rather different from those of converters and raw materials producers, and are solely related to the need for creating and maintaining a link between the identification of food contact materials and the identification of food and food components to fulfil Article 18 of Regulation 178/2002/EC.

4.3.2 Structure of the document

Some elements in the Guidelines are common to all materials and articles, while internal codes of practice are different in relation to the chemical and manufacturing processes. For this reason the Guidelines have been divided into two sections, the former dealing with all common elements and the latter composed of several subsections, each of them dealing with one specific material. The structure of the Guidelines is reported in Fig. 4.2.

4.3.3 Involved stakeholders

The different stakeholders involved along the supply chain of food-contact materials and articles are reported in Fig. 4.3. Taking as the central point where the food contact material or article is manufactured, i.e., the converters

Fig. 4.2 Structure of the Industrial Guidelines for Traceability of Food Contact Materials and Articles.

or producers, we can identify an 'upstream' and a 'downstream', as indicated. Converters transform materials that have been produced by upstream suppliers into finished articles or semi-finished goods, consisting essentially of the same materials. Producers manufacture articles directly from starting materials, using processes involving chemical, as well as physical change. To achieve the objective of tracing a food contact material or article it is necessary that the relevant information be passed along the chain from one stakeholder to the next and that such information is managed so as to maintain the link between incoming goods and outgoing products of the concerned stakeholder.

The scheme reported in Fig. 4.3 assumes that the whole chain is within the European Union, where Regulation 1935/2004/EC is fully applicable. However, in some cases, part of the chain can be outside the EU, therefore another business must be put in the scheme, namely the importer. Import may take place at different levels, such as importing

- starting materials by the converters and producers
- empty packaging by distributors or fillers
- food contact articles by distributors or retailers
- filled food contact materials and articles by distributors or retailers.

It is evident that importers of food contact materials in the EU can only guarantee that suppliers and goods imported are appropriately identified and are accompanied by a declaration of compliance ensuring that the imported products fulfil the EU legislation in the relevant area of food contact materials and articles. But importers are not in a position to ensure that the same rules of internal traceability are followed by manufacturers located outside the Community. These manufacturers have a legal obligation to comply with the food contact regulation in force in the EU when selling here but they are not subjected to the same internal traceability. This creates discrimination between converters and producers located within or outside the EU, the former being forced to sustain extra costs that are unlikely to result in additional benefit to consumers.

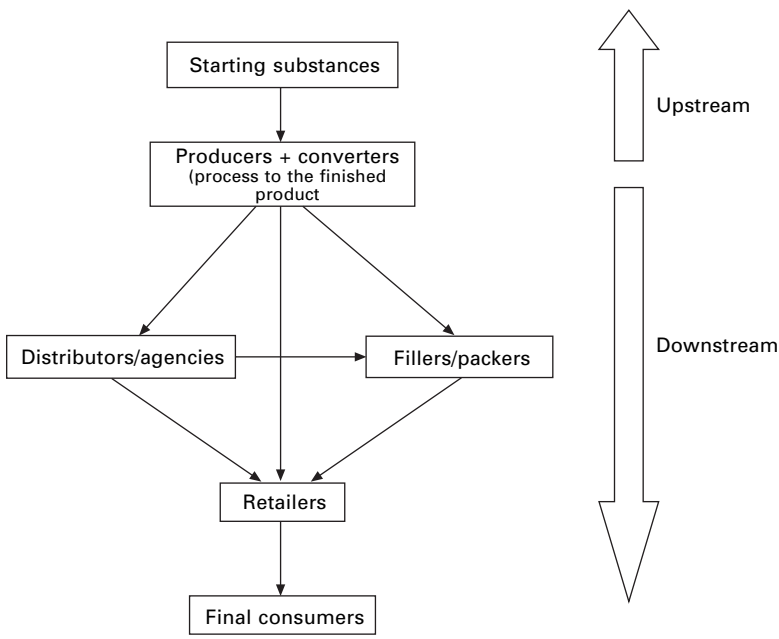

Fig. 4.3 Parties involved in traceability of food contact materials and articles.

4.3.4 Use of the guidelines and future trends

The Industrial Guidelines paper on traceability of food contact materials is not conceived as a procedure but rather as guidance to develop specific procedures that can be adapted to the needs of each single industry. It is expected that all elements addressed in it would be reflected in the company's quality system. For this reason they do not explicitly suggest the use of any specific quality or system of Good Manufacturing Practice. Some companies may not have the critical mass for being accredited through a certified quality system. Nevertheless, they should always establish an equivalent traceability system internally. ISO 9000 is not the only system requiring industry to establish procedures for traceability. Other systems, such as those in place in many industries, have the same requirement.

Whatever procedure is adopted, it is essential that every manufacturer of a food contact material or article maintains a documented system aimed at identifying and preventing the production of defective products and, in the case of delayed defects detection, allowing appropriate product recall. The Guidelines are also conceived as an open document, to which other sector associations can contribute with a description of their own practices (in Annex II), thereby increasing their relevance and creating a shared background to attain the objective.

4.4 Ensuring the traceability of food contact materials

4.4.1 Boundaries of traceability

As shown in Fig. 4.3, the traceability chain ends at the retailer. The other end of the chain, the starting point for traceability of a food contact material or article, is logically placed at the point at which it or its components or ingredients are first put on the market with the intention of being 'for food contact use'. For materials or articles, or their components/ingredients that are imported from outside the European Union, traceability shall extend back to the importer responsible for putting them on the EU market for the intended food-contact application. One of the questions that has been raised is the traceability of repeated use household goods, such as plastic containers, wooden spoons, glass items, trays, etc. Although these materials or articles can follow the same procedure as disposable goods up to retailing, it is very difficult to set up systems of traceability for their entire lifetime. Even labelling or marking of each single item can hardly help, as repeated washing and handling may delete it or make it unreadable. On the other hand, if the objective of the European Commission, while setting rules for traceability, was to protect consumers from chemical contamination caused by migration, repeated use of materials and articles would reduce migration and make the need for traceability less and less important as use proceeds. For this reason, in the preparation of the Industry Guidelines, it was decided to limit the downstream boundary to retailers.

4.4.2 Industrial practice

Traceability within stakeholders' operations

Incoming starting materials
To attain a suitable level of traceability, each business operator must ensure that the incoming starting materials that he uses are supplied with information from the relevant supplier in order to ensure full and unequivocal identification of the starting material to be made. In the case of a converting or producing operation, such information should include:

1. The name of the supplier and the type or grade of the starting material.
2. The place and date of production, batch number or another equivalent identification number that will unequivocally identify the starting material.
3. In the specific case of starting materials for food contact plastics, documentation of compliance with details of the legislation with which they are complying.
4. Documented analysis that, depending on the nature of the starting materials, reports the key attributes against the agreed specifications.

Procedures for qualification of starting materials and suppliers are normally requested by all quality systems, both ISO and GMP. Qualification includes the confirmation of technical suitability for the intended use, as well as control of compliance with the relevant legislation, either general safety requirements in Regulation 1935/2004/EC or, in the case of plastics, in Directive 2002/72/EC and its amendments and, as appropriate, the relevant legislation of the EU Member Countries. As far as the technical attributes are concerned, such qualification is often carried out through audits with the aim of ensuring that the supplier's process is under control, and therefore the relevant technical attributes of the starting materials are constantly maintained. Audits may be also backed up by further analyses to confirm such suitability. These procedures and practices ensure that all measures are taken to guarantee that, if a starting material has a defect that may cause negative effects in the finished product, this defect is identified before it can cause problems. This provides, via traceability, a backup system addressing defects that may have escaped the quality control and quality assurance processes.

The process described above is applicable in particular to business operators that produce or convert materials and articles for food contact. However, the concept of 'starting material' is different depending on the position of an operator in the supply chain. For example, for a polymer-producing company monomers and additives represent starting materials, while plastic pellets, as well as additives, adhesives, printing inks, etc., are starting materials for a company producing plastic goods. Finally, the finished plastic material may be seen as a starting material for food companies that use it for packaging food. The level of modification that the starting materials undergo within each operation also defines the level of accuracy of the internal traceability

needed to fulfil the requirement of Article 17. It is evident that complex processes, such as those used in plastics converting, require accurate records of the different steps (as will be described in section 4.5), whilst a lower degree of internal rework, such as cutting and sealing of the same plastic operated by a food packer, would certainly require a less sophisticated record system. However, regardless of the complexity of the internal rework, it is worth noting that internal systems of traceability are absolutely necessary to obtain complete materials traceability, and that simply fulfilling Article 17 (i.e. tracing 'one step back and one step forward') can hardly serve the objective of identifying critical starting materials at the retail level.

Shipped materials and articles

To fulfil the requirements of Article 17 of Regulation 1935/2004/EC, food contact materials or articles must be unequivocally identified when they are shipped to the next operator in the value chain that is a food company or a retailer. The converters or the producers have to ensure that information capable of operating such identification is transferred to customers. The necessary information consists of: (i) name and address of converter or producer; (ii) commercial name and grade/number of the material or article; (iii) production date and identification of the product.

The product's identification may consist of the lot number or another equivalent code, e.g., identification of the production shift, reel number, etc. The material or article, and/or its container, and/or the accompanying documentation shall always report the information mentioned above.

Several tools capable of carrying such information can be used, such as alphanumeric descriptions, bar codes, labels, RFID tags or the freight documentation that accompanies the shipped goods. The use of these tools depends on cost and on the further use of the material.

Some examples are:

- the usual means of identification for food and beverage metal cans such as labelling, bar-coding and inkjet coding, applied either to individual cans or to batches according to feasibility and appropriateness;
- the label used as an information-conveying tool for transport packaging containing rigid packaging such as plastic trays, glass containers, PET pre-forms etc.;
- in the case of plastic cutlery, the information printed on its container (usually a plastic bag) or onto a label stuck to it;
- in the case of film reels that will be further cut before being used, the information on a label stuck on the wrapping or in the core, or printed on the conveying tool.

It must be pointed out that it is not important how the information is conveyed to the next stakeholder in the distribution chain, but it is of fundamental importance that it is complete, unambiguous and maintained along the chain.

Traceability along the supply chain

Besides the implementation of internal systems of traceability within each operator in the supply chain, an important concept that must be introduced here is that traceability is achieved only if each single operator of the chain respects the rules of identification enabling it to go back to its supplier(s). In other words, the information that accompanies the materials and articles when they leave the manufacturing company must be maintained downstream to the retail stage. This may not be an easy exercise, because different identification rules may apply for distributors and fillers with respect to manufacturers. In an ideal supply chain, composed entirely of companies operating under ISO 9000, traceability will always be guaranteed, as every single step of the chain will be documented. Of course, this is not the case as not all distribution chains are composed entirely of certified companies. However, since companies operating under a certified quality system are required to control their suppliers and to ensure that the supplied products are appropriately identified, the system of traceability tends to be widened because suppliers (including distributors) and transport companies doing business with these companies will also be required to implement equivalent systems.

Traceability along the whole supply chain is a key point. If the information provided by a business operator to the next one in the chain is not appropriately maintained, managed and propagated, then traceability will be inevitably lost, and the effort of the supplying operator will be wasted regardless of the internal degree of accuracy. In other words, one single point of break can put at risk the whole work of the supply chain. This is indeed a weak point of the system that must be very carefully taken into consideration by control authorities whenever detecting failures. If a failure in the traceability system is detected by the authority, it might be easier for the authority to ask for more burden to be put on the concerned material or article, e.g., manufacturing information and a product's or manufacturer's identification printed on each single item introduced to the market. If the problem resides with lack of accuracy in the propagation of the identification from one operator to another, this may simply not be the solution, as free riders will break the law anyway.

It must be clear for the control authorities that Article 17 represents a challenge for the operators of the food contact materials and articles chain not only to align, harmonise and deepen their internal and inter-chain system of product tracing and recall, but also to control appropriately, identify and penalise illegal behaviour. As outlined in section 4.2.1, there are three types of food contact materials and articles for which traceability must be ensured: (i) materials and articles already in contact with food, (ii) those manufactured for food use but not yet in contact with food at the retail stage, and (iii) those that can reasonably be expected to be brought into contact with food or to transfer their constituents to food under foreseeable conditions of use. The traceability for these three categories can be different, in particular in relation to the traceability of food set forth by Article 18 of 178/2002/EC.

Materials and articles already in contact with food
For materials and articles sold to the final consumer already in contact with food, filling represents the boundary to the downstream end of traceability. In fact, when they are filled with food, their identification overlaps that of the food itself, which must be guaranteed through Article 18 of the above mentioned Regulation 178/2002/EC (Fig. 4.4). In practice, 'best-before' date (mandatory for all foodstuffs), date of packaging and/or lot number are expected to contain, or link to, information relative to the food contact material or article. It is, however, necessary that the fillers maintain records of the specific references of the material or article that has been used for each foodstuff, and that the link between the two flows is not interrupted. It is not important how the link between food and the material used for its packaging is maintained by each body in the chain, whether it consists, for instance, of document filing or electronic archiving, as long as it is proven that it is unequivocal and unambiguous. For example, companies may choose to archive the material's shipment documentation with its reference lot number, or to put in a spreadsheet the material's reference codes versus time, if the process is continuous.

Materials and articles not yet in contact with food
These are materials and articles in a stage of their production and marketing prior to the stage at which they are brought into contact with food, or alternatively materials and articles sold as such in the retail stage without being in contact with food. For this reason their identification system does not overlap with the food identification system. In this case, it is necessary that the identification

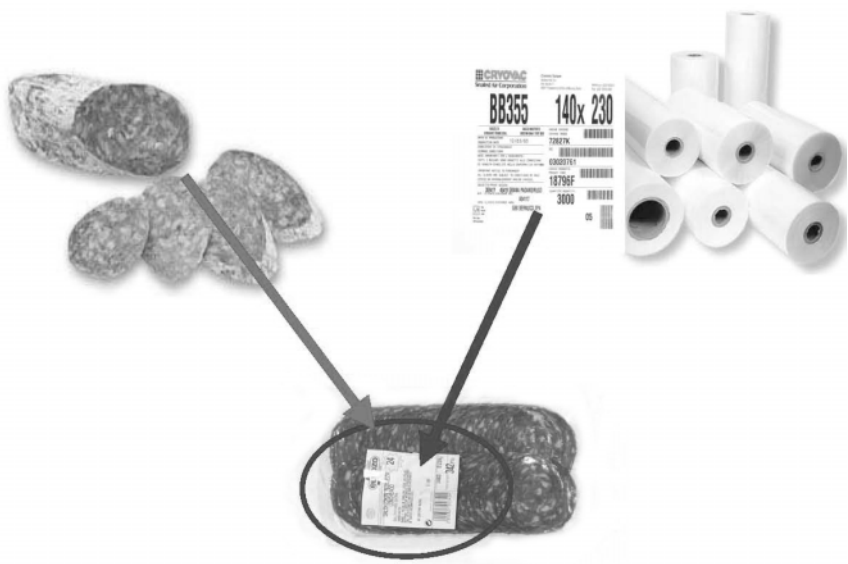

Fig. 4.4 Merging of traceability of food packaging materials into food traceability.

(e.g. manufacturer's name, date and place of production, code, etc.) be maintained up to the retail stage. The tools already employed for the identification of food contact materials can be also used for food contact articles.

Material and articles that can reasonably be expected to be brought in contact with food or to transfer their constituents to food under foreseeable conditions of use

In relation to the previous two sections, this is not a separate category of food contact materials and articles when it comes to traceability information and its flow in the supply chain. The peculiarity here is the point at which the material or article is identified as coming into contact with food, and the fact that this contact can be indirect. Therefore the starting point of the traceability chain can be quite different from that of more traditional food contact materials and articles, but the end point still is the retailer, at which point the material is either in contact with food or not. Thus the previous two paragraphs apply, depending on the circumstances.

4.5 Case study: traceability of plastic materials for food contact

4.5.1 Types of food contact plastics and their components

Plastics for food contact can be rather difficult to trace, owing to the large variety of components and the various processes used to obtain the final product. Considering the finished product that comes in contact with food, a first classification can be made as follows:

1. Products composed of one type of plastic only. Examples are monolayer foils used, e.g., in packaging for bakery or in the form of bags for household application. It is worth noting that a mono-material film, consisting, e.g., of polypropylene, may contain more than one component. If the film is coloured, this is obtained by mixing a polypropylene matrix with a colourant carried by another polypropylene, normally of lower molecular weight.
2. Products composed of more than one type of plastic, either mono-component, such as multi-layer films or laminates, or multi-components, such as plastic bottles and caps.
3. Multi-layer products that can still be classified as 'plastic for food contact' as the food contact layer consists of plastic, but that contain other types of materials such as adhesives, aluminium foils, paper, etc. These materials are often referred as multi-material multilayers.

Plastic materials consist at the minimum of polymers (sometimes referred as 'resins') and one or more additives; the additives can be added to improve the processability of the polymer (e.g., antioxidants, slipping agents, etc.) or to impart specific physical and technological properties to the finished product

(such as colourants, plasticisers, antifog agents, etc.). The former are normally added by the producer of the polymer, whilst the latter are introduced in the formulation either by the manufacturer of the finished product, or by an intermediate operator (as in the case of coloured plastics) who is identified as 'compounder' or producer of a 'compound' or 'masterbatch'. It becomes evident, then, that even relatively simple finished products, such as those composed of only one type of plastic, may contain several components that make the tracing exercise rather complex.

4.5.2 Raw materials for production of food contact plastics

The raw materials used for manufacturing food contact plastic materials are:

- resins, most of the time purchased in the form of pellets and then submitted to various processing steps
- additives, added in-line during the production of the material or articles, or used off-line to produce a compound that is further processed for the manufacture of the material or articles
- plastic films or sheets, purchased as reels and then either coated and/or printed and laminated to another substrate
- primers, inks, varnishes and coatings, used in the printing process
- adhesives and tie-layer resins, used to laminate or bond together various layers
- non-plastic substrates such as paper, aluminium foil, etc.

Obviously, traceability can be attained only if the identification elements of each of the above raw materials are properly obtained by the relevant suppliers, but the most difficult part consists of the management of such identification elements in the various steps of storage, transformation and warehousing of finished goods.

4.5.3 Processing of plastics for manufacturing food contact products

Raw materials may undergo different types of processing that lead to the finished food contact article. The processing is selected on the basis of the type of finished product desired and its properties. Plastic films or sheets, either monolayer or multilayer, may be produced via extrusion. If a colourant or another additive is added, then the extrusion step is preceded by a compounding phase, where the matrix polymer is mixed with a coloured masterbatch (colour concentrate). The extruded film may undergo an orientation treatment in-line, where the film is drawn to obtain specific mechanical and physical properties such as mechanical strength, reduced gas permeability and ability to shrink. The semi-finished product consists of a reel of a width depending on the width of the extruder's head. Reels produced in extrusion are called 'master reels' and are too wide to be used in food packaging machines, therefore they undergo slitting and originate a larger number of reels. Each reel may undergo further processing, such as printing.

Although films or laminates represent a simple example of plastic product for food wrapping, one may see that the various steps require that the information to trace the material is transferred from one step to another, making the whole process rather difficult. This becomes more complex if other manufacturers are involved in intermediate steps, e.g., compounding, printing, etc. Most of the plastic food packaging materials commonly present in the market are composed of more than one layer, either co-extruded or glue laminated. From a traceability viewpoint these materials may be represented as a multiplication of the single steps needed for the production of a single layer. Schemes of production of a co-extruded and a laminated material are presented in Figs 4.5 and 4.6. Each of the different components

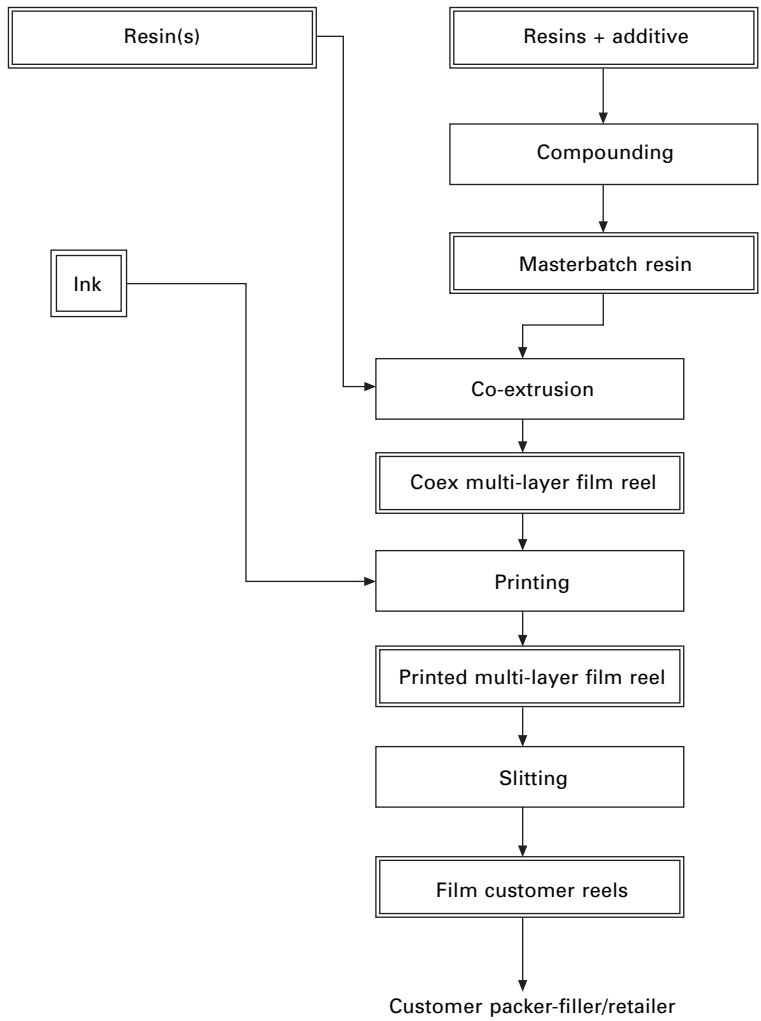

Fig. 4.5 Manufacturing of a co-extruded multilayer film.

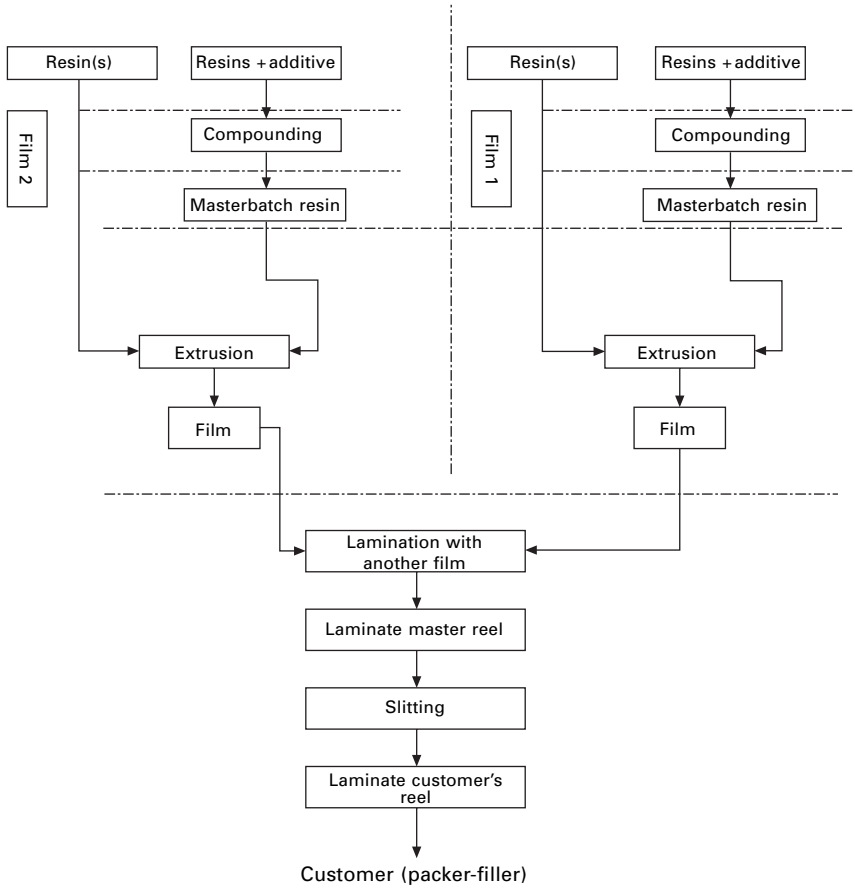

Fig. 4.6 Production of a laminated film.

of the final co-extruded or laminated product will undergo a separate procedure that would eventually result in one single identification code when they are put together.

4.5.4 Limits of traceability systems in plastic processing

Bulk storage of resins

In many cases resins for the production of plastic food packaging materials are shipped in large quantities and stored in silos. These are normally refilled before they are empty and so they generally contain more than one batch of the resin. Although for physical reasons one may reasonably assume that batches are fed to the extruders in a first-in-first-out regime, mixing of batches to a certain extent is virtually unavoidable. This implies that a one-to-one correlation between production codes of the food contact product and

resin batch cannot be fully guaranteed. Of course this is not an issue for extruders fed from bags or single containers, but the use of silo storage by plastics processing companies is so widespread that discontinuing such practice is unrealistic and economically unjustified. Some measures may be adopted for reducing the uncertainty in the identification of the resin batch number versus product manufacturing. For example, recording the dates of feeding of silos and relevant batch codes would allow identification of which batches were present in the silos at the moment of production of a given material. Nevertheless extruders may store resins from more than one vender in the same silos. Therefore manufacturing companies may decide to adopt separate batch management.

On the other hand, one single silo may feed multiple extruders, thus making the whole materials flow rather complex and variable. If the finished material shows any delayed defect or is found non-compliant because of the resin stored in the silos, the manufacturer should then be ready to recall all materials produced from all batches that were present in the silos on the day of manufacturing the defective one. This implies a greater risk for the manufacturer, who is not in a position to identify with great precision the batch responsible for the defect or non-compliance, and will be required to recall more material than necessary to ensure that all products containing the defective resin batch are withdrawn. Normally the probability of lack of conformity or presence of defects, in particular leading to unsafe products, is so low that the risk for manufacturers is most of the times worth taking.

Reworked materials

Reworking of scrap materials is a common practice in plastic processing operations. Trims of films can be recycled in-line or stored in baskets and recycled in another production run. In the former case trims belong to the same finished product batch code, so no traceability problems would arise, while in the latter case several batches of trim stored in a basket can together be recycled into another film batch. Establishing a one-to-one correlation between the resin batches composing the trims and the final film batch would result in an extremely overcomplicated exercise. Also, defective batches of finished products may be reworked into the same type of product or even incorporated into other products with different composition. This is a practice that is adopted for maximising resin yield and reducing landfilling or other loss of raw materials. All these practices imply a high degree of complexity in the traceability systems, up to the point that manufacturers have to decide the extent of risk that they are willing to accept by limiting tracing back of raw materials, for example, to the scrap products that undergo reworking. Also in this case producers might be forced to recall more than necessary in case of defective or non-compliant product, but again frequency of damage is normally so low as to justify risk taking.

Printing inks
Inks used for printing food contact materials and articles normally have a rather complex composition. They may be purchased as ready-to-use colour series, where each single product of the same series differs from the others only in the pigment used. They can be directly loaded into either flexo- or rotographic machines, or as concentrated colours (in the form of viscous liquid or paste) that are added with chromic or technological varnishes, then solvent diluted, before use. Also, several additives may be used in ink preparation (antifoaming agents, adhesion promoters, antistatic additives, etc.). Alternatively, primers for surface treatment to improve sticking of colours may be used. In addition, protective overprint varnishes may be used for avoiding print deterioration and scratches. All of these components ultimately become integral parts of the finished product, and in principle all of them should undergo full traceability. Apart from possibly solvents, such components are left in only minimum quantities after evaporation at the end of the process, as they are not an intentional component of the finished product. In industrial practice all purchased batches are often stored in one single container, where they mix and, since they are liquid, lose reference to the original batch.

Different colours may also be mixed in different proportions to obtain special desired effects, as well as recovered when in excess and back flushed in the original container. Clearly, printing practices do not allow batch-to-batch correlation unless very sophisticated controls are put in place, the cost of which is hardly worth the risk. Transmission of colour to food is unlikely through plastic materials, as plastics are in general good barriers to large molecules such as organic colourants, but it might occur when porous paper is printed and laminated to thin low density plastic foils (such as LLDPE). For such reasons it is appropriate to establish recording systems that are able to provide indications not only as to the type of ink and ink components used (which is straightforward), but also to the batch or batches and the shift or shifts of production. An acceptable level of traceability may be ensured by recording the date of supplying of inks and ink components, relevant identification, type of storage system (e.g. identification of the container) and any production records that relate the respective storage system with the product and its relevant date of printing.

4.6 Conclusions

Traceability systems already exist in the food contact material distribution chain, mainly to address quality problems that may arise with use. ISO-certified companies, as well as companies operating using Good Manufacturing Practice, not only adopt these systems internally, but also require their suppliers, service companies and manufacturers to use them, so that traceability is a common and widespread feature of food contact materials in the European

market. The aim of Article 17 of Regulation 1935/2004/EC may be interpreted from one side as a tool for the harmonisation of the various systems, and from the other side as a message for consumers as to the strengthening of control on the whole food manufacturing and distribution chain.

4.7 References

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7. Regulation (EC) No 1830/2003 of the European Parliament and of the Council of 22 September 2003 concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms and amending Directive 2001/18/EC.
8. Codex Alimentarius Commission 2-7/07/2001 (with comments of EU Commission).
9. Letter from Health and Consumers Protection Directorate-General to EuPC, dated 7 Oct. 2002 (SANCO D3/OS D430796 (2002)).
10. www.crl-fcm.jrc.it, Section 'Industry reports'.

Part II

Assessing the risks and improving the safety of food contact materials

5

Compliance testing of chemical migration from food contact materials

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5.1 Introduction

Food may be in contact with a wide variety of materials before it is consumed: during production and processing in the factory, during storage in packaging and during final processing and consumption. To ensure that the food is not contaminated with migrants from the food contact materials, resulting in unwanted changes of the composition of the food, all kinds of regulations for food contact materials are established. It can be difficult for producers, traders and users of food contact materials to know with which regulations the material must comply and how to ensure that it complies with the relevant legislation and intended use. In this chapter we will present how food contact materials can be tested for compliance with the relevant legislation in the European Union (EU).

In principle two approaches to testing can be distinguished. Conventional compliance testing is a target analysis of migrants, based on knowledge of the composition of the food contact material, and a non-target approach for the non-intentionally added substances (NIASs). The approaches are complementary. The main difference between conventional compliance testing and non-target compliance testing is that in conventional compliance testing the investigation is focused on the ingredients (monomers, additives, etc.) used and on how much of these ingredients are present and can potentially migrate to the food. In the non-target compliance approach all possible components that can migrate to the food are included (with the focus on components that were included in the polymer without the intention to be added, which are components like oligomers, by-products, reaction products, impurities, etc.).

Conventional testing follows the following discrete steps:

1. Gathering information about the composition of the material
   This first step is to obtain information about all raw materials and production aids used in the production process of the food contact material. When the product is manufactured on site this is quite simple, but when an end product or a precursor is obtained from another party this can be more difficult. Secondly, detailed information about the raw materials (such as monomers, additives, catalyst, etc., used in the production of the coating, polymer or paper) and other ingredients used to produce the raw materials is required.
2. Select relevant legislation
   As mentioned above, the kind of material, together with the country in which the material is produced and sold, determines with which legislation the product must comply. A detailed strategy is given in section 5.2.
3. Check whether composition is in accordance with the legislation
   In principle all the ingredients used must be on the EU positive list in the relevant legislation. Although some of the EU positive lists are not complete (like the additive list of the 2002/72/EC at this moment) or exclude some components like catalysts, all the materials must be safe and must comply with the framework Regulation (EC) 1935/2004 Article 3. How to deal with this is again described in section 5.2.
4. Performance of the relevant tests
   Besides compliance of a product's composition with legislation, one needs to demonstrate that the product complies with the limits set for overall migration, specific migration, residual content and requirements. This is described in section 5.3 in more detail.
5. Non-target compliance testing
   Instead of looking for residual contents and/or specific migration which are covered by the previous step, in non-conventional compliance testing a non-target analysis is performed. This follows discrete steps:
   - Separate the components in the migration solvent to as many peaks as possible using a wide variety of analytical equipment.
   - Reduce the separated peaks to a smaller subset of peaks, which are relevant, using structural information and concentration data.
   - Identify the relevant components.
   - Determine the concentrations of the components.
   - Evaluate possible toxicological effects.

The testing methodology described in this chapter (except for purity requirements) applies only to end products.

5.2 Administrative compliance evaluation

The principle of administrative evaluation is simple: information is requested on how the food contact material is produced; this information is compared

with relevant legislation and relevant tests are selected. The reality is far from simple. As can be seen from Fig. 5.1 the person who brings the food contact material in contact with the food can be many steps remote from the person who knows the exact composition of the food contact material. In the example in Fig. 5.1 a common situation is illustrated in which one company knows every ingredient of a PET granulate, but does not know the details of the final product and its application. One company knows every ingredient of the colourant masterbatch but also does not know the details about the final product and application. But the PET bottle producer, who has to declare that his bottles are suitable to be used in contact with food, does not know all details of ingredients of the raw materials used.

In many cases raw material suppliers are not keen on providing detailed information about the ingredients used (like catalysts, additives, monomers, etc.). Instead, each party delivers a certificate of compliance to his client. Such a statement usually contains information on which legislation the product complies with and which tests must be performed on the final product to ensure compliance with this legislation. Alternatively, some raw material suppliers want only to provide information on which specific migration or residual content needs to be performed under a non-disclosure agreement or to a third-party lab. Finally, the producer of the end product has a statement from his supplier saying which tests should be performed and he has to demonstrate that his product complies by means of testing using the temperature and time conditions needed to cover the product's intended use by his clients (food fillers). Then he issues a certificate of compliance to the food filler. When materials intended to be used to produce food contact materials, or food

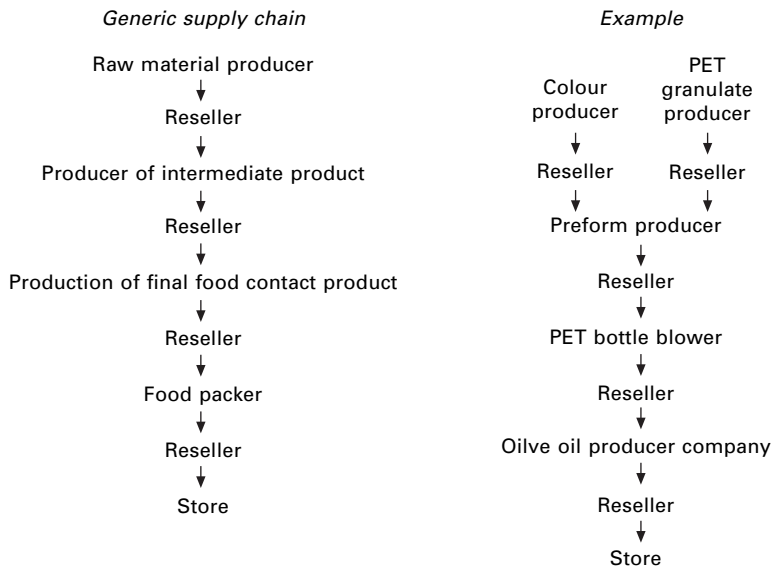

Fig. 5.1 Supply chain of food contact material.

contact materials themselves, are sold, they must be accompanied by a written declaration of compliance as is laid down in Article 16 of (EC) 1935/2004:

> Article 16
> Declaration of compliance
> 1. The specific measures referred to in Article 5 shall require that materials and articles covered by those measures be accompanied by a written declaration stating that they comply with the rules applicable to them. Appropriate documentation shall be available to demonstrate such compliance. That documentation shall be made available to the competent authorities on demand.
> 2. In the absence of specific measures, this Regulation shall not prevent Member States from retaining or adopting national provisions for declarations of compliance for materials and articles.

Alternatively, a third-party (independent) company can be asked to gather the details of all materials and ingredients used through the complete supply chain, in order to evaluate whether the food contact material complies with legislation and which experiments should be performed. The information obtained is very confidential in many ways. Both the ingredient information as well as information about which companies deliver to which company should not become known to the final product producer as well as all other parties. A reseller, for example, could be concerned that if his client knows where he buys his materials he will be passed over. Therefore, this whole procedure will be performed under non-disclosure conditions.

When all the information about the composition of the final product is gathered it has to be compared with the relevant legislation. Evidently it is of critical importance to know what the relevant legislation is and to be aware of the latest updates to this legislation. In Table 5.1 the European Directives and regulations that exist at this moment are shown. In Table 5.1 also the repealed Directives are listed because in some statements of compliance references are made to repealed legislations. This could be an indication that the certificate is obsolete. The Regulation (EC) 1935/2004 is applicable to all food contact materials, demanding general safety requirements. One of the most important articles of (EC) 1935/2004 is Article 3:

> 3. Materials and articles, including active and intelligent materials and articles, shall be manufactured in compliance with good manufacturing practice so that, under normal or foreseeable conditions of use, they do not transfer their constituents to food in quantities which could:
>
> (a) endanger human health;
>
> or
>
> (b) bring about an unacceptable change in the composition of the food;
>
> or
>
> (c) bring about a deterioration in the organoleptic characteristics thereof.

Table 5.1 Active and repealed EU directives and regulations

		Plastics	Coatings	Adhesives	Ceramics	Regenerated cellulose	General	Other	Rubber
National	Additional[3] legislation	various[1]	various[1]	various[1]	various[1]	various[1]	various[1]	various[1]	various[1]
EU	Active directives[2]	2002/72/EC 2004/1/EC 2004/19/EC 2005/79/EC	–	–	84/500/EEC 2005/31/EC	93/10/EEC 93/111/EEC 2004/14/EC	78/142/EEC 80/766/EEC 81/432/EEC	–	93/11/EEC
	Repealed directives	90/128/EEC 92/39/EEC 93/9/EEC 95/3/EC 96/11/EC 99/91/EC 2001/62/EC 2002/17/EC	–	–	–	83/229/EEC 86/388/EEC 92/15/EEC	76/893/EEC 80/590/EEC 89/109/EEC	–	–
			2002/16/EC 2004/13/EC 2001/61/EC		–	–	–	–	
	Regulation		EC 1895/2005		–	–	–	–	–
						EC 1935/2004			

[1]At national level there could be national legislation. For more details see Table 5.2.
[2]The EU directives must be implemented into the national legislation.
[3]Beside the implemented EU directives some countries do have additional legislation for one or more food contact materials (for details see Table 5.2).

For some food contact materials the EU has made Directives, which are implemented in the national legislation of EU Member States. Apart from these implemented Directives some Member States have additional legislation for one or more food contact material types. A summary can be found at http://ec.europa.eu/food/food/chemicalsafety/foodcontact/sum_nat_legis_en.pdf and the present status is given in Table 5.2.

Special attention should be paid when a certificate of compliance mentions only one or more EU Directives, as the EU Directives do not cover all materials and all ingredients of the food contact materials. For plastics, for example, only the monomers list is complete; the additives are only partly covered. As a result, even when there is a certificate of compliance with EU Directives, it could be that some unlisted additives are present. Also catalysts or polymer reaction products may be present, and their potential migration into food during use must be taken into consideration, keeping the relevant national legislation and Article 3 of (EC) 1935/2004 in mind. After evaluation of the composition and/or certificates of compliance, it should be clear whether the material's composition complies with the relevant legislation and which migration has to be checked in the end product to demonstrate compliance with the legislation.

5.3 Conventional experimental compliance testing

Conventional compliance testing of food contact materials simulates food contact by bringing food contact materials into contact with a food simulant (using certain temperature and time conditions). It then determines what is migrating from the food contact material to the food by testing how much in total migrates (overall migration). For some chemical components specific migration or residual content must be performed. Furthermore, additional experiments like sensory evaluation, purity of ingredients, colour release or determination of the amount of volatiles must also be performed.

5.3.1 Mimicking food contact

To avoid possible arguments about what kind of food should be chosen to perform migration testing, EU legislators have agreed on four food simulants, which are able to mimic foods:

- Simulant A, water, mimicking aqueous foodstuffs
- Simulant B, 3% acetic acid, mimicking acidic foodstuffs
- Simulant C, 10% ethanol, mimicking alcoholic foodstuffs
- Simulant D, olive oil, or another approved oil, mimicking fatty foodstuffs.

Not all four simulants need to be included in testing. Directive 85/572/EEC defines which simulants need to be used to simulate certain foods. Alternatives for olive oil may be used if needed (like sunflower oil). In some cases it is

Table 5.2 Summary of national legislation in the EU (source: http://europa.eu.int/comm/food/food/chemicalsafety/foodcontact/sum_nat_legis_en.pdf)

Member State	Other	Adhesives	Ceramics	Glass	Enamel	Metals alloys	Cork	Wood	Textile
Austria	–	–	+	–	+	–	–	–	–
Belgium	–	–	–	–	–	–	–	–	–
Cyprus	–	–	–	–	–	–	–	–	–
Czech Republic	–	–	+	+	+	+	+	+	–
Denmark	Mandatory registration[1]	–	+[2]	–	–	–	–	–	–
Estonia	–	–	–	–	–	–	–	–	–
Finland	–	–	–	–	–	+	–	–	–
France	–	–	+	+	+	+	–	+	–
Germany	–	+[3]	+[4]	+[4]	+[4]	–	–	–	–
Greece	–	–	–	–	–	+	–	–	–
Hungary	–	–	+	–	+	+[5]	–	+	–
Ireland	–	–	–	–	–	–	–	–	–
Italy	–	–	+	+	+[6]	+[7]	–	–	–
Latvia	–	–	–	–	–	–	–	–	–
Lithuania	–	–	–	–	–	–	–	–	–
Luxembourg	–	–	–	–	–	–	–	–	–
Malta	–	–	–	–	–	–	–	–	–
Netherlands	–	–	+	+	+	+	+	+	+

Table 5.2 Continued

Member State	Other	Adhesives	Ceramics	Glass	Enamel	Metals alloys	Cork	Wood	Textile
Poland	–	–	+[8]	–	+[8]	–	–	–	–
Portugal	–	–	–	+[8]	+[8]	–	–	–	–
Slovakia	–	–	–	+	–	+	+	+	+
Slovenia	Yes: colours[9]	+	–	+	+	+	–	+	+
Spain	Yes[10]	–	–	–	–	–	–	–	–
Sweden	–	–	–	–	–	+	–	–	–
UK	–	–	–	–	–	–	–	–	–

+ : National legislation applies; – : no national specific legislation

1. Mandatory registration for producers and importers of plastics, ceramics, glass and regenerated cellulose.
2. Also for glass and ceramic products.
3. BfR recommendation.
4. DIN standard.
5. National legislation and standards.
6. Limitation on lead.
7. Specific measures for stainless steel, tin-free steel, tin containers.
8. National standards.
9. Rules on the requirements concerning the hygiene suitability of consumer goods.
10. Plastic materials legislation, prohibition of recycled plastics, register on substances and manufacturers.

Table 5.2 Continued

Member State	Paper board	RCF	Plastics	Varnish coating	Printing inks	Silicone	Wax	Rubber	Ion-exchange resin
Austria	–	–	–	–	–	–	–	–	–
Belgium	–	–	–	+[11]	–	+[11]	–	–	+[11]
Cyprus	–	–	–	–	–	–	–	–	–
Czech Republic	+	–	–	+	+	+	–	+	–
Denmark	–	–	–	–	–	–	–	–	–
Estonia	–	–	–	–	–	–	–	–	–
Finland	+	–	–	–	–	–	–	–	–
France	+	–	+	+	–	–	–	+	–
Germany	+[3]	–	+[3]	–	–	+[3]	+[3]	+[3]	–
Greece	+	–	+	+	–	–	–	–	–
Hungary	–	–	–	–	–	+[12]	–	+[12]	–
Ireland	–	–	–	–	–	–	–	–	–
Italy	+	+	+	+	–	+	–	+	–
Latvia	+[13]	–	–	–	–	–	–	–	–
Lithuania	–	–	–	–	–	–	–	–	–
Luxembourg	–	–	–	–	–	–	–	–	–
Malta	–	–	–	–	–	–	–	–	–
Netherlands	+	+	+	+	+	+	+	+	–
Poland	+[8]	–	–	–	–	–	–	–	–
Portugal	–	–	–	–	–	–	–	–	–
Slovakia	+	–	–	+	–	–	–	+	–
Slovenia	+	–	–	+	–	–	–	+	–
Spain	–	–	+	–	–	–	–	–	–
Sweden	–	–	–	–	–	–	–	–	–
UK	–	–	–	–	–	–	–	–	–

11. Resolutions (adoption pending).
12. For teats.
13. Paper and cardboard materials and articles cannot release more than 0.5 mg cadmium from 1 kg of paper and not more than 3 mg of lead from 1 kg of paper.

not possible to use olive oil as a food simulant because of technical reasons and alternative simulants may be used like isooctane and 95% ethanol.

The time and temperature conditions that must be chosen to mimic contact with the food are regulated for plastics in Directives 82/711/EEC (basic rules), 93/8/EEC (basic rules, 1st amendment) and 97/48/EC (basic rules, 2nd amendment). Additional information can be found in CEN methods for overall migration (EN 1186-1:2002) and specific migrations (EN 13130-1:2005). In many cases national legislation also applies the use of such simulants, temperature and time conditions, to other, non-plastic, food contact materials. For ceramics a specific time/temperature/food simulant has been chosen: 22 °C for 24 hours using 4% acidic acid as food simulant regardless of the real-life application, as described in Directives 84/500/EEC and 2005/31/EC.

5.3.2 Overall migration testing

The reason for determining overall migration is that the food contact material may bring about an unacceptable change in the composition of the food (Article 3 of the framework Regulation (EC) 1935/2004). The methods of determining the overall migration into the aqueous simulants (A, B and C) are as follows:

- Bring the food contact material in contact with the simulant for a selected time and temperature (see section 5.3.1).
- Separate the sample from the simulant and evaporate the simulant.
- Determine the weight of the residue and calculate overall migration. As a consequence volatile chemicals, which migrate, are not included in the overall migration value for the aqueous simulants.

Because the fatty food simulant olive oil cannot be simply evaporated, the determination of the overall migration into olive oil is more complicated. The value of overall migration is measured by determining weight loss from the sample. But because the sample might have absorbed components of the fatty simulant during contact, the weight loss of the sample must be corrected for the amount of absorbed fat. The procedure of determining the migration into fat is:

- Determine the weight before contact (W1).
- Bring the food contact material in contact with the simulant for a specific time and at a defined temperature (see section 5.3.1).
- Separate the sample from the simulant and remove as much simulant as possible.
- Determine the weight after contact (W2).
- Determine the amount of fat absorbed in the sample using a suitable method (F).
- Calculate the migration (migration is W1–W2+F).

Migration into fat is a very complicated factor and errors can be made very easily resulting in higher or lower values. The following critical issues need to be considered during the determination of overall migration into fatty foodstuffs:

- The weight before and after the contact time is determined. Therefore it is important that in case the material contains moisture, the amount of moisture is identical whilst determining W1 and W2. This could be achieved by conditioning the sample before determining W1 and W2, by means of vacuum drying or using constant relative humidity.
- During conditioning volatile components (not being water) are removed resulting in a lower value for overall migration.
- In determination of the amount of fat absorbed by the sample (F), not all the fat is extracted, resulting in a value for F which is too low.

Besides the above there are many more sources of possible error. More detailed information about the determination of overall migration can be found in CEN methods, which are listed in Table 5.3. The use of olive oil is preferred over the use of alternative simulants because in most cases 95% ethanol or isooctane is a more stringent simulant resulting in a much higher value of overall migration than the value that would be obtained when olive oil is used.

The EU limit of the overall migration is 10 mg/dm^2 or 60 mg/kg. Because olive oil is a severe solvent compared with most fatty foods, a reduction factor ranging from 2–5 may be applied depending on the food. Chocolate has, for example, a reduction factor of 5, which means that the value obtained for the overall migration into simulant D must be divided by 5 before checking it against the limit (Directive 85/572/EEC). Furthermore, it should be kept in mind that analytical error in the determination of the overall migration was determined by the EU as 2 mg/dm^2 or 12 mg/kg for the aqueous food simulants (A, B and C), whilst the error is 3 mg/dm^2 or 20 mg/kg for the fatty food simulant (D).

5.3.3 Specific migration testing

Specific migration is the amount of a specific component that migrates from the food contact material to the food during contact. There are several ways to demonstrate compliance of the specific migration limits (SMLs) set in EU food contact legislation. The generic approach is shown in Fig. 5.2. For every component with a specific migration limit that is present in a material the procedure in Fig. 5.2 must be completed.

Worst-case calculation

If the amount of a component that is available to migrate is so small that even if everything were to migrate to the food the migration limit cannot be exceeded, it is clear that the SML cannot be exceeded. This calculation can

Table 5.3 The official CEN methods to determine overall migration

EN 1186-1:2002	Materials and articles in contact with foodstuffs – Plastics – Part 1: Guide to the selection of conditions and test methods for overall migration
EN 1186-2:2002	Materials and articles in contact with foodstuffs – Plastics – Part 2: Test methods for overall migration into olive oil by total immersion
EN 1186-3:2002	Materials and articles in contact with foodstuffs – Plastics – Part 3: Test methods for overall migration into aqueous food simulants by total immersion
EN 1186-4:2002	Materials and articles in contact with foodstuffs – Plastics – Part 4: Test methods for overall migration into olive oil by cell
EN 1186-5:2002	Materials and articles in contact with foodstuffs – Plastics – Part 5: Test methods for overall migration into aqueous food simulants by cell
EN 1186-6:2002	Materials and articles in contact with foodstuffs – Plastics – Part 6: Test methods for overall migration into olive oil using a pouch
EN 1186-7:2002	Materials and articles in contact with foodstuffs – Plastics – Part 7: Test methods for overall migration into aqueous food simulants using a pouch
EN 1186-8:2002	Materials and articles in contact with foodstuffs – Plastics – Part 8: Test methods for overall migration into olive oil by article filling
EN 1186-9:2002	Materials and articles in contact with foodstuffs – Plastics – Part 9: Test methods for overall migration into aqueous food simulants by article filling
EN 1186-10:2002	Materials and articles in contact with foodstuffs – Plastics – Part 10: Test methods for overall migration into olive oil (modified method for use in cases where incomplete extraction of olive oil occurs)
EN 1186-11:2002	Materials and articles in contact with foodstuffs – Plastics – Part 11: Test methods for overall migration into mixtures of C-labelled synthetic triglycerides
EN 1186-12:2002	Materials and articles in contact with foodstuffs – Plastics – Part 12: Test methods for overall migration at low temperatures
EN 1186-13:2002	Materials and articles in contact with foodstuffs – Plastics – Part 13: Test methods for overall migration at high temperatures
EN 1186-14:2002	Materials and articles in contact with foodstuffs – Plastics – Part 14: Test methods for 'substitute tests' for overall migration from plastics intended to come into contact with fatty foodstuffs using test media iso-octane and 95% ethanol
EN 1186-15:2002	Materials and articles in contact with foodstuffs – Plastics – Part 15: Alternative test methods to migration into fatty food simulants by rapid extraction into iso-octane and/or 95% ethanol

be made using data that are already available such as the chemical's ingredient specification or the amount of chemical added. As an alternative the residual amount present expressed per unit of area (QMA) can be determined. If the value obtained is above the specific migration limit mathematical modelling can be used to calculate how much can potentially migrate to the food.

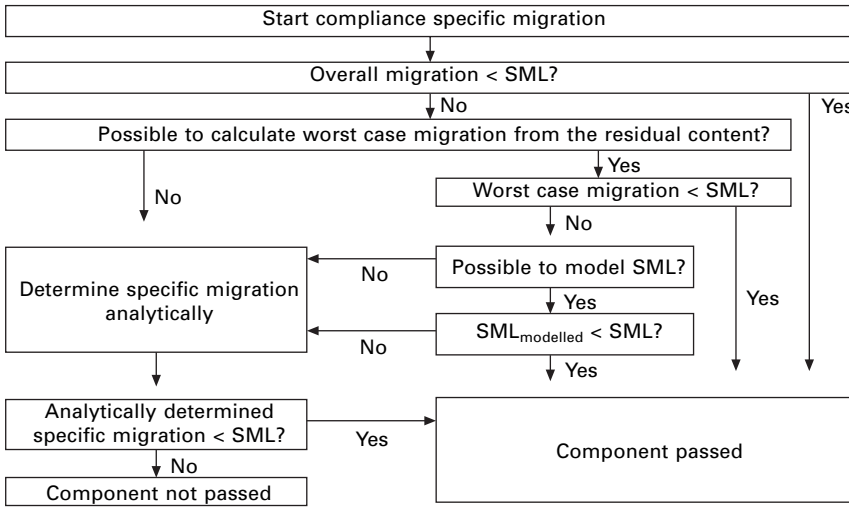

Fig. 5.2 Generic scheme for evaluation of specific migration.

Mathematical modelling

Mathematical modelling of specific migration is described in more detail in Chapter 8 of this book. Mathematical modelling can be a relatively cheap and fast way to determine maximum specific migration. Mathematical modelling can be done using several programs available on the Internet or others that are commercially available. The following considerations must be taken into account when using mathematical modelling.

- The concentration of the component in the food contact material must be known.
- The component may not be charged.
- The concentration of the component should be homogeneous in the food contact material (an antistatic additive is therefore excluded).
- Sufficient information about the migration behaviour of components in the polymer must be known (so far, modelling can be performed only in some polymers). Research continues to expand the application range.
- The temperatures to which the polymers are exposed must be below certain limits because above these (which are unique for each type of polymer) the diffusion behaviour of the migrant changes and cannot be calculated using the migration models.
- It is possible to demonstrate that specific migration is smaller than the SML, but because mathematical modelling provides an overestimation of migration it is not possible to state that an SML is exceeded.

Specific migration covered by overall migration

If the total amount that migrates is smaller than the SML, in principle the SML cannot be exceeded. However, this approach should be used very carefully.

- Analytical error of overall migration is quite large, as is shown in section 5.3.2, therefore analytical error must be added to the overall migration value found before it is compared with the SML.
- When overall migration into aqueous simulants is determined, the simulant is evaporated. Therefore, this approach of checking an SML via overall migration cannot be used for volatile components with values of overall migration into aqueous simulants, because they will not be included in overall migration.

In practice, using overall migration to check that SMLs are not being exceeded can be done only when:

- a small area of packaging is in contact with large amounts of food (for example, a cap on a bottle)
- a large value for the SML applies
- the food contact material is in contact with an object with a large reduction factor (see section 5.3.2).

Analytical determination of specific migration
If the steps described above could not demonstrate compliance with an SML, then specific migration must be determined analytically. After the simulant is separated from the sample (see section 5.3.1) specific migration can be determined using a wide variety of analytical techniques, such as high performance liquid chromatography (HPLC) and gas chromatography (GC) with a wide range of detection methods.

General information about how to determine specific migration is available in CEN document 'EN 13130-1:2004 Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 1: Guide to test methods for the specific migration of substances from plastics to foods and food simulants and the determination of substances in plastics and the selection of conditions of exposure to food simulants'. CEN has also established methods for the determination of some specific migration. Table 5.4 is a list of components for which CEN methods are established. Another source of methods for the determination of specific migration can be found at http://cpf.jrc.it/smt/. At this website of the Joint Research Centre methods are collected and made public online. A summary of the methods available at the website of JRC is given in Table 5.5.

5.3.4 Residual migration testing

Restrictions for the residual amount of a component instead of a specific migration limit are set by the legislator in cases where specific migration of a component is difficult to obtain (for example, because the component is very volatile) or impossible to determine directly (for example, if the component is very reactive and would react with the food simulant). There are two ways to determine the residual content, by worst-case calculation or by analytical determination. The generic approach is shown in Fig. 5.3.

Table 5.4 CEN methods for specific migration testing

EN 13130-1:2004	Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 1: Guide to test methods for the specific migration of substances from plastics to foods and food simulants and the determination of substances in plastics and the selection of conditions of exposure to food simulants
EN 13130-2:2004	Determination of terephthalic acid in food simulants
EN 13130-3:2004	Determination of acrylonitrile in food and food simulants
EN 13130-5:2004	Determination of vinylidene chloride in food simulants
EN 13130-7:2004	Determination of monoethylene glycol and diethylene glycol in food simulants
CEN/TS 13130-9:2005	Determination of acetic acid, vinyl ester in food simulants
CEN/TS 13130-10:2005	Determination of acrylamide in food simulants
CEN/TS 13130-11:2005	Determination of 11-aminoundecanoic acid in food simulants
CEN/TS 13130-12:2005	Determination of 1,3-benzenedimethanamine in food simulants
CEN/TS 13130-13:2005	Determination of 2,2-bis(4-hydroxyphenyl)propane (Bisphenol A) in food simulants
CEN/TS 13130-14:2005	Determination of 3,3-bis(3-methyl-4-hydroxyphenyl)-2-indoline in food simulants
CEN/TS 13130-15:2005	Determination of 1,3-butadiene in food simulants
CEN/TS 13130-16:2005	Determination of caprolactam and caprolactam salt in food simulants
CEN/TS 13130-18:2005	Determination of 1,2-dihydroxybenzene, 1,3-dihydroxybenzene, 1,4-dihydroxybenzene, 4,4'-dihydroxybenzophenone and 4,4′ dihydroxybiphenyl in food simulants
CEN/TS 13130-19:2005	Determination of dimethylaminoethanol in food simulants
CEN/TS 13130-21:2005	Determination of ethylenediamine and hexamethylenediamine in food simulants
CEN/TS 13130-23:2005	Determination of formaldehyde and hexamethylenetetramine in food simulants
CEN/TS 13130-24:2005	Determination of maleic acid and maleic anhydride in food simulants
CEN/TS 13130-25:2005	Determination of 4-methyl-1-pentene in food simulants
CEN/TS 13130-26:2005	Determination of 1-octene and tetrahydrofuran in food simulants
CEN/TS 13130-27:2005	Determination of 2,4,6-triamino-1,3,5-triazine in food simulants
CEN/TS 13130-28:2005	Determination of 1,1,1-trimethylolpropane in food simulants

Calculation

If the amount of a component is already known to be so small that the residual content limit is not exceeded, this is sufficient. This can be calculated using already available information like ingredient specification, the amount of chemical added, etc. One consequence is that this worst-case calculation is not possible for monomers, but only for additives and processing aids. In real-life this approach could be used in rare cases only and an analytical determination is the method most commonly used.

Table 5.5 Methods available online at http://crl-fcm.jrc.it

Component			Online information available			
Name	PM	CAS #	Analytical method	IR spectrum	NMR spectrum	EI mass spectrum
Acetic acid, vinyl ester	10120	00108-05-4	+	+	–	+
Acrylamide	10630	00079-06-1	+	+	–	+
11-Aminoundecanoic acid	12788	02432-99-7	+	+	–	–
1,3-Benzenedimethanamine	13000	01477-55-0	+	–	–	–
2,2-Bis(4-hydroxyphenyl)propane	13480 & 40060	00080-05-7	+	+	+	+
2,2-Bis(4-hydroxyphenyl)propane bis(2,3-epoxypropyl) ether	13510	01675-54-3	+	+	–	+
3,3-Bis(3-methyl-4-hydroxyphenyl)-2-indolinone	13600	47465-97-4	+	–	–	–
1,3-Butadiene	13630	00106-99-0	+	–	–	+
Caprolactam	14200	00105-60-2	+	+	–	+
Carbonyl chloride	14380	00075-44-5	+	–	–	–
1,2-Dihydroxybenzene	15880	00120-80-9	+	+	–	+
1,3-Dihydroxybenzene	15910	00108-46-3	+	+	–	+
1,4-Dihydroxybenzene	15940	00123-31-9	+	+	–	+
4,4′-Dihydroxybenzophenone	15970	00611-99-4	+	+	–	+
4,4′-Dihydroxybiphenyl	16000	00092-88-6	+	+	–	+
Dimethylaminoethanol	16150	00108-01-0	+	+	–	+
Ethylene oxide	17020	00075-21-8	+	–	–	+
Ethylenediamine	16960	00107-15-3	+	+	–	+
Formaldehyde	17260	00050-00-0	+	–	–	–
Hexamethylenediamine	18460	00124-09-4	+	+	–	+
Hexamethylenetetramine	18670	00100-97-0	+	+	–	+
Maleic acid	19540	00110-16-7	+	+	–	–
Maleic anhydride	19960	00108-31-6	+	+	–	–
Methacrylonitrile	21490	00126-98-7	+	+	–	+
4-Methyl-1-pentene	22150	00691-37-2	+	+	–	+
1-Octene	22660	00111-66-0	+	+	–	+
1,3-Phenylenediamine	23050	00108-45-2	+	+	–	+
Propylene oxide	24010	00075-56-9	+	–	–	+
Tetrahydrofuran	25150	00109-99-9	+	+	–	+
2,4,6-Triamino-1,3,5-triazine	25420	00108-78-1	+	+	–	+
1,1,1-Trimethylol propane	25600	00077-99-6	+	+	–	+

Analytical determination of residual content

If a calculation is not possible or the value calculated is larger than the limit, the actual residual content has to be determined. Before the amount can be determined using suitable analytical equipment, the residual components have to be released from the food contact material. This can be done using one of several methods.

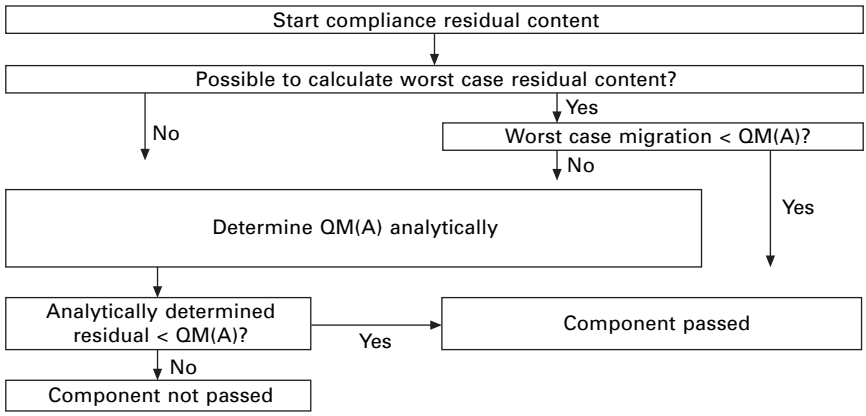

Fig. 5.3 Generic scheme for evaluation of residual content.

- Exhaustive extraction of the analyte using soxhlet or reflux; this method can be performed for non-volatile components. Thin samples like films can be extracted directly. Thicker materials need to be reduced in size using methods like cryogenic grinding of the material. The solvent used to extract samples can be analysed using suitable analytical equipment.
- Dissolving the polymer using a good solvent and then precipitation of the polymer using a poor solvent (like methanol) for the polymer; care should be taken that the analyte is not precipitated or included in the polymer. After removing the polymer, the solvent can be analysed using suitable analytical equipment.
- Dissolving the polymer in a good solvent, with a high boiling point, in a headspace vial; the analyte can be determined directly using GC with headspace sampling and injection. The main advantage is that no loss of volatiles can occur. However, attention should be paid to matrix effects that can occur when polymer is present in the solvent, which may result in another equilibrium of the solvent/vapour distribution of the analyte.
- If the residual content of a material has to be determined the sample should be dissolved using a suitably aggressive solvent, followed by determination using analytical equipment like ICP-MS or AAS.

CEN has also generated standardised test methods (Table 5.6).

5.3.5 Other tests

At European or national level some additional tests exist. In this section some examples of these additional tests are given. This list is not complete; many other tests exist. Please consult national legislation closely to view all relevant tests.

Organoleptic evaluation

Article 3 of Regulation (EC) 1935/2005 states that the food contact material

Table 5.6 CEN methods for residual content determination

CEN/TS 13130–17:2005	Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 17: Determination of carbonyl chloride in plastics
CEN/TS 13130–22:2005	Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 22: Determination of ethylene oxide and propylene oxide in plastics
EN 13130–4:2004	Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 4: Determination of 1,3-butadiene in plastics
EN 13130–6:2004	Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 6: Determination of vinylidene chloride in plastics
EN 13130–8:2004	Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 8: Determination of isocyanates in plastics
CEN/TS 13130–20:2005	Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 20: Determination of epichlorohydrin in plastics

may not cause an organoleptic change during contact. This must be tested on the final product using the foodstuff that will be in contact with the food, with contact conditions that mimic real life ones. Standardised methods are described in national legislation in Germany (DIN10955), the Netherlands (packaging and food utensil) and in method ISO 4120-1983. The organoleptic test is very important to avoid customer complaints, but is a very difficult test to use. Attention should be paid to the test panel, which should include a good selection of members able to determine differences in flavour and taste after training, test set-up (test and reference samples must be filled identically and must be safe for testing by the panel) and the test facilities.

Purity and physical parameter specifications

In some cases certain restrictions apply to the ingredients used in production, sometimes in addition to migration limits, for example, minimum viscosity, minimum molecular weight, carbon chain length and purity of the additives used. Examples of some specifications as mentioned in EU Directives are those for:

- polydimethylsiloxane
  - (Mw > 6800)
  - minimum viscosity of 100×10^{-6} m^2/s (= 100 centistokes) at 25 °C.
- waxes, refined, derived from petroleum based or synthetic hydrocarbon feedstock. The product should have the following specifications:
  - content of mineral hydrocarbons with Carbon number less than 25, not more than 5% (w/w)
  - viscosity not less than 11×10^{-6} m^2/s (= 11 centistokes) at 100 °C
  - average molecular weight not less than 500.

- white mineral oils, paraffinic, derived from petroleum based hydrocarbon feedstock. The product should have the following specifications:
  - content of mineral hydrocarbons with Carbon number less than 25, not more than 5% (w/w)
  - viscosity not less than 8.5×10^{-6} m^2/s (= 8.5 centistokes) at 100°C
  - average molecular weight not less than 480.
- Carbon Black
  - toluene extractable: maximum 0.1%, determined according to ISO method 6209
  - UV absorption of cyclohexane extract at 386 nm: <0.02 AU for a 1 cm cell or <0.1 AU for a 5 cm cell, determined according to German BfR, BIII, Reinheitsprüfung von Rußen, Stand 1.7.1972
  - benzo(a)pyrene content: max 0.25 mg/kg Carbon Black.

Compliance testing of the end product cannot be performed because the ingredients are not present. The company that uses a material with restrictions has to have data that the materials used do indeed comply with the restrictions as laid down in the legislation.

Colour release

When food is in contact with food contact material, the colour of the food contact material must remain on the food contact material and may not colour the food. Staining of the food is an unacceptable change of the food as described in EC Regulation 1935/2004. In both the German and Dutch legislation, tests are made to check if colour is released from the packaging. In both sets of tests food contact material is brought in contact with white filter paper which is wetted with a food simulant for a certain time and temperature under a constant pressure. Then the filter paper that was in contact with the food contact material should be inspected and compared with a filter paper which was also wetted and stored under identical conditions, but was not in contact with the sample to be tested. No colour release or differences between the filter paper in contact with the sample and the blank should be detectable.

Volatiles

For silicon materials some volatile components can remain in the silicon material after polymerisation. These volatiles can be removed by treating the material at high temperatures. In both France and Germany a maximum amount of volatiles that may be present is laid down in the legislation. The method of determination is:

- Prepare the silicon material (cut to prescribed sizes).
- Remove water from the silicon material using water free calcium chloride.
- Determine the weight of the silicon material.
- Expose the silicon material for a certain time to a certain temperature.
- Determine the weight of the silicon material.
- Calculate the weight loss.

This is a very straightforward method, which can easily be used to determine the total amount of volatiles. This is quite important because silicon materials are used more and more, and the new applications are often at high temperatures, such as silicon bake forms for use in ovens.

5.4 Non-target migration testing

By applying the procedures mentioned above, monomers and additives can be adequately tested. However, other components, the NIASs, can be present in the food contact material and potentially migrate to food. Such unlisted components are gaining renewed attention. In principle, they are already regulated in Article 3 of Framework Directive EC 1935/2004, i.e., food contact materials should not endanger human health. Unlisted substances that could be found in food contact materials may include:

- impurities in starting substances
- reaction intermediates
- decomposition products
- reaction products
- oligomers.

Renewed attention to unlisted substances is stimulated by efforts to enhance consumer protection. Recent examples of unlisted substances originating from packaging materials are:

- semicarbazide formed as a decomposition product of azodicarbonamide used as a blowing agent for plastics (e.g. Stadler *et al*. 2004)
- chlorohydrins and cyclic reaction products formed from epoxidised soybean oil used as a stabiliser (e.g. Biedermann-Bremm *et al*. 2001).

In these cases migrants from food packaging, with possible toxicological alerts, were found in food although these substances were not intentionally added or used for the food packaging, but were formed during preparation and/or use of the food packaging. These examples show the need to pay attention to unlisted substances. It is therefore necessary to develop a pragmatic and cost-effective strategy to address the issue of unlisted substances that is accepted by both industry and legislative authorities.

5.4.1 Current status and opinions on screening and analysis of migrants

Compared to target analysis used for specific migration studies, trying to detect all possible migrants in food simulants by screening methods offers a whole new perspective. Due to the lack of legislative requirements to analyse all substances migrating from food contact materials, only very few papers deal with this subject. The main principle for methods suitable for screening

of migrants is that they should be able to detect, identify and quantify a large range of chemical components varying in chemical structure, polarity and molecular weight. Some possible strategies for the analysis of unlisted substances have already been addressed by a few authors (Feigenbaum *et al* 2002, Grob 2002). The scheme proposed by Feigenbaum *et al*. has also been published in Annex II of the EC Practical Guide on materials and articles in contact with food. In principle, the schemes combine well-known analytical techniques for analysing a wide range of components, such as headspace gas chromatography (GC) for volatile components, atomic absorption spectroscopy (AAS)/induced coupled plasma (ICP) for elemental analysis, GC for semi-volatiles and liquid chromatography (LC) for non-volatiles. An additional step may be the application of gel permeation chromatography (GPC)/size exclusion chromatography (SEC) to determine and isolate the fraction of migrants with a molecular mass below 1000 daltons (Da), which is thought of as the toxicologically relevant limit. Figure 5.4 shows a schematic representation of an analytical strategy based on those of Feigenbaum *et al*. and Grob. In principle, with this analytical strategy a wide range of different migrants can be detected.

Headspace GC-MS is the preferred method for the analysis of very volatile migrants. Practically the same GC conditions can be used as for GC-MS. Due to the coupling to MS, identification is also relatively easy. The heating time and temperature are the main experimental variables. The major drawback of headspace GC-MS is quantification. As a result of the principle of headspace GC-MS, i.e., partitioning of compounds between gas phase and liquid phase, the chemical properties will have a significant influence on the partition of each molecule between gas phase and liquid phase. Therefore, quantification is almost solely possible by using external standards of the same compound (Grob and Barry 2004).

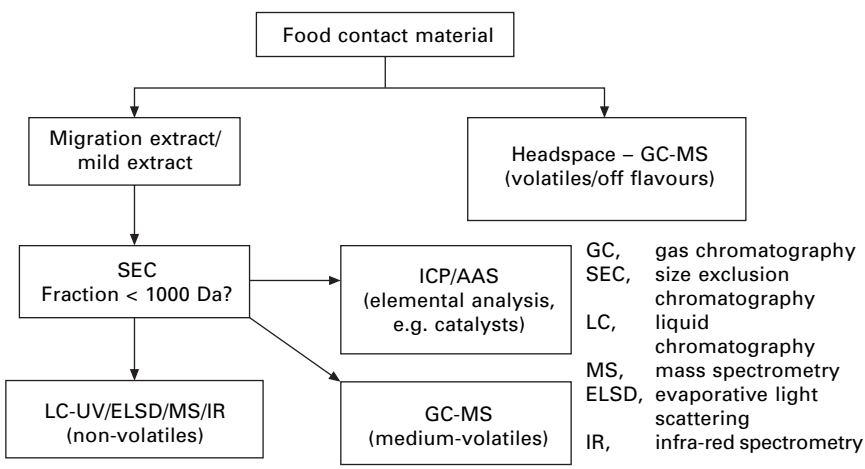

Fig. 5.4 Possible analytical scheme to detect substances migrating from food.

Size exclusion chromatography (SEC) or gel permeation chromatography (GPC) separate samples based on molecular size and thus in most cases on molecular weight. It is the preferred technique for separating low molecular weight components from high molecular weight components based on their molecular mass. As mentioned above, the fraction of migrants below 1000 Da is thought to be toxicologically relevant. As a result it may be advisable to isolate the fraction of migration extracts below 1000 Da before any further analysis. However, a major drawback of SEC or GPC is that the separation is in principle based on molecular size. Separation purely on molecular mass is possible only using calibration standards of specific compounds, e.g., polystyrene. This implies that only polystyrene can be exactly separated on molecular mass. For every other compound separation on molecular mass is approximate. It is therefore difficult to separate the fraction below 1000 Da exactly. In many cases the fraction below ~1500 Da is isolated. GPC/SEC separation can be carried out according to standardised methods DIN 55672, OECD 118 and 119. However, it is questionable whether isolation of the fraction below 1000 Da is really necessary.

Further analysis of the migration extract is preferably carried out using GC-MS and LC-MS. For GC-MS it is impossible to detect components with a molecular mass above 1000 Da due to volatility and the mass range of quadrupole MS detectors. With LC-MS the mass range can be chosen and thus the highest mass can be set at 1000 Da. Multi-methods exist with which almost all elements in the periodic system can be analysed in extracts at low levels. Combination of induced coupled plasma (ICP) and atomic absorption (AAS) coupled to MS is the preferred method. Quantification of each element is also possible with this method.

GC-MS is the method of choice for medium volatile migrants. Relatively standard GC methods can be applied that are able to detect many different types of components, except for very polar components. The only variable that might influence the application of GC is the food simulant or extraction solvent. Almost all organic solvents can be directly injected into the GC system using non-polar columns where only the start temperature has to be adapted to the specific boiling point of the solvent. Aqueous solvents are more troublesome for standard GC methods and special GC columns that are compatible with water should be used. With these columns the separation of polar components is also possible. MS detection coupled to large databases makes GC-MS ideal for identification of migrants. The major drawback of GC-MS is the separation and detection of less volatile components and very polar components, although high temperature columns might increase the volatility range significantly. For example, Irganox 1010 (m/z 1075) has been detected using HT-GC-FID (Feigenbaum *et al*. 2002).

LC coupled to a combination of MS, PDA and fluorescence is the preferred complementary technique. With LC basically all components can be separated that are soluble in the mobile phase. Separation in LC can be based on polarity, solubility and molecular mass. Moreover there are large numbers of

columns each with different properties and the combinations of mobile phases and additives are numerous. Separation and sensitivity are highly influenced by different experimental conditions like mobile phase, temperature, pH, column, etc. It is therefore very difficult to obtain a single LC method that is suitable for a large number of different types of migrants. This is complicated further when MS detection is used whilst there are also numerous variations in type of MS detectors (ion trap, time-of-flight, triple quad), type of ionisation (APCI, ESI) and settings. Furthermore, ionisation is highly influenced by mobile phases and pH. The most often used method is a reversed phase LC method with a C18 column and a mobile phase gradient from water to acetonitrile or methanol. The optimal additives and pH depend mostly on the type of detection. However, before applying this analytical strategy to screen for migrants in food packaging some considerations have to be made with respect to:

- realistic (migration) extract
- sample work-up/pre-treatment
- identification of migrants
- quantification of migrants
- sensitivity/limit of detection.

Realistic (migration) extract
It is very important that a realistic extract be analysed that reflects the food as accurately as possible. For safety reasons it is necessary to obtain a worst-case extract although this should not be exaggerated. In food packaging legislation food simulants can be used that resemble officially the various food types, i.e., 3% acetic acid, water, 10% ethanol and olive oil. Aqueous simulants are relatively easily compatible with LC and can therefore be used for screening of migrants. However, GC is less compatible with aqueous solutions and care should be taken. Possible solutions are the use of water-compatible GC columns, e.g., Aquawax, or the use of derivatisation in which the aqueous extract is freeze-dried, followed by derivatisation of polar functional groups using, e.g., methylation, butylation or silylation. With the latter method polar components are made less polar and can thus be analysed with 'regular' GC methods. However, derivatisation is not straightforward and should be carefully optimised before application. Furthermore, databases like those of Wiley and NIST do not contain many EI spectra of derivatised components.

Olive oil is a very troublesome food simulant with respect to analysis. It is therefore advised not to use olive oil for screening of migrants. Alternative fat simulants are 95% ethanol and iso-octane and these may be more compatible with techniques like GC and LC. However, these two simulants are very different from each other. Iso-octane is very non-polar and therefore exaggerates the migration of non-polar components; 95% ethanol is very polar and therefore exaggerates the migration of polar components. Another option might be to carry out mild extraction using conditions that are relatively worst-case but

still realistic, and solvents that are readily compatible with the various analytical methods. Possible examples of these solvents are iso-propanol/iso-octane 1:1 (v/v), dichloromethane, diethyl ether and tetrahydrofuran. Further research is necessary to show whether these solvents are realistic options and which extraction conditions resemble worst-case, but realistic migration conditions.

Sample work-up/pre-treatment
Ideally (migration) extracts are analysed directly without any sample work-up or pre-treatment. Every extra step in the sample work-up or pre-treatment might result in the loss of (volatile) migrants that may be toxicologically relevant, or the 'creation' of migrants due to contaminants. This can be partially solved by carrying out blank experiments in which a blank solvent undergoes the same procedure. There is a large chance that direct injection of the migration extracts does not lead to sufficient sensitivity and that further concentration is necessary. In this case contamination and loss of migrants should be minimised at all times. Further complication might occur when the solubility limits of specific compounds are exceeded and the components precipitate.

Separation
The first aim in the screening of migrants is the ability to detect and separate as many components as possible. A combination of headspace GC, ICP/AAS, GC and LC is an adequate set-up to cover a large range of different compounds from very volatile compounds to non-volatiles, non-polar to polar and organic versus inorganic. Individual methods should be optimised to increase separation. Migration extracts might contain a large amount of migrants with a large variation in concentration that might interfere with separation. This often results in co-elution thereby complicating both identification and quantification. In the case of small and large peaks co-eluting, the former one might not be visible at all and remain unnoticed. Multi-dimensional separation like GC × GC and LC × LC are the answers to co-eluting peaks (Dalluge *et al*. 2003). In these methods, different separation mechanisms are applied in two dimensions. For example, in GC × GC components can be separated in the first dimension on volatility whilst in the second dimension the peaks are separated on polarity. A demonstrative example is shown in Fig. 5.5 where a GC × GC-TOF-MS is shown for a migration extract of a polyethylene (PE) food packaging.

It can be clearly seen that along the first dimension a series of large peaks due to PE oligomers are separated whilst in the second dimension more polar components, like additives, are separated. With GC-MS, small peaks due to degradation products of additives might be invisible due to the large peaks of the PE oligomers. The advantage of GC × GC-TOF-MS is that the same mass spectral information and databases can be used and sensitivity is equal to or higher than that of GC-MS. An additional advantage of GC × GC is the possibility of group-type separation where components with similar

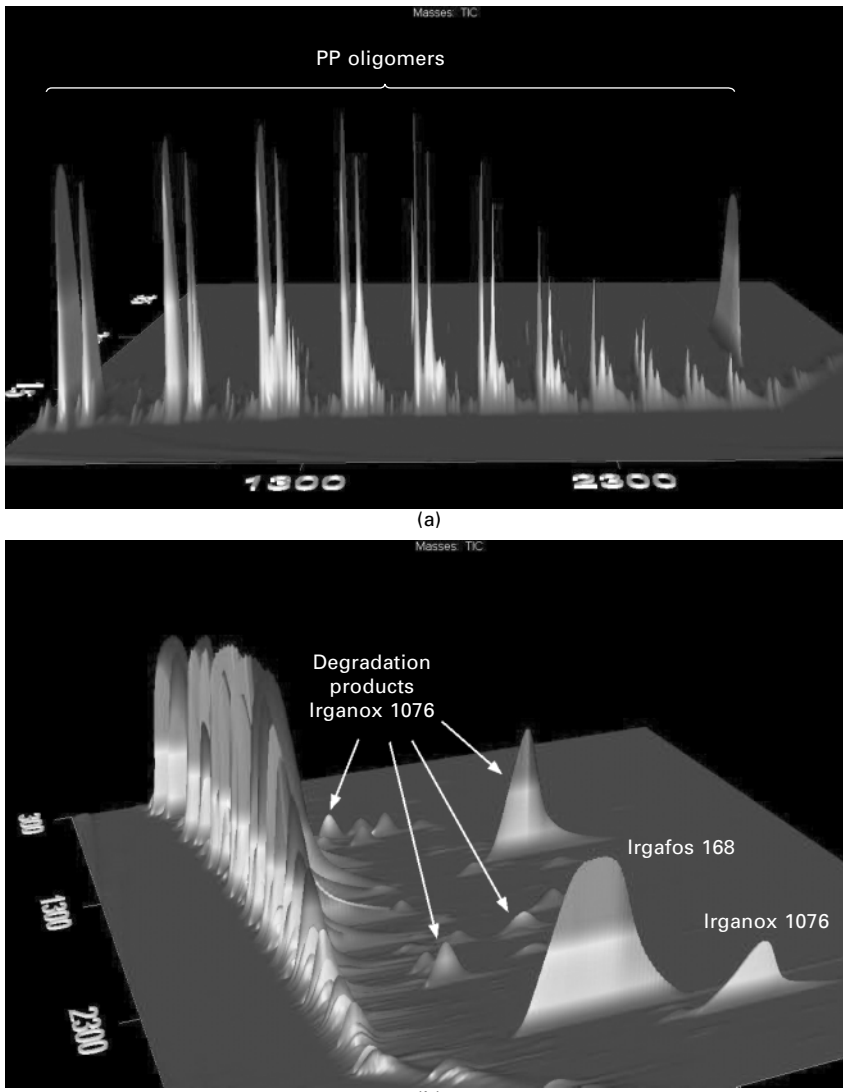

Fig. 5.5 GC × GC-TOF-MS chromatograms of a PP migration extract: (a) view along the first dimension (separation on boiling point), (b) view on the second dimension (separation on polarity).

functionality form groups on the GC × GC chromatogram (Mondello *et al*. 2003). This might be a useful way to screen classes of compounds, e.g., aromatic amines or isocyanates.

For LC × LC the situation is a bit different. First of all this method is not as well developed as GC × GC and is mostly applied for proteins where a combination of ion exchange-RPLC is used or to polymers where a combination of LC × SEC is most often used. Moreover, a major drawback of LC × LC

is the fact that due to the two dimensions the peaks are diluted and therefore sensitivity decreases, which is already a critical factor for LC. Furthermore, on-line LC × LC-MS methods are not available at the moment. There is a lot of development in the field of LC × LC and without a doubt this technique might play an important role in the future for screening of migrants. The combination of NPLC × RPLC might be very helpful to increase separation based on polarity.

Identification of migrants

A wide range of detection techniques can be used, although unknown migrants can be identified almost solely by means of mass spectrometry (MS). The advantage of GC-MS is the relatively straightforward method used to detect a wide range of components. Identification is relatively easy on the basis of existing mass spectral databases. Although ionisation of molecules may differ amongst molecules, almost all molecules ionise under the conditions of GC-MS, i.e., electron impact ionisation. Identification with GC-MS mainly depends on the presence of large databases. This often results in either complete identification or no significant match. In some cases it is possible to characterise the component using specific mass traces. For example, a mass/charge ratio (m/z) of 149 is often indicative for phthalates. If identification is not possible using databases, other types of MS might be helpful. For example, chemical ionisation (CI) gives in addition to electron impact (EI) the molecular mass of the component. This is often difficult to determine due to strong fragmentation with EI. Chemical ionisation in combination with high resolution MS might give the elemental composition of the molecule. By applying CI and ion trap MS it is then possible to obtain structural information by MS/MS experiments. A possible identification strategy for unknown migrants using GC-MS based techniques is shown in Fig. 5.6.

MS is the preferred technique for screening of migrants using LC. The ionisation process in LC is relatively soft and does often lead to very simple mass spectra containing mainly the molecular ion. In certain cases the component can be identified based on retention time and molecular mass derived from the molecular ion. However, this is mainly true for well known

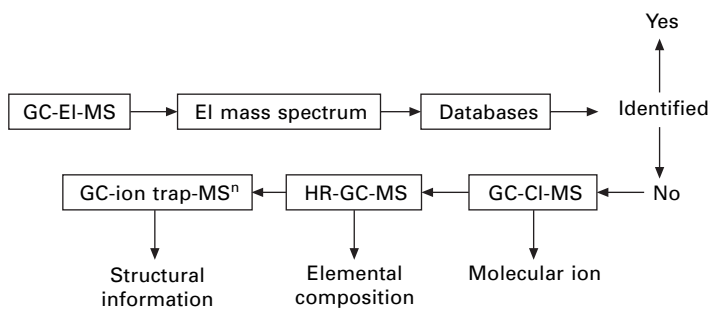

Fig. 5.6 Possible identification strategy for unknown migrants using GC-MS.

components. Moreover, the mass spectra can be complicated by adduct formation, especially in electrospray ionisation. Very apolar components (e.g. aromatics, alkanes) cannot be ionised at all with LC-MS and will therefore not be visible in LC-MS chromatograms. No large databases exist for LC-MS and therefore identification of unknown peaks in the chromatogram is often very difficult, expensive and time-consuming, if possible at all.

Recent developments in MS analysers are giving some new perspectives in the field of identification. Especially with high resolution MS, like TOF-MS and even better FT-ICR-MS, the exact molecular mass and thus the elemental composition can be obtained (Hendrickson and Emmett 1999). Using various databases of chemicals on the Internet, it is often possible to identify the component based on the chemical composition. Of course this should be validated by analysing the specific component using LC-MS and comparing the retention time and mass spectrum. MS/MS experiments, using ion trap MS analysers, are in certain cases necessary to obtain some additional structural information in order to decide which chemical composition obtained from high resolution LC-MS is the most likely.

Quantification of migrants

The most common method of quantifying components is the use of calibration standards from the pure compound. However, in the case of degradation products or decomposition products this is not possible due to the absence of a commercially available reference compound. Furthermore, the quantification of all migrants present in a migration extract is very time-consuming and thus expensive. A possibility might be the use of a mix of reference compounds that resemble different types of compounds. This would assume similar ionisation efficiency for compounds with similar chemical structures. In this way a specific peak is, after identification, categorised in a specific class of compounds and is semi-quantified using the relevant reference compound. For example, for a migration extract of PE food packaging a mixture of alkanes, butylated hydroxytoluene and Irgafos 168 might be used as reference compounds for PE oligomers, anti-oxidants and degradation products of anti-oxidants. It is essential that information from the supplier can be obtained regarding what type of ingredients are used and thus what type of migrants can be expected. Although this approach is not 'waterproof', it is relatively easy and holds true in many cases for GC-MS. However, for LC-MS it would be very difficult to use the same approach as ionisation depends very much on chemical structure. For certain types of molecules parallel detection using PDA or fluorescence might be helpful and these types of detection might be more quantitative. After a component is identified and seems to be toxicologically relevant, exact quantification might be possible using reference compounds.

Sensitivity/limit of detection

Assuming that all migrants can be detected by the various analytical methods,

the concentration of the migrant in the extract determines whether the migrant is visible in the chromatograms. If a component is not visibly present in the chromatograms it cannot be further addressed. However, this does not mean that the component is of no toxicological risk. The toxicological properties of a specific compound and the extent of its consumption via food determine what concentration is allowed in the migration extract, using the assumptions made in food contact legislation. As a result the acceptable concentration of compounds in migration extracts might differ by orders of magnitude. As a result analytical methods should be sensitive enough to detect the most toxic compounds above certain toxicological thresholds. An example of such a threshold is the Threshold of Regulation of 1.5 μg/day as proposed by Begley (1997). This means that every compound is allowed if the consumption does not exceed 1.5 μg/day. At first instance this seems an adequate rule of thumb for the screening of migrants. However, using the current assumptions in the EU that 1 kg of food is consumed every day and is in contact with 6 dm^2, this means that 1.5 μg/day corresponds to 1.5 μg/kg food = 1.5 μg/6 dm^2 packaging. Assuming standard migration conditions of 2.34 dm^2 packaging in contact with 100 ml simulant, this results in a concentration of (1.5/6)*(2.34/100) = 0.00585 μg/ml = 5.85 ng/ml. Hence a detection limit of 5.85 ng/ml is necessary to ignore all undetected migrants. For most components this is not feasible using the analytical techniques discussed above. Possible solutions to this problem are enrichment of the migration extract by evaporation, also as discussed above. Concentration by at least a factor of 10–100 is necessary. Another option might be the use of actual exposure data instead of relying on the various assumptions made in the current legislation. This is explained in some more detail in a later section.

At this moment, no analytical technique or strategy exists with which all possible components can be detected, identified and quantified. Despite this, the current status of analytical techniques is able to at least give a good indication of the presence of migrants in food simulants. Analysis of migration extracts by the scheme shown in Fig. 5.4 enables the detection of a wide range of non-polar/polar compounds, small/large compounds and volatile/non-volatile compounds. Table 5.7 gives an overview of literature dealing with the screening of migrants from food contact materials including the type of food packaging and the analytical methods used.

5.5 Future trends and requirements for screening and analysis of migrants

Despite the limitations of the current analytical techniques and the scheme shown in Fig. 5.4, the field of analytical chemistry is improving day by day and some new promising techniques and approaches may result in a major improvement in the screening of migrants. However, the whole idea behind the screening of migrants, especially those unintentionally added and not

Table 5.7 Overview of literature dealing with screening of migrants

Packaging material	Analytical methods			Reference
PP, PVC, HDPE, LLDPE, PS, PC, PET, PA6	AAS, GC-FTIR-MS, thermodesorption GC-MS, headspace GC-MS, NMR, HPLC, GC-FID, GC-IR, GC-MS, HT-GC-FID	Extraction		Feigenbaum *et al.* 2002
LDPE, HDPE, PP, PA66, PA6, laminates	(purge and trap) GC-MS	Migration	Identification and quantification	Skjevrak *et al.* 2005
Phenolic resins for can coatings	GC-MS, GC×GC-FID, NPLC-GC, SEC, CI-MS	Dissolution	Pure compound, identification	Biedermann and Grob (submitted)
cPET, thermoset polyester, poly (ethersulphone), poly(4-methyl-pent-1-ene)	GC-FID, GC-MS, headspace GC	Extraction	No quantification	Gramshaw *et al.* 1995
PA 12	GC-FID, HPLC-UV, LC-MS	Migration	Monomers, oligomers	Stoffers *et al.* 1993
PA6, PA6,6	GC-FID, HPLC-UV, EI-MS, FAB-MS	Extraction		Soto-Valdez *et al.* 1997
Polyester can coatings	GC-FID, LC-MS, HPLC-UV/ELSD	Migration		Schaefer *et al.* 2004
PA6	LC-MS, HPLC-UV			Barkby and Lawson 1993
PA6, PA6,6	GC-MS, HPLC-UV	Migration in food		Gramshaw and Soto-Valdez 1998

included in the EU positive lists, is the protection of the consumer. The influence of a certain compound on human health is determined by the principal toxicological properties of that compound and the exposure of a consumer during daily diet towards that compound. The detection, identification and quantification of compounds in migrant extracts are therefore only a part of the whole risk assessment. It is important that aspects of exposure and toxicology are addressed. Without proper exposure and toxicological assessment, the development of adequate screening methods for migrants is of limited use.

5.5.1 Exposure

One of the most important issues regarding safety of food contact materials is exposure of consumers to specific migrants in combination with the toxicity of the migrants. Current EU legislation on food contact materials is primarily

based on toxicity, and analytical capabilities and exposure are not adequately integrated, in our opinion. From the available toxicity and migration data, a specific migration limit (SML) is derived and several assumptions are made:

- 1 kg of food eaten every day
- 1 kg of food corresponds to 6 dm^2 of packaging
- packaging always contains the substance
- migration of the substance at SML
- consumer body weight of 60 kg.

As a result, an additive or monomer on the positive list can be used for any type of packaging/application provided that the SML is not exceeded. Although these assumptions lead to a relatively easy enforcement of the legislation, it is questionable whether this is a realistic approach. The assumptions mentioned above are on average all justifiable but on the individual level strong deviations may occur depending on the consumer (e.g. age, body weight, high consumers), the food-type (e.g. solid food vs. liquid food, fat food vs. aqueous food) and the type of packaging (commonly used materials vs. rarely used materials, small/flat packaging vs. large/cubic packaging). To obtain the actual exposure of consumers towards food contact materials and substances present in these food contact materials, the following data are required:

- food consumption: what types and amounts of food are consumed by individuals representative of all ages and EU countries
- food packaging: what packaging materials are used for different foods, including surface area/weight ratio.

Additional information on the chemical constituents of the packaging material, i.e., type and amount of monomer and additives and their migration characteristics, would give the opportunity to calculate the actual exposure to specific migrants. Note that this information is also essential for the interpretation of the analytical results obtained in the screening of migrants. The more information is known prior to analysis, the better the chance that compounds can be identified.

For the NIAS, there is a more urgent need due to Article 3 of the Framework Regulation (EC 1935/2004) and new upcoming legislation and the same approach to exposure should be used. The only drawback to the NIAS is the fact that these substances are often unknown and thus the toxicity of these substances cannot be used, and therefore it is almost impossible to apply the acceptable or tolerable intake of these NIAS. The combination of actual exposure and toxicology will help to determine the acceptable level of a specific migrant in the migration extract.

5.5.2 Toxicology

The toxicological characteristics of substances on the EU positive lists for chemical migrants are normally obtained through time-consuming and

expensive toxicity testing. From a practical and economic point of view it is unthinkable that these tests should also be carried out for all unlisted substances present in migration extracts. Indeed reference substances are usually not available to carry out these tests and testing of a migration extract may not provide the correct results. To circumvent this problem, activities were undertaken for Europe by the ILSI Europe Threshold of Toxicological Concern Task Force (Kroes *et al*. 2000, 2004). A Threshold of Toxicological Concern (TTC) principle evolved from a review of the Threshold of Regulation used by the FDA (Munro 1990) and further developments (Munro *et al*. 1996). The TTC principle was defined assuming threshold values for many chemicals based on their chemical structures and the known toxicity of chemicals that share similar structural characteristics. Using a decision tree, based on that of Cramer *et al*. (1978), a specific compound is assigned to a specific structural class of compounds each with its own specific threshold. The TTC Task Force concluded that the TTC principle could be applied to low concentrations of chemicals in food without available toxicity data, provided that there is a sound consumer intake estimate. Especially for chemicals migrating from food contact materials into food, a sound intake estimate based on food consumption data and packaging material data is very important in order to apply the TTC principle.

A schematic overview of the different structural classes and their TTC values is shown in Fig. 5.7, adapted from data in Cramer *et al*. (1978) and Kroes *et al*. (2000, 2004). If the intake of a specific compound is below the TTC value, there should not be a safety concern. In case the intake exceeds the corresponding TTC value, a risk assessment is required on the basis of compound-specific toxicity data. In the latter case, the use of structure-activity relationships (SARs) may be of value.

A very important class of components are the genotoxic compounds. Table 5.8 gives an overview of various classes of chemicals with structural alerts for genotoxicity. This list is not exhaustive but shows classes of chemicals that might be present in food contact materials. It has been proposed that for proper risk assessment of food packaging materials, it should be demonstrated that this class of components is not present above the TTC value. Whilst genotoxic chemicals have the lowest TTC value, it will be an enormous challenge to obtain a strategy to which this can be applied, given the unacceptability of genotoxic carcinogens being used in packaging.

5.5.3 Future risk assessment of unlisted migrants

A protocol for risk assessment of unlisted migrants should be developed that is pragmatic, cost-effective and accepted by both industry and legislative authorities. In this protocol, exposure, toxicology and chemical analysis should be combined. A possible combination would be the approach described above of relating exposure to the threshold of toxicological concern (TTC) principle. This would determine the analytical boundaries for screening of

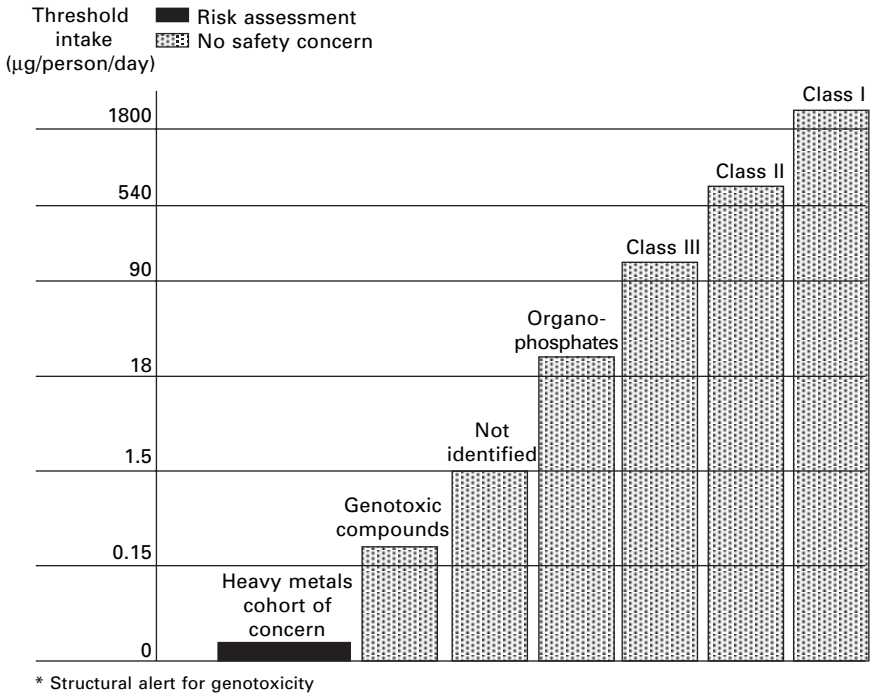

Fig. 5.7 Threshold levels and different structural classes used in the Threshold of Toxicological Concern principle (adapted from Cramer *et al*. (1978) and Kroes *et al*. (2000, 2004)).

Table 5.8 Classes of chemicals with structural alerts for genotoxicity that might be present in food contact materials

Alkyl esters of phosphonic or sulfonic acids	Propiolactones and propiosulfones
Aromatic and aliphatic nitro groups	Aromatic and aliphatic aziridinyl-derivatives
Aromatic azo groups (reduction to amine)	Aromatic and aliphatic substituted primary alkyl halides
Aromatic ring N-oxides	Urethane derivatives (carbamates)
Aromatic mono- and d-alkyl amino groups	Alkyl N-nitrosamines
Alkyl hydrazines	Aromatic amines and N-hydroxy derivatives
Alkyl aldehydes	Aliphatic epoxides and aromatic oxides
N-methylol derivatives	Center of Michael reactivity
Monohalalkanes	Halogenated methanes
N and S mustards, β-haloethyl	N-chloramines

migrants from food packaging materials. But the current status of analytical chemistry will most probably not be sufficient to meet the standards necessary for analysing a wide range of different components at low concentrations. The analytical strategy should be at least able to detect a wide range of

different components varying in molecular mass and polarity as well as identification of relevant migrants above a certain threshold (determined by exposure and toxicology).

Recent developments in analytical chemistry that might be interesting for the analysis of unlisted substances are HR-GC-MS and LC-FT-MS for identification purposes, and GC × GC-TOF-MS and LC × LC for the analysis of complex mixtures of migrants. The TTC principle separates chemicals in classes based on chemical structures. Therefore, screening on classes of components by, e.g., isotopic or fluorescence labelling or derivatisation of functional groups might be a good way of avoiding laborious peak-by-peak identification and quantification.

5.6 Sources of further information and advice

http://crl-fcm.jrc.it/ The website of the Joint Research Centre of the EU with information about analytical methods for specific migrations
http://www.efsa.eu.int/science/afc/afc_opinions/catindex_en.html The EFSA website with up-to-date opinions regarding components and issues around food contact materials
http://europa.eu.int/eur-lex/en/search/search_lif.html The official EU website with Directives and legislations
http://www.foodcontactmaterials.com Legislative information regarding EU, national and FDA issues regarding food contact materials
http://ec.europa.eu./food/food/chemicalsafety/foodcontact/documents_en.htm A summary of information (link through page to Summary of the national legislation, List of abbreviations and explanations, Addresses of European and National Authorities, Contacts of European Professional Organisations, Questions and Answers, list of the EU and national legislations, Practical Guide – information/explanation on EU legislation on food contact materials, Synoptic Document, substances listed in EU Directives and Note for Guidance, National Contact Point for Petitions)
http://www.cenorm.be/CENORM/BusinessDomains/TechnicalCommitteesWorkshops/CENTechnicalCommittees/Standards.asp?param=6175&title=CEN/TC+194 The CEN website with the most recent specific and overall migration testing CEN methods

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6

Exposure estimation – the missing element for assessing the safety of migrants from food

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6.1 Introduction

A fundamental principle of toxicology is that any biological effects increase as the dose increases, in other words 'the dose makes the poison', the often-stated phrase normally attributed to Paracelsus (1493–1541). This philosophy may seem, to some, to be lacking today in the EU, where migrants from food packaging are concerned. The rapid advances in analytical techniques and equipment over the last two decades have resulted in detection limits for known substances migrating being substantially reduced and many substances being detected, which were hitherto unexpected, primarily because earlier analytical techniques never detected them. Consequently, this has resulted in food scares and questions being raised about the safety of food contact materials with respect to substances that migrate into the foodstuff. However, even toxic substances cannot endanger human health if they are not consumed or are consumed only at very low levels – the '*de minimus*' principle. Risk to a contaminant in food, irrespective of its source, is a combination of the hazard of the substance (toxicity) and how much of that substance is consumed (exposure).

$$\text{Risk} = \text{hazard} \times \text{exposure}$$

Thus to ensure the safety of food packaging, not only is it necessary to consider the toxicity of any migrating species (hazard evaluation), but also how much is consumed (consumption estimation) and how much is present in the foodstuffs (occurrence estimation) consumed. This approach by Rees and Tennant (1993) is suitable for chemicals that have a chronic effect, but for those that have acute toxic effects the amount of food containing them

consumed in one meal or one day may be important. In this case estimation of a lifetime exposure is unwarranted and the maximum amount likely to be consumed in one eating occurrence must be considered. This chapter primarily considers how exposure to migrants from food packaging may be estimated, and these would be encompassed by the chronic classification.

Exposure assessments are fundamental to determining a tolerable daily intake (TDI), which is based upon the hazard (toxicology) and the exposure. Exposure assessments also offer other benefits to the risk manager. For example, they enable a level below which the toxicity need not be tested, provided it is not genotoxic, and a value of 1.5 μg/person/day is frequently referred to as a threshold of regulatory concern (TORC) in the USA and sometimes as a threshold of toxicological concern (TTC) in Europe. An ILSI publication (Barlow 2005) gives more details. It is possible by using probabilistic (stochastic) modelling to derive what level of migration equates to a TTC (Castle *et al*. 2006). Depending upon the structure of a substance it is possible (ILSI 2000, Monroe *et al*. 1996, Cramer *et al*. 1967, Kroes *et al*. 2004) to have an exposure of a known substance up to 1800 μg/person/day (Cramer Class III), without having to evaluate the toxicity of the substance. There has been much debate about thresholds and they will not be considered further here, but for more details the reader should consult the references given under threshold further reading amongst others. What is clear, however, is that in order for a threshold to be applied it is necessary to estimate the exposure of any individual to any substance migrating from packaging. This is considered by many as a major weakness in the EU risk assessment process, as it currently stands.

Several methods can be used to estimate the intake of a food contaminant and the choice will depend upon the accuracy and detail of the required estimate (Parmar *et al*. 1997). No single method can meet all of the choice criteria, therefore the methods have to be selected and combined on a case by case basis. The choice depends upon (Kroes *et al*. 2002) the objectives of the study, the foods of interest, the needs for group vs. individual data, the needs for relative vs. absolute intake, characteristics of the population, the time-frame of interest, the level of specificity needed for describing foods and available resources.

Rees and Tennant (1993) summarised four guiding principles for chemical intake (a migrant is part of the chemical intake) as:

1. The estimate should be appropriate for the purposes to which it is put.
2. The estimate should have an assessment of accuracy.
3. Any underlying assumptions used should be clearly stated.
4. Critical groups of the population should be taken into account when these groups are disproportionately affected by the chemical.

In the absence of adequate raw data to enable a ‘true’ exposure assessment for a migrant from packaging materials it is necessary to estimate the exposure. Different approaches may be used, ranging from the EU assumption of

6 dm^2/kg, to that of the US FDA, which in essence uses a *per capita* approach based upon industry statistics, to the latest probabilistic modelling techniques. With the advances in computer technology and statistics, it is now possible to employ 'state of the art techniques' often referred to as stochastic or probabilistic modelling, where the gaps in the data are addressed by using a 'Monte Carlo' (random number generation) approach. Here the most likely values for the different parameters affecting exposure to any migrant from packaging and others are chosen at random and used to construct an exposure scenario.

In this chapter the different facets of the parameters for assessing exposure, who and what should be covered by an exposure assessment are discussed before different data sets which should ideally be available in order that a realistic assessment of exposure can be made. This is then followed by a review of the different approaches which can be used with today's data. Approaches can range from very crude to very refined. It could be argued that exposure to migrants from food packaging materials is more difficult to estimate realistically than that from food additives or other contaminants, such as pesticides, because in many surveys of the consumption of foodstuffs, the food is described but not its packaging. Determining, estimating or guessing the packaging of each and every foodstuff consumed adds another dimension to an already difficult problem. Many of the approaches (e.g. Rees and Tennant 1993, 1994, Parmar *et al*. 1997, Kroes *et al*. 2002) were developed for estimating exposure to food additives, flavourings or contaminants but not contaminants arising from packaging of the foodstuffs. This requires additional information.

6.2 What is exposure?

Exposure to a substance found in foodstuffs, irrespective of source, is derived as follows:

- For each individual
  - Exposure for food item = concentration of the substance in a food item × weight of item consumed.
  - Exposure for meal = sum of exposure of all items consumed during that meal.
  - Exposure over lifetime = sum of exposure for all meals.
- For the population
  Exposure for population = distribution of exposure for every individual obtained by repeating the above three steps for the entire population.

The exposure intake for any population is a sum of the products of the concentration (c) in mg/kg or µg/kg of the migrant within the food item eaten and the weight (w) in kilograms of that item, and is expressed as (Holmes *et al*. 2005)

$$DD_{jk} = \frac{1}{W_j} \sum_{l=1}^{n(k)} w_{jkl} c_{jkl} \qquad 6.1$$

Here, DD_{jk} is the daily dose for any individual j on day k consuming up to $n(k)$ items on that day. W_j is the weight of the individual j and c_{jkl} is the concentration of the migrant in the food item l, whilst w_{jkl} denotes the weight of item l on day k eaten by individual j.

A distribution curve similar to that shown in Fig. 6.1 can be obtained. From the 'y' axis it is possible to select any percentile consumer and 'read off' the exposure on the 'x' axis. If all of these data existed with no uncertainty, then there would be no need to estimate exposure. Having obtained an exposure curve, it is then necessary to decide what percentile value should be used for the consequent risk assessment. The percentile to use for the 'protection' of any population to any risk is a political and not a scientific decision. The regulators and politicians have to be realistic as 100% of the population can never be protected all of the time. The considered opinion of many is that the diet of the consistent 100th percentile consumer would result in serious health problems due to nutritional factors long before any effects due to migrants from packaging would be a factor. The definition of the high consumer varies, but for food contact materials, either the 90th, 95th or 97.5th percentile is typically used for the high consumer (Kroes *et al*. 2002) rather than the maximum value.

This does not mean that 10, 5 or 2.5% of the population are unprotected, but as a consequence of the derivation of the percentile, a high consumer of one food type is most unlikely to be a high consumer of another and certainly not for a lifetime. Furthermore, the maximum level consumer is unlikely to maintain this consumption over long periods of time and therefore is not representative of high level intakes in relation to chronic exposure (Benford and Tennant 1997). The use of the 95th percentile has been considered as a

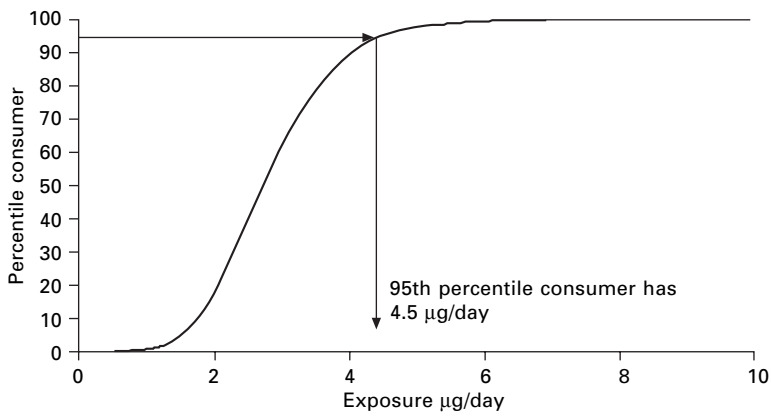

Fig. 6.1 Cumulative exposure curve for a population showing an exposure ('x' axis) for a given percentile ('y' axis) (Holmes *et al*. 2005).

good compromise (Chambolle 1999) between a high level of protection for the consumer and the uncertainty (or precision) in the intake estimates. However, as a consequence there is correlation between the percentile selected and the necessary precision and the sample size. For a given sample size the nearer one gets to the 100th percentile the fewer the consumers. It is now possible to statistically treat scenarios for high consumers with small sample sizes but the uncertainty of any estimate increases.

Whilst it is necessary to consider all sources for a substance to be found in foodstuffs for a full exposure assessment, this chapter considers only contamination of food from its packaging. For the presence of substances which could be in packaging as well as in the raw food (however few), any contamination from food processing equipment and any migration from cookware or cooking utensils in the home, once the food has been emptied from its packaging are outside the scope of this chapter. Today, the exposure to a substance migrating from packaging into food cannot be determined exactly, as consumption data with the packaging of the foodstuff consumed do not exist for the whole of the European population. Indeed, very limited data exist for the EU and in some cases even the surveys of the foodstuffs are barely adequate, but their prime purpose is for nutrition.

6.3 Who and what should be considered in any exposure assessment?

Exposure to a given amount of a given contaminant may not present an issue for one individual, but may be a serious issue for another. Thus the questions, which must be considered in any exposure assessment, include the sensitivity of the individual, in the sense that an infant has a much lower body weight than the conventional assumption used in the EU that a person weighs 60 kg. Also a child, whilst having a lower body weight, consumes a relatively higher proportion of foodstuffs/kg of body weight, which results in a higher exposure in terms of mg or μg/kg body weight (Castle 2004). Edler *et al.* (2002) address the consumption of infants and children with reference to their relative immaturity compared to adults, particularly with respect to their immune systems and potential inability to eliminate compounds from their system (toxicokinetics) or the response of target organs (toxicodynamics).

Regulatory limits based upon toxicological data have a safety factor, typically 100-fold to allow for differences between species (10-fold factor), as most testing is on rats rather than mankind, and variability between humans (another 10-fold factor) (Renwick *et al.* 2000). Additionally, in order to address potential areas of concern, it may be desirable to distinguish between different consumers and their habits. Certain groups may be more vunerable due to age, dietary habits, ethnicity, gender, genetic make up, any medical conditions, etc. As an example, consider a teratogen and its potential to be effective. A pregnant woman consuming a teratogen may result in damage to the foetus, whilst it

could be argued that an infant consuming a teratogen will not affect the development of the foetus, because the infant cannot become pregnant. Consult Edler *et al*. for further details on the treatment of sensitive groups.

The protection of the high consumer from contamination by migrants from the packaging of the food they are consuming is important not only for governments and their advisory bodies, such as EFSA, but also for industry. Obtaining a realistic estimate of exposure to a particular migrant(s) for the high consumer is always an issue with the current lack of data. However *per-capita* estimates normally include non-consumers, which reduce the exposure to the consumer population. They cannot be used to express exposure for non-average consumers, particularly the high consumer. However, it is accepted by some (Rees and Tennant 1994) that multiplying the per-capita estimate by three gives an estimated exposure for the high consumer (97.5th percentile), but whilst this may be valid for individual foodstuffs it is less likely to hold when a chemical can be present in several foodstuffs, or by two for the 90th percentile (Rees N., private communication 1998). A pragmatic approach to estimating exposure for the high consumer is to derive the *per capita* estimate and multiply by a factor of three. Moy (2005) considers that the high consumer of a single food consumes three times the *per capita* consumption, whilst for the whole diet a factor of two is more appropriate. Thus estimates of exposure for the population to a migrant from a food packaging material are needed and they will have varying degrees of refinement.

Another factor which could result in non-average exposure is loyalty, either to a brand or to a type of packaging which could impact any estimate of exposure. Packaging loyalty is when a consumer will always drink a can (or glass bottle or PET bottle) of beverage irrespective of brand, as distinct to a brand loyal consumer who will always drink the same brand of beverage irrespective of its packaging. Packaging loyalty or brand loyalty will skew any exposure estimate. Packaging loyal, high consumers are subjected to a higher exposure (if the migrant originates from that packaging) than a non-packaging loyal consumer, if there is more than one form of packaging for that foodstuff.

Brand loyalty is the preference of a consumer for a particular brand of the same foodstuff, but this has implications as described in SCOOP (Report EUR 17528EN). The exposure for a brand loyal and non-loyal consumer could vary significantly if there were, for example, a different food additive present in one brand compared to another, for example, present in biscuit X but not Y or Z. Do brand loyal biscuit X consumers eat biscuit X at the same level as brand loyal biscuit Y consumers eat biscuit Y and do the aggregated (non-brand loyal and brand loyal) biscuit consumers (biscuits X, Y and Z) eat biscuits at the same levels as the brand loyal consumers of biscuits X and Y? If the additive is only present in say biscuit X, then the aggregated biscuit consumption would under-estimate the exposure to the additive for the brand loyal consumer who only ate biscuit X, but would over-estimate the exposure for the consumer who only ate biscuit Y, but would be most representative

for the non-loyal biscuit consumer. However, until more information is available from dietary surveys about brand loyalty, it must not be assumed that if only a single brand of the products in a particular food item contain the migrant then there is less concern, even if the brand has a small market share, partly because brand loyal consumers may belong to a vulnerable group for whatever reason. Today dietary intake studies generally contain inadequate data to accurately determine the exposure of brand loyal consumers.

Another factor, which may influence the realistic concentration data, is store loyalty, which is in reality a sub-set of brand loyalty. This applies in those situations where for whatever reasons, such as lack of mobility, the consumer is effectively forced to purchase from a local store. If they purchase 'own brand' foodstuffs and if these foodstuffs have a different concentration of the migrant data set compared to the overall concentration data compiled during a survey, such as the FSA BADGE survey (2000), then it is necessary to ensure that if the concentration data are higher the consumers who purchase only 'own brands' are protected. It could be argued that if the concentration data are lower, then these data should also be used.

One of the simplest approaches for packaging loyalty is to assume that if a consumer initially consumes a foodstuff in a particular type of packaging then they will always consume that item in the same packaging (100% loyalty), whereas the non-packaging loyal consumer will consume that foodstuff item with its packaging randomly selected in proportion to the market share of the packaging for that type of foodstuff. If a food item is packaged in more than one material, then there will always be a proportion of the population who consume the food item, but due to packaging loyalty they will never be exposed to that migrant from that source.

6.4 What data are needed in order to estimate exposure?

In order to estimate exposure to a given migrant(s) the following data are required:

1. consumption of foodstuffs
2. packaging of foodstuffs consumed
3. concentration data of migrant(s) in foodstuffs consumed.

It is necessary to combine data from different sources. These data can be simplistically considered as concentration of migrant(s) and weight of foodstuff consumed containing that (those) migrant(s). However, obtaining these data is normally not straightforward and many assumptions are required. Whilst all EU member states conduct food consumption surveys, their prime purpose is for nutritional information. Few contain detailed information on the packaging of the foodstuffs consumed. Some of the surveys do not contain detailed information on the foodstuffs actually consumed and by whom. These surveys today have to be used as the basis for assessing the consumption of foodstuffs,

whilst taking account of the associated uncertainties. Information about the consumer, the weight of food consumed and an adequate description of the food items consumed are considered critical input data.

Packaging may be defined for some of the food items recorded in some survey data, but this is not the norm. The packaging of non-defined items has to be assigned based on their estimated market shares, based on any available marketing data, and/or expert judgement. Concentration data for a given migrant can be obtained from simulant studies or by determining its concentration in the foodstuffs of concern or by mathematical modelling. Clearly, not all of these data are readily available and, in most cases, very limited data exist. Therefore it is necessary to make assumptions based on available information and expert judgement, but in so doing the impact of the assumptions on the estimate needs to be evaluated. Of the data required, concentration data for a particular type of packaging, even if assumptions are used, are frequently easier to obtain and could be considered to be more reliable than the other inputs of the packaging used and who consumed what.

6.5 Obtaining concentration data

6.5.1 Introduction

The actual concentrations of any substance migrating from the packaging into each and every foodstuff are uncertain. In order to evaluate the exposure to any substance, it is necessary to determine the amount of each and every foodstuff consumed, which may have been in contact with the substance, and the concentration of the substance in each and every foodstuff consumed. Surveillance surveys do not measure the concentration of a substance in every foodstuff, but are typically more targeted towards those foodstuffs in which the substance(s) being surveyed are considered to have their highest levels.

6.5.2 Different approaches for obtaining concentration data

In many cases concentration data in real foodstuffs are unavailable, particularly for new substances. Thus simulant data for migration is typically used. Foodstuffs are assigned a chemical mixture (a simulant), which is believed to represent the foodstuff, in both Europe and the USA. In Table 6.1, the simulants considered to represent different foodstuffs according to EU Directives 2002/72/EC and its amendments, 82/711/EEC and 85/572/EEC are given. Note that solid foods may or may not need to be tested depending upon whether they are fatty in nature. The simulant must be used under conditions which will simulate the most extreme case the packaging is likely to encounter, during the processing of its contents (e.g. sterilisation, pasteurisation). For further details on which foodstuff is represented by which

Table 6.1 Food simulants specified in the EU for testing plastics for migration (CEU 2002, 2003)

Simulant code	Composition of the simulant	Foodstuffs that the simulant represents
A	Water	Aqueous foods with a pH > 4.5
B	3% w/v acetic acid	Acidic foods pH ≤ 4.5
C	10% v/v ethanol	Alcoholic foods and beverages
C	Ethanol at concentration in foodstuff	Concentration of ethanol (v/v) actually present
D	Olive oil or alternative fat simulants	Fatty foods
D/X		Test value divided by reduction factor X, in the range 2–5, because olive oil is considered too aggressive for many fatty foods
O	No testing required	For example, fruits with peel or dry foodstuffs

simulant and under what conditions (times and temperatures) consult these Directives.

It should be noted that at this point in time, the value for the migration into the fatty food simulant 'D' may be subject to a reduction factor (D/X) with 'X' varying from 1 to 5 for different fatty foods in recognition that olive oil is overly aggressive for real foodstuffs in many instances. The simulants for different foodstuffs may change in light of new knowledge, as is the case for milk which is being changed to 50% ethanol instead of water. In the USA the simulants used are similar, but as always there are slight differences between EU and USA. For further details of the simulants used by the US FDA consult http://www.cfsan.fda.gov/.

One of the main issues with concentration data is how the non-detectable (ND) values are treated. In many instances the substance(s) of interest is non-detectable in either food simulants or real foodstuffs. In a UK FSA survey (2000) for BADGE (bisphenol A diglycidyl ether) in canned foodstuffs, in more than 95% (105 of 111 targeted samples tested) of the foodstuffs tested the levels were non-detectable. Using targeted foodstuffs in any surveillance will always skew any results to a higher level, in that only foodstuffs considered most likely to contain the substance will typically be analysed.

If the migrant species of interest is not present in particular food packaging materials, the foodstuffs consumed in that packaging will have a true zero concentration data set or they can be excluded from any estimate of exposure. However, if it is possible that the migrant species could be present in the packaging of that foodstuff, even if it cannot be detected in the foodstuff, then it is necessary to make allowances for its presence. It is clear that if the value is ND it cannot be assumed that the value is zero and on the other hand, it cannot always be at the limit of detection (LOD). Therefore it is necessary

to try to use more realistic values, of which there are many approaches. Normal or Gaussian distributions between zero and the LOD are often used. In reality this gives a mean value for the ND of half the LOD. Assuming a normal distribution, between 0 and the LOD, will effectively give similar results as a Gaussian one. When it is plausible that the migrant may be present and the migrant is toxic or when levels below the LOD may make a significant contribution to the overall exposure then it is necessary to use a value between zero and the LOD (Kroes *et al*. 2002). The emerging use of probabilistic (stochastic or Monte Carlo random number generation) modelling of exposure to migrants enables the NDs to be handled in a number of different ways, with values between zero and the LOD being statistically generated according to whatever distribution is required.

Improving the detection limit in many cases is one of the most efficient ways to demonstrate lower exposure. For example the exposure to BADGE in canned foodstuffs (food and beverages) was estimated (Oldring *et al*. 2006) using a stochastic model (probabilistic – Monte-Carlo approach) with two different LODs of 0.3 μg/dm^2 and 0.5 μg/dm^2 and the exposure was effectively halved, primarily because many of the foodstuffs consumed were acidic, aqueous or alcoholic where the concentrations of BADGE and its regulated derivatives were non-detectable.

Food surveillance surveys may contain a range of values for the concentration data for a given food or group of foods. Some may be ND whilst others are above the LOQ. For exposure assessments, it is possible to use various approaches to utilise this data, from assuming that the migrant is always present at the highest level recorded or the average level or the mean, etc. Another approach is to fit the actual data to a statistical distribution, for example, normal or lognormal. This enables a more representative value for migrant concentration to be used. An arguably improved treatment would be to use probabilistic modelling to randomly select concentration values in the statistical distribution range, with possibly weighting around the mean, in order to better represent the realistic concentration of the migrant in a food or range of foodstuffs.

Parmar *et al*. (1997) consider that in the absence of statistical tools, fewer than 20 samples is unlikely to give a sufficient range of results even if the contaminant is present in all samples, whereas more than 100 could be considered as being wasteful of resources. Fifty to 100 samples should normally be adequate, but not necessarily if the contaminant is unevenly distributed with the bulk of the samples being ND. The FSA BADGE survey would be one such example of where more than 100 samples were taken, but they were targeted towards those foodstuffs where there was a probability that they contained BADGE, even though the bulk of these were ND.

Food surveillance surveys give concentration values in either μg/kg (ppb) or mg/kg (ppm). However, concentration data derived using simulants normally give results in μg/dm^2 or mg/dm^2, therefore in order to relate these values to concentrations in foodstuffs it is necessary to know the actual surface to

weight (volume) of the packaged foods. In practice this is seldom known and in the EU the factor typically used is 6 dm^2/kg. Data from Bouma *et al.* (2003), Holmes *et al.* (2005) and ILSI (1996) indicate that in practice 6 dm^2/kg is too low by a factor of at least two. However, this under-assumption is compensated by the over-assumption of 1 kg of the foodstuff always being packaged in the same material of 6 dm^2. To compound this dilemma, is the apparent growth in single person consumption.

In many EU member states, there is a growth in the number of people living alone. This impacts their consumption habits. Previously they may have lived with two or more persons and food items purchased would most likely have been such that they could be divided between them, thus the pack size would most likely have been much larger than that for the single person. For example, it could have been common to purchase a 200–500 g piece of cheese to share, with a surface area to volume ratio which could have been in the range ten to one (10 dm^2/kg). In contrast the single person consumer may purchase two slices of cheese weighing 25 g with (say) 2 dm^2 of packaging, which would give a surface to volume ratio of twenty to one. However, the amount consumed is the critical factor and, in all probability, the amount of cheese actually consumed by that individual will not have changed, but the exposure to any migrating species from the packaging could have increased if the amount of migration remained the same and the same packaging material were used.

It is generally recognised that values measured in simulants are normally worst case as the simulant normally extracts more of the substance than the foodstuff. Yet another approach is to use a strong solvent, such as acetonitrile, and extract all of the substance which could potentially migrate. If the estimate of exposure does not give cause for concern then it could be argued that there is no need to conduct simulant studies. An area which still needs resolution is the lag-time for multilayer packaging. Species which could migrate and are not in the food contact layer may over a period of time diffuse through the layers and eventually enter the foodstuff. For products with long shelf lives, this is a possibility. Guidelines are still being developed at the EU Commission level as to how lag times can be simulated.

Another approach to obtain migration data particularly for some plastic materials is the use of modelling. Today this approach is only suitable for certain materials but is accepted by the EU Commission. Diffusion within, and migration from, food contact materials are predictable processes that can be described by mathematical equations. Mass transfer from a plastic material, for instance, into food simulants obeys Fick's laws of diffusion in most cases. Physico-mathematical diffusion models have been established, verified and validated for migration from many plastics into food simulants and are accepted in the USA and in the EU.

Because of the complex, heterogeneous and variable nature of foods, compared to simple food simulating liquids, no general tool for modelling migration into foods is yet available. An EU project with the acronym

'FOODMIGROSURE' (www.foodmigrosure.com) was initiated with the objective to develop a migration model for estimation of mass transfer from food packaging plastics into foodstuffs by extension of the existing model for food simulants to more complex foodstuffs as contact matrices. These models probably represent the only practical way that the complete combination of relevant parameters, including variable food composition, in-pack processing and storage times and temperatures can be encompassed when compiling concentration datasets large enough to accurately describe the foodstuffs as eaten by European consumers. For further details on the use of modelling to predict migration from food contact materials consult Brandsch *et al*. (2002), Reynier *et al*. (2002) and O'Brien and Cooper (2002) (see section 6.9.1).

When concentration data for the chemical(s) of concern are considered it is necessary to relate them to their actual relevance. For example, do we use values at the highest level permitted, highest reported, mean or median or, most importantly, in the foodstuffs consumed? In addition if the consumer purchases one or more pre-packed foodstuffs and then prepares a meal from them how are any potential migrants from the processing considered?

6.5.3 Packaging of foodstuffs containing the migrant(s) of interest

Closely related to concentration data is the type of packaging from which the migrating species can originate. For the purposes of estimating exposure to migrants from food packaging, the focus has to be on the primary packaging. This would be, for example, the packet for a packet of crisps, whereas secondary packaging would be the bag containing the 12 packets of crisps. Whilst some dietary surveys may contain detailed descriptions of food items and who consumed what, very few have information on the packaging of the foodstuffs consumed; for example, in four NDNS (UK) surveys the packaging of some items (e.g. beer canned or beer bottled) is sometimes described, though this is not the norm. The primary focus of dietary surveys to date is, understandably from a nutritional point of view, on what was eaten rather than its packaging. In the case of raw foodstuffs with a thick outer covering, such as bananas or oranges, the packaging is most likely irrelevant, but with raw fish or meat or processed foods knowledge of the packaging is paramount in order to determine the potential exposure to a given migrant.

In order to obtain an estimate of exposure it is necessary to combine data derived from surveys of the food consumption with data derived from surveys of food packaging. Even then there could be issues as the food packaging may be identified as plastic without identifying the plastic. In some instances the packaging may be multilayer, and expert knowledge or analysis would be the only certain methods of determining the food contact layer. This is further compounded by the growth in mixed packages. For example, it is not uncommon in the UK to purchase fresh (raw) meat or fish in a mixed package consisting of an expanded polystyrene tray with a paper bottom insert and a plastic (but which plastic?) film over-wrap. Yet another complication is that

for a definitive packaging description, such as 'a bottle of', the nature of the closure is frequently unknown and, furthermore, unless the bottle is described as glass, PET, PVC, etc. uncertainty still remains despite a valid description from a consumer's viewpoint.

One of the most straightforward approaches with the lack of packaging data is to use the total production of packaging materials for different foodstuffs, with corrections for imports and exports, and divide by the population. This is in essence the per-capita approach which is discussed later (section 6.7) and this was undertaken for canned foods and beverages (Dionisi and Oldring 2002). This has the disadvantage that it will under-estimate exposure due to the non-consumer.

The UK NDNS (National Diet Nutritional Surveys) probably have the most information about the packaging of the foodstuffs consumed by the whole of the population, but it is restricted to UK dietary habits. In one of the most recent food consumption surveys (Duffy *et al*. 2006b), the actual items of food packaging were collected and identified, thereby becoming the first food nutritional survey to determine the packaging of the food consumed, albeit for a limited number of children (*ca*. 600). A project sponsored by the FSA (project A03051) with Newcastle University is nearing completion and packaging of the foodstuffs consumed by children of different ages has been identified wherever possible. European industry is undertaking projects to improve the knowledge of the packaging of the foodstuffs consumed.

Bouma *et al*. (2003) undertook a survey in the Netherlands of the packaging of 606 foodstuffs, mainly retail, and analysed the food contact layer using FTIR, as well as determining the surface area to weight ratio. Polyolefins (polypropylene (27%) and polyethylene (34%)) accounted for the majority of the packaging, with polyvinylchloride, polystyrene, polyethylene terephthalate and paper and board being the next most frequent forms of packaging. However, even knowing that the packaging is derived from a particular polymer may still be inadequate for a more refined exposure assessment. Whilst it is adequate for assessing the exposure to the monomers of the polymer, it will not necessarily help with the additives. For example, different additives may be present in structurally different forms of the polymer, such as low or high density polyethylene, polystyrene or high impact polystyrene, polypropylene or orientated polypropylene. Nonetheless, this is a major improvement to the previous situation. The surface area ratios ranged from 6–95 dm^2/kg; however, the higher values were for herbs, etc. For bakery products, meat, fish, fruit, vegetables, salads, microwaveable meals, nuts and sauces the typical range was from 10–30 dm^2/kg.

The Food Standards Agency commissioned a PIRA International study of packaging materials used for dietary staples. This report refers to data from Mintel Food and drink reports (see below). It also gives a possible stepwise approach to allocate packaging to different staple foodstuffs, which should be considered as an appropriate protocol. Duffy *et al*. (2006a) summarised the situation regarding some of the available sources of information on packaging of foodstuffs.

In 1995, the EU commissioned Maurice Palmer Associates (MPA) to undertake a survey of packaging of foodstuffs across Europe. They primarily focused on the UK and Italy, but the data were not correlated with foodstuff consumption. The data collected from the UK and Italy were extrapolated to the remaining 15 EU Member States, but because many assumptions were necessary, the confidence in the results varied from about 60% for Ireland, Finland and Sweden to a high of 90% for the UK market (ILSI 1996). MPA concluded that the different databases for food packaging materials for 15 EU Member States had a considerable amount of detailed information and probably contained far more detail than would be needed to derive food consumption factors, although the information could if necessary be refined on a country by country market share or packaging type basis. It is believed that this data has not been put to many, if any, uses to date as far as packaging of foodstuffs consumed is concerned.

ILSI (1996) derived some pseudo food consumption factors for the EU based on the MPA data. The food contact area for all packaging was 20.1 dm^2/person/day. As plastics accounted for 62% this equated to 12.4 dm^2/person/day. Whilst at first sight these may be seen as being significantly higher than the EU assumption of 6 dm^2/person/day, if the USFDA assumption of 3 kg/person/day instead of 1 kg/person/day is used there is much better agreement (18 dm^2 vs. 20.1 dm^2/person/day). The use of polyethylene in Benelux and Ireland is about 9–10.4 dm^2/person/day compared to 4–4.6 dm^2/person/day for Spain, Portugal and Greece. This illustrates the difficulty of attempting pan-European treatments for exposure to migrants from food contact materials. PVC, PS/ABS were <1 dm^2/person/day, with France having the highest usage. These results seem to tie in with the Bouma *et al*. study.

There are databases that contain amongst other data some information on packaging of foodstuffs, ranging from crude (e.g. box) to more specific (polypropylene), but they are not ideally suited to estimating exposure to migrants. They may provide supplementary information which could be of use when other sources of the migrant needs to be considered. Examples are the Dutch Grootverbuik Product Informatie database (www.gpi.nl) which covers foodstuffs supplied to the catering, hospital and restaurant industries. Whilst the Dutch EAN DAS (www.eandas.nl) contains information on packaging of fast moving consumer goods (FMCG), only 35% are food products. Other sources of food packaging information are commercial food and consumer databases that monitor trends in the consumer product market. The Mintel Global New Products Database (www.gnpd.com) monitors worldwide consumer packaged goods markets and covers the food, beverage and non-food sectors. The Innova Food and beverage database also collects information on ingredients, packaging and formulation of foods and beverages (www.innova-food.com).

Again, the level of packaging information in these databases ranges from crude to more specific. The German Association for Packaging Market Research (GVM) collate data on the packaging types used for foods at the retail rather

than consumer level. The Fraunhoefer Institute undertook a survey of packaging of foodstuffs for a single supermarket chain based in Munich. Market power and Euromonitor, for example, collate packaging information across some or many of the EU Member States, although this is not their primary purpose. Overall these databases are a useful source of general packaging information. However, information is not routinely recorded on the actual food contact layer used for the food, the polymer type if the packaging is plastic or if the packaging is a multilayer. It is this level of detail that is needed to refine exposure assessments to chemical migrants from packaging materials. Also, these databases were not created to directly link with food consumption data and therefore give an overview only of the types of packaging used for foods available on the market but not the packaging used for foods that are actually purchased and consumed. In the absence of any other data they are an invaluable source of information in order that more realistic estimates of exposure can be made.

6.6 Obtaining food consumption data

6.6.1 Overview of dietary surveys

In order to obtain estimates of exposure, it is necessary to obtain information about the different foodstuffs consumed, preferably with details about their packaging. However, data with this extent of detail hardly exist, thus the first step must be to obtain data about the consumption of different foodstuffs. Some consumption surveys are focused on individual consumers, whilst others are directed towards household purchases and others to the whole of the population. Today there are three broad categories for sources of data for food consumption, covering the food supply chain, households and individuals, namely:

- food balance sheets (FBS), which outline food availability and the market supply situation
- household budget surveys (HBS) which record the food brought (but not consumed) into the household
- food consumption or dietary surveys which try to capture the foodstuffs consumed by an individual during a specified period. Some workers (e.g. Kroes *et al*. 2002) further divide this into duplicate diets and individual consumption surveys.

Food balance sheets, whilst being regularly updated, primarily consider raw food commodities and do not reflect the packaging of the foodstuffs consumed. However, they are useful in indicating trends that can be used in any exposure assessment.

Some countries undertake shopping basket or household budget surveys (HBS), which involve simply recording the contents of a shopping basket for a known family size. However this has many shortcomings. Consider a

family of two adults and two children (under 12 years old). If the shopping basket contained amongst other items eight soft drinks and eight beers, then it is unlikely (hopefully!) that the consumption would be two soft drinks and two beers per person. This is of concern, as the consumption calculated from the basket would not represent the actual consumption by each individual. Furthermore, the packaging type is not recorded, but there are a few surveys of packaging of foodstuffs in retail outlets (Bouma *et al*, 2003), which could be used to give an indication of the most likely packaging or at least its market share. In a household budget survey, if no allowance is made for waste food, compared to that actually consumed, then this will increase any estimates of exposure. Normally foodstuffs not consumed at home are not recorded, resulting in a potential underestimate of exposure. Household budget surveys are normally repeated every 3–10 years and are normally of lower cost than surveys of the dietary habits of individuals, thus most countries conduct household surveys, but only for nutritional purposes. Even though the structures of household budget surveys vary significantly from country to country, these surveys could be used to compare and differentiate between population intakes in different countries across the EU at a relatively high level.

There are a number of different approaches for determining the foodstuff consumption of individuals which can be broadly sub-divided into record keeping or recalling the food items consumed. An advantage of surveys of individuals is that additional data about the individuals, such as age, actual body weight, gender, socioeconomic status, ethnicity, etc., can be used in combination with their dietary habits and this enables a more complete picture of exposure to be obtained, particularly when sub-groups of the population could be of special interest. Any survey cannot feasibly survey every person in the population, thus, it must be representative of the whole of the population under consideration. The methodology for ensuring that surveys are representative is outside the scope of this chapter.

In recording methods, an individual records in a diary all the items consumed and typically the amounts consumed over a period of time, which normally is in the range of one to seven days. The weight of non-consumed food on the plate should be deducted from the original weight on the plate, in order to allow for wastage. Ideally foodstuffs consumed outside the home should also be included. In the case of homemade recipes, such as cakes or meat pie, either their ingredients and weights should be recorded or, as in the UK and Ireland (and some other European countries), standard recipe databases could be used to assess the consumption of the individual items. The SCOOP report mentions different recipe approaches.

In recall approaches a trained interviewer asks individuals what they ate in the immediate past, typically the preceding 24 or 48 hours. The interview can be face to face or over a telephone. A major disadvantage is that it relies on the memory of the interviewees. If the interview is over the telephone, it also relies on details of the individuals, such as body weight, being accurately

reported. A refinement of the recall method is the dietary history where the interviewee is asked to recall their eating habits over a longer period of time.

Food frequency questionnaires determine the frequency with which certain foodstuffs are consumed over a given period. Thus it is necessary to pre-define the foodstuffs of interest and these may be targeted to a nutrient(s) or food(s) of specific interest. They are rarely conducted for specific contaminants arising from the packaging of the foodstuffs consumed. It is possible (Parmar *et al*. 1997) to combine the food frequency questionnaire with portion sizes (MAFF for example) in order to obtain an estimate of food intake, particularly where consumption data are limited.

For surveys of individuals a consideration is the duration of any survey. It is clear that it is impractical to undertake surveys for the lifetime of individuals. The period of any survey does not reflect eating habits over the whole of the lifetime of an individual and certainly not the population, with the longest individual surveys typically being of one week's duration. Some surveys re-visit the consumer over the course of a year, which gives a better indication of longer-term consumption, but all surveys over or under-estimate the consumption of particular items for any individual over their lifetime. However, it is necessary to consider how a one-day survey relates to that for the consumption for one week or one month, let alone one year or a lifetime. It is clearly impracticable to use a single meal survey, whilst a one-day survey is recognised to represent an acute intake (Kroes *et al*. 2002). They also recognise the need to consider other scenarios; habitual intake corresponding with the usual intake of individuals during a particular stage of their life, needing corrections for within individual subject variations; high intake as a sub-category of habitual intake, such as binge drinking; lifetime intake corresponding with integration of habitual intake values.

It is the normal dietary intake which is needed and short-term studies can give only a snapshot of exposure during that time frame. It may be necessary to correct the short-term studies; consult Kroes *et al*. (2002) for further details. The longer the period of the study (and the better the method of recording items consumed) the more reliable the results because they reflect longer-term eating habits. In the SCOOP report it is recognised that as the number of days for a survey increase, the percentage of consumers for a particular foodstuff increases, as will the non-consuming days for consumers. Therefore the reported intakes for consumers will decrease over time of the survey.

There are additional factors which must be considered when the packaging of the foodstuffs has to be taken into account. There is no denying that a short-term dietary survey being used to assess exposure from migrants from the packaging of the foodstuffs consumed cannot represent the longer-term picture for at least two reasons, firstly the packaging of a foodstuff in many instances will (almost certainly) change over the lifetime of the consumer; for example, the growth in PET for beverages has been enormous and will impact any exposure assessment. The FDA recognise this and have adjusted

their food packaging factors for PET accordingly. Secondly, an important consideration is that the eating habits of the consumer will almost certainly change over their particular lifetime. As an example, wine in the 1960s was not consumed in large quantities in the UK, whilst today UK consumers are one of the largest wine consumers in the EU.

A major weakness of a short-term (24 hour survey) is that it may depend upon the day of the week, when the survey was conducted. For example, in some European countries the diet on a Friday would consist of more fish than any other day and consequently this would impact on the packaging and the potential migrants present. Another issue is the season of the year and when the consumption surveys were conducted. Seasonal foods, particularly in Southern Europe, may have very large differences in consumption and out of season only the preserved or frozen seasonal foods may be consumed in contrast to the fresh ones, which may have been consumed in season. This will impact the packaging of the foodstuff significantly.

Under and over-reporting are potential sources of errors and there are different approaches to make allowances for these phenomena. However, in the case of estimating exposure to migrants from food packaging it is considered that the sources of error from uncertainty about the packaging of many of the foodstuffs consumed far outweigh any errors due to under or over-reporting. Other types of approaches for obtaining data on dietary habits include total diets, which can be derived using different approaches. Data from the above sources can be used to construct model diets for either the 'average consumer' or a group of consumers who are considered as high risk for whatever reason. Duplicate diets are used where the amount and type of food consumed is duplicated – with an equivalent portion of the food item being placed in a bucket for example – or replicated – purchasing the same items from the same stores. In addition to giving information about the dietary consumption they can also give the concentration of the migrant in the foodstuffs consumed, which is in essence an exposure assessment. The USFDA use model diets and prepare annually meals based on these diets in order to analyse for contaminants. However, there are some disadvantages of duplicate diets. The analysis of a complex mixture of foodstuffs for relatively low levels of contaminants is difficult due to interference, therefore it is time consuming and costly. If the contaminant of interest occurs only in certain foodstuffs, then its level in the mixture of food would be diluted, thereby demanding greater sensitivity in analysis to avoid the conclusion that it is non-detectable. In some countries the portion size is published by the authorities, such as MAFF (food portion sizes), whereby the amount consumed can be estimated from the portion size and the contents of a household budget survey.

6.6.2 Comparability of consumption data across Europe

The relevance of consumption data for different countries is always a

consideration when an exposure assessment is being undertaken, unless it is for a single country where all of the consumption and concentration data were obtained in that country. In many instances it is necessary to cross-correlate data and the dietary habits of different countries need to be considered. There is no single pan-European survey of foodstuff consumption, therefore different sources of data need to be considered.

The GEMS (WHO Global Environmental Monitoring programme) approach divides the World into different regional diets. The EU is divided into four groups, of which the diets of the individuals in the countries of that group are considered to be similar enough to warrant the same treatment for the purposes of foodstuffs consumed. The foodstuffs considered are primarily for nutritional purposes, particularly for staple foodstuffs, but illustrate similarities and differences between groups of countries. Examples of the 15 food groups are cereals, vegetables, nuts and oilseed, fish and seafood, fruit, milk and milk products, meat and offals, animal oils and fats. The groups for the European countries are:

- Group B: Cyprus, Greece, Italy, Portugal, Spain
- Group D: Bulgaria, Romania
- Group E: Austria, Belgium, Czech Republic, Denmark, France, Germany, Hungary, Ireland, Malta, Netherlands, Poland, Slovakia, Slovenia, United Kingdom, Luxembourg
- Group F: Estonia, Finland, Latvia, Norway, Sweden, Lithuania.

Even the usefulness of this grouping of countries with similar diets has been questioned by some in the WHO (Moy 2005). Whilst it represents the staple diets for nutritional purposes, it certainly does not reflect the types of packaging for the same foodstuff. Intuitively, whilst UK and France are in the same group, from experience it is clear that the French tend to purchase the same foodstuff differently, for example, vegetables or meat tend to be purchased fresh rather than processed, which has an important effect on the contamination of migrants from its packaging. In other words, whilst French, Greek and UK consumers may actually eat 100 g of chicken, there is a high probability that the packaging of the chicken is totally different, even though for some nutritional purposes the foodstuffs consumed are considered equivalent.

Questions arise about the compatibility of food consumption surveys across Europe. There are a number of pan-European dietary studies, such as DAFNE (European union DAta Food NEtworking (Trichopolou and Lagiou 1997)), CALEUR (van de Vijver *et al*. 1999), TRANSFAIR (Hulshof *et al*. 1999), all of varying quality (Kroes *et al*. 2002) for providing comparative dietary intakes across countries. The DAFNE project is targeted towards creating a European food data bank based upon household budget surveys. The European food consumption survey (EFCOSUM) aims to define a method for monitoring food consumption in nationally representative samples of all age–sex categories in Europe in order to provide internationally comparable data.

Lowik *et al*. (1998) studied the consumption factors for eight European countries and reviewed available intake data, as well as its relationship to lifetime intakes and variability between individuals. One of the major issues is that different countries have different food coding systems. As an example, the SCOOP report summarises some of the food consumption databases where the number of individual codes for a number of European countries (14) ranges from 43 to 30,000 depending on country. Even with one category, for example the general classification fine bakery ware, the number of individual food codes for this sub-group ranges from two to 1312 depending on country. Efforts have been made to develop more pan-European coding systems. The CIIA (Confédération industrie international agroalimentaire) have classifications for different foodstuffs, but the usefulness of their classification for exposure assessments has been questioned (SCOOP), partly because the CIAA categories and sub-categories refer to foods as marketed or as ingredients in food processing, whilst the food codes in dietary intake databases refer to foods as consumed. Other potential issues on the food coding systems are also raised in this report.

Attempts have been made at unifying the different food codes used across Europe. A 33 Euro food group (EFG) classification has been proposed (EFCOSUM) into which the different categories used in Europe would approximately fit, using least common denominators. Many countries have different protocols for collecting consumption data, although there are recommendations as to what should be done (e.g. Kroes *et al*. 2002). This situation is further compounded by none of the systems being primarily constructed for the packaging of the foodstuffs consumed.

Kroes *et al*. (2002) concluded that the variation in comparable indices, such as the 95th percentile across countries is less than the variation within a particular country. This was also the conclusion of Lowick *et al*. (1998). Thus the relatively large within country variations mean that complete coverage of the EU Member States for the high consumer is unwarranted. Lowick *et al*. (1998) also concluded that levels of consumption above the 95th or 97.5th percentile are more likely outliers, which would not be maintained over long periods of time. Therefore maximum levels were not considered representative of a high level for chronic intake.

6.7 Estimating exposure to migrants from food contact articles

6.7.1 Introduction

The percentile of the population to consider and any at risk or vulnerable groups in an exposure assessment was discussed in section 6.3. Today there is no universally recognised single approach to estimating exposure, particularly to migrants from food packaging. ILSI (2002) undertook a workshop focused on determining exposure to migrants from food contact materials, but a

standardised approach or methodology was never agreed; however, the need for more data was identified. Exposure assessments can be determined in a number of ways which can be summarised as:

- Simplistic (or simplified/straightforward), normally using a worst-case assumption, as is the case in the EU today with the 6 dm^2/kg food/person/day. This approach is a subset of a deterministic approach.
- Deterministic, where a fixed value of consumption (normally of a given foodstuff or family of foodstuffs) normally at the high end is combined with a high or most likely the highest level of migration found.
- Probabilistic, where statistical modelling is used to predict those values related to the unknown inputs required in order that a more refined estimate of exposure may be obtained.

Today for risk assessment in the EU it is assumed that each, and every, person eats 1 kg of food, packaged in the same material, every day of their life. Furthermore, it is assumed that the surface area to volume ratio of this package is 6 dm^2/kg. In the allocation of migration limits for a substance, it is assumed that the substance always migrates at the highest level, corresponding to its TDI, for all packaging and all foodstuffs, therefore migration at 1 mg/kg equals exposure at 1 mg/person/day. This has the advantage that exposure to a substance for any migrant is independent of its packaging, with a few exceptions. This is unlike the US FDA, where the use of a substance can be restricted to a particular application, including type of package or foodstuff. The major disadvantage is that in most cases, different types of packaging contain different substances and their migration behaviour frequently depends upon the foodstuff and its processing in the package. Consequently, the current EU approach arguably over-estimates exposure to migrants and therefore applies stricter restrictions, which do not necessarily improve consumer safety but could restrict consumer choice. There are some counter-arguments that this approach under-estimates the exposure for infants, but this is currently the subject of debate (Castle 2004) and in reality there are a number of projects being undertaken or in the process of being reported which may clarify this situation.

Whilst most people recognise the shortcomings of the current EU approach for food contact materials, there is no simple solution, as the data required with the necessary detailed information do not exist. EU Member states have nutritional surveys of varying quality. Their prime purpose is to enable authorities, etc., to determine the 'nutritional health' of their population. For example, the amount of salmon, vegetables, fruit, salt or sugar consumed is, quite rightly, considered more important for the surveys than the packaging of the foodstuffs consumed. In some cases, such as exposure to heavy metals in tuna or dioxins in salmon, then this is an invaluable first step in assessing the exposure. Should the resulting value give cause for concern then there is a need to refine the assessment by obtaining more details about the foodstuff items containing the substance of concern consumed.

The deterministic approach is better suited to food additives or contaminants and not migrants from food packaging, provided there are adequate data on the foodstuffs consumed. In these cases the types of food which could contain the additive are known from the food item description, as well as the amount consumed. The concentration of a food additive in the foodstuff is either predetermined or can be measured. Taking a high consumption (97.5 percentile) of the foodstuffs containing relatively high levels of the additive and using a relatively high concentration value will enable an exposure assessment to be made. If the exposure is below the TDI, then there is no cause for concern and no further efforts should be devoted to improving the estimate of exposure. However, it is necessary to consider the relevance of taking high concentration values with high consumption and in some cases only one of the two input parameters would be at the high levels with the other at a lower level (possibly the average level). The deterministic approach is also of value for groups of concern where model diets or actual consumption data exist. The simplistic approach described above could be considered as a simplified deterministic one.

Using data from food frequency questionnaires and portion sizes in combination with a concentration value would give a deterministic estimate of exposure (Parmar *et al*. 1997), particularly if the contaminant could occur in more than one type of foodstuff. If average or maximum concentration data are used, then an estimate of exposure can be obtained. This approach would also cover rarely consumed foodstuffs where the migrant was specific to these. If the contamination is only in one foodstuff or one source of foodstuff is known to be the major contributor to the intake, then it is possible to use a single point estimate using a single average or maximum concentration data value. A more realistic approach would be to use a distribution of concentration data. Probabilistic modelling is ideally suited where there are data gaps, allowing confidence limits to be put on any exposure estimate. This approach is considered later.

Estimates of exposure need to be in units which are meaningful. Many toxicologists use mg/kg body weight/day to assess risk. The body weight can be that recorded in surveys or the EU assumption of 60 kg body weight per person. The use of μg/person/day enables one to determine if a threshold has been exceeded. Another expression for exposure is mg/kgdiet. All assumptions made should be clearly stated and all sources of data used indicated. An estimate of the likely error bounds for any estimate is important, as is a statement as to who is being 'protected' by the estimate.

6.7.2 Approaches to determining exposure to migrants from packaging of foodstuffs

There are a number of different approaches (Rees and Tennant 1993, Parmar *et al*. 1997, Kroes *et al*. 2002) which can be used in order to obtain estimates of consumption of different foodstuffs and any exposure to chemical

contaminants in the foodstuffs. In essence they fall into three categories (Rees and Tennant 1994) which are:

- per capita
- model diets or worst case scenarios
- surveillance methods or duplicate diets.

Per capita estimates of food chemical intake can be made for virtually every European country. They permit comparison between different European countries. There are in essence two basic approaches for undertaking this estimate: multiply the average food consumption of the whole population by anticipated or actual levels of the migrant; divide the total available food chemical by the number of individuals in the population. Obviously this approach is unsuitable for migrants, but ideally suited for food additives.

An advantage of the per capita approach is that it is cost effective and relatively straightforward. If the estimated levels of exposure are significantly lower than those which could cause concern, then arguably further refinement of the estimate of exposure is unjustified. Wherever possible per capita data should not be averaged, but a range retained in any subsequent calculations. The better the manufacturing data and demographic data the 'better' and more reliable the per-capita estimate.

The total diet method, which can be used for food intake studies, utilises data on food purchases based on household budget surveys. They can give the average consumption of different foodstuffs, normally grouped. It is possible for these foodstuffs to be purchased and analysed. This enables the food groups which contribute the major sources of exposure for a given migrant to be identified. If the migrant is restricted to one type of packaging, then it is necessary to select those foods packaged in that packaging. This does not facilitate estimating exposure for individual consumers as the household budget surveys are frequently for families which may or may not be consumers of all items.

Another approach is the model diet where, based on consumer statistics, a diet is proposed that models that of the average or possibly (with adequate data) the non-average consumer. This is of value when limited consumption data exist or when the major source of contamination is one food group. This approach can be considered to be cost effective for a deterministic approach but is subject to errors when many foodstuffs are involved. If the groups for the model diets are based upon 'good' and 'appropriate' data then it may be possible to use model diets for different age groups or 'at risk' groups.

It is also possible to model different scenarios as shown in Table 6.2 (Rees and Tennant 1994) where extreme and reasonable scenarios are used. If the worst-case scenario does not give cause for concern then there is no need to refine any exposure estimate. For example, assume that for a given migrant, migration is at the SML and that all the foodstuffs which could be packaged in the material are packaged in that material. This can be considered as a useful screening technique because if the exposure estimate does not give

Table 6.2 Matrix of intake estimates using the 'scenario' approach (Rees and Tennant 1994) and Rees, N., private communication (1998)

		Food consumption	
		Typical (per capita or average)	Worst case (above average or high level)
Occurrence of migrant in foodstuffs	Typical (mean or most common value)	Likely. The exposure calculated is likely in the majority of consumers, particularly if averaged over a year	Possible. Fewer consumers are likely to have exposure of this level, but may require consideration if the dietary pattern is habitual
	Worst case (maximum value or high percentile)	Possible. Fewer consumers are likely to have exposure at this level but may require consideration if there is a good chance of selecting high migrant levels on a regular basis	Unlikely. Whilst this may be possible, there should be an assessment of whether it is probable on a regular basis and what the toxicological implications may be

cause for concern, then there is no need for further refinement. This approach is useful if there are limited data or a sudden 'unexpected' issue occurs where no data exists. These estimates by definition are imprecise.

An approach to provide data with reduced uncertainty limits is the purpose of surveillance surveys. Simulants are used for relating concentrations in real foodstuffs, whereas a surveillance survey actually measures the concentration, thus there is no doubt about the relevance of simulant derived data to what it would be in the foodstuff the simulant is simulating. However, it is still necessary to allocate migration concentration values to those foodstuffs which were not part of the survey. This can be achieved by either assuming certain foodstuffs are similar in migration characteristics to those which have been tested in the survey or by using stimulant migration data. Surveillance surveys enable those foodstuffs which are most at risk from contamination to be identified, consequently these surveys are frequently 'targeted' and if due consideration for this is not made then any data could be skewed to a higher concentration level and hence an unrealistically high exposure assessment. However, surveillance surveys need to be run in conjunction with consumption surveys to maximise the accuracy of the estimates.

One of the most sophisticated approaches is the duplicate diet method where for every item consumed an identical amount of the item is put aside for analysis at a later date. This approach enables all sources of the substance of interest to be included and gives a realistic and arguably the most accurate way of obtaining an exposure assessment. This is a good way of examining at-risk groups, but it is expensive. The interpretation of the data beyond the

survey period is difficult (Kroes *et al*. 2002). In the case of migrants from packaging, not only is it necessary to ensure that the foodstuffs consumed were representative, but it is necessary to know if the packaging of the foodstuffs consumed during the survey period was typical for each consumer.

6.7.3 The USFDA approach to estimating consumer exposure to migrants from food contact materials

The USFDA approach to assessing exposure to migrants from FCMs is explained in CFSAN/Office of Food Additive Safety, April 2002 and is available on their web site (http://www.cfsan.fda.gov/). It describes the use of exposure estimates for use in food contact notifications (FCNs) which would normally be based upon simulant rather than food migration data, as is the case for new materials. The USFDA approach is described in more detail in Chapter 2. In the USFDA approach a consumption factor is combined with a food distribution factor and concentration data to derive an estimate of exposure from all food types and all FCMs containing the substance of interest.

The consumption factor (CF) describes the fraction of the daily diet expected to contact specific packaging materials and represents the ratio of the weight of all food contacting a specific packaging material to the weight of all food packaged. To account for the variable nature of food contacting each food-contact article, the FDA has calculated food-type distribution factors (f_T) for each packaging material to reflect the fraction of all food contacting each material that is aqueous, acidic, alcoholic and fatty. Tables for both factors are supplied by the USFDA. This is then combined with concentration data to obtain an exposure estimate, assuming a daily consumption of food and drink of 3 kg per person per day. This gives an estimated daily intake (EDI) for a substance per source of packaging. If there is more than one source the EDIs are combined to give a cumulative estimated daily intake (CEDI).

The concentration of the substance in the food contacting the food-contact article, <M>, is derived by multiplying the appropriate f_T values by the migration values, M_i, for simulants representing the four food types. This, in effect, scales the migration value from each simulant according to the actual fraction of food of each type that will contact the food-contact article.

$$<M> = f_{\text{aqueous and acidic}}(M_{10\% \text{ ethanol}}) + f_{\text{alcohol}}\,(M_{50\% \text{ ethanol}}) + f_{\text{fatty}}(M_{\text{fatty}}) \quad 6.2$$

where M_{fatty} refers to migration into a food oil or other appropriate fatty-food simulant. The concentration of the substance in the diet is then obtained by multiplying <M> by CF. The EDI is then determined by multiplying the dietary concentration by the total weight of food consumed by an individual per day, assuming that an individual consumes 3 kg of food (solid and liquid) per day.

$$EDI = 3 \text{ kg food/person/day} \times \langle M \rangle \times CF \quad 6.3$$

A concentration in the daily diet of 1 ppm corresponds to an EDI of 3 mg substance/person/day. This approach is designed to deal with single use (e.g. food packaging) rather than repeated use (e.g. non-stick frying pan) FCMs.

6.7.4 Probabilistic (stochastic) modelling

This section explains the background to the use of probabilistic, also known as stochastic, modelling for estimating exposure to migrants from the packaging of foodstuffs. Not all exposure assessments need the refined approach of probabilistic modelling. However, it is a tool gaining greater acceptance for assessing exposure where there are data gaps. Probabilistic modelling has been used by Lambe *et al*. (2002) to assess the intakes of flavours. Petersen (2000) compared theoretical and practical aspects of probabilistic modelling.

Probabilistic modelling overcomes the lack of data by estimating the most likely exposure to a given migrant(s), using input data with uncertainties but also deriving confidence limits for any assessment. The treatment of data with uncertainties is one of the strengths of probabilistic modelling. Probabilistic models can deal with data rich and data poor inputs. Another factor to consider is variability and whether it should be separated from uncertainty. This gives rise to one- or two-dimensional probabilistic models, with the one-dimensional model combining uncertainty and variability and the two-dimensional model propagating them separately (Hart A., private communication). The theory of probabilistic modelling is outside the scope of this chapter.

Probabilistic modelling uses the principles of statistics and in essence is based upon the Monte Carlo approach. It repeatedly (typically > 1000 iterations) calculates the exposure to obtain an estimate of the mean and the uncertainty for any given percentile using different input parameters, some of which are randomly generated. Where there is uncertainty about the actual value of a parameter, lower and upper limits can be set, with a most likely value. The statistical model randomly generates values between the lower and upper limits for each iteration, with the majority of the values being distributed about the most likely value, using whatever distribution between minimum and maximum centred around the most likely is considered appropriate. This means that values near to the most likely one are used more times in the total number of iterations than those values towards the lower and higher limits. A more detailed description of such a model is given in Holmes *et al*. (2005) It is recognised that a number of groups are working in this area including, for example CSL, Crème and Rikilt. It should be borne in mind that there are only a few mathematical/statistical models. The differences in use are in how the data are input and the results obtained.

In order to estimate exposure to migrants from food packaging materials,

the data required are similar to those for any other method of exposure assessment, namely:

1. consumption of foodstuffs
2. packaging of foodstuffs consumed
3. concentration data of migrant(s) in foodstuffs consumed.

Clearly not all of these data are readily available and, in most cases, very limited data exist. Thus it is necessary to make assumptions, but in doing so the impact of the assumptions on the estimate needs to be evaluated. Probabilistic modelling facilitates this requirement.

Inputs can be considered as being either fixed or variable being varied between upper and lower limits, depending upon the accuracy, amount and availability of the required input data. Where some input data have considerably greater uncertainty or variability than others, then it is questionable if the amount of effort and treatment required for the less uncertain or less variable parameters is justified. The case of migrants originating from packaging is a good example. Today, for most cases, significantly less is known about the packaging of all the foodstuffs consumed than the types and amounts of foodstuff consumed, thus uncertainty arising from the accuracy of the amount of foodstuff consumed could be considered insignificant compared to what it was packaged in. Possible treatments for a few of the more important variable input parameters will be considered here as examples of how the uncertainty in input data was treated using as an example the CSL model (Holmes *et al*. 2005).

In the UK NDNS surveys, in some instances, the food item description described the packaging. Examples are 'canned' or 'not canned' or 'bottled'. In these cases it is possible to associate the likely concentration of the migrant(s) with the foodstuffs consumed, being either definitely present or absent. In other cases, where the packaging of the foodstuff was unclear, it is necessary to use 'expert judgement' or market share to allocate the most likely packaging to the food item description and the most likely concentration of migrant in that food item. Being undefined, there is some uncertainty about the value to be used. Thus a lower and upper limit are allocated, and for each iteration of the Monte Carlo model a different value for the packaging, between lower and upper limits, is selected, with the majority being around the most likely value using a triangular distribution.

Obtaining concentration data was considered earlier (section 6.5). In the case of the UK NDNS food surveys, the description of some food items consumed are a home-made meal rather than a pre-packaged one, without a breakdown of the amount of each ingredient. Having identified those items which could be in the packaging(s) of interest, it is then necessary to apply a correction factor because if only part of the food item contains the migrant, then the concentration data need to be adjusted accordingly. For example, if a food item description consists of three food components and 100 g of the food item consumed and the migrant is present in only one of the three food

components, then the 100 g of food item consumed does not contain 100 g of the food containing that migrant. Therefore it is necessary to reduce the concentration of the migrant in that weight of foodstuff consumed by the use of a factor. Values can be varied between lowest estimate of its content in the meal, most likely and highest with a different value being used for each iteration, with the majority of the values being around the most likely.

Yet another use of this factor could be to correct for subsequent dilution of a packaged item to one that is consumed. As an example 10 g of powdered soup may give 100 g of soup reported as being consumed. Another example is that 2 g of milk may be in 100 g of a cup of coffee reported as being consumed. Expressing the concentration data in a weight per unit area enables a surface volume to weight ratio to be applied rather than the conventional factor of 6 dm^2/kg. In most cases, if not all, the actual surface to volume ratio is unknown. Therefore it is necessary to allocate appropriate ranges, with again a different value between minimum, most likely and maximum being used per iteration.

It should be possible to derive a cumulative exposure curve for the whole of the population and, ideally, for consumers only. It is desirable to obtain estimates of exposure for any selected sub-set of the population, to ensure adequate protection of vulnerable groups. Depending upon the quality of the food consumption survey and associated data this may or may not be easy to achieve. If non-consumers are included in an exposure estimate, as is the case in typical per-capita estimates, then the estimate of exposure will be below the actual exposure and the amount of under-estimating will depend upon the ratio of non-consumers to consumers.

Having obtained a value it is necessary to determine the confidence limits (error bounds) for this estimate. In this way, the impact of any uncertainty surrounding the initial assumptions used can be evaluated. A representation of a mean value for the population and 95% confidence limits for any given percentile is shown in Fig. 6.2. As can be seen, the difference between the upper and lower values of an exposure estimate for a given percentile increases the nearer the selected percentile is to 100%.

From a probabilistic approach it should be possible to derive the exposure for any age group or any percentile, as shown for example in Fig. 6.3. In Fig. 6.3, upper and lower limits are represented by the line either side of the mean estimate represented by the diamond. In addition the effect of gender, socio-economic class, ethnicity, etc., can be evaluated, provided they have been identified in the food intake survey, although as the group studied becomes smaller greater uncertainties inevitably arise. Exposure can be expressed as mg/kg actual body weight or mg/person/day or mg/kg diet.

It is also of value to identify the main contributors to any estimate of exposure in order that any parameters driving the estimate can be investigated further, as illustrated in Fig. 6.4 (Holmes *et al*. 2005). In some cases major contributors to exposure may be due to high concentrations of the migrants in the foodstuffs, but in others it may be that even though the concentration

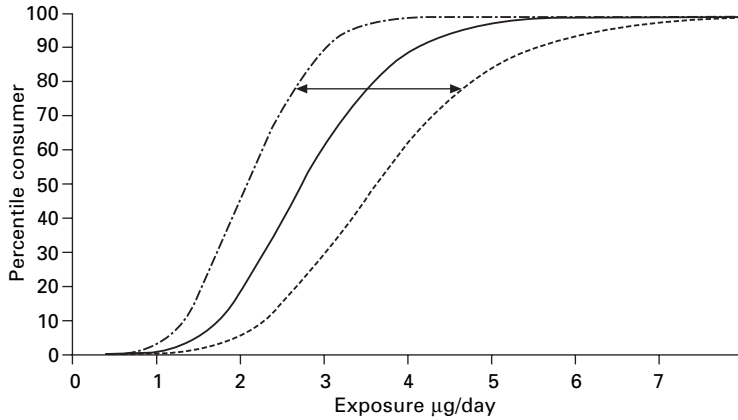

Fig. 6.2 Mean estimate for any given percentile, with upper and lower confidence limits.

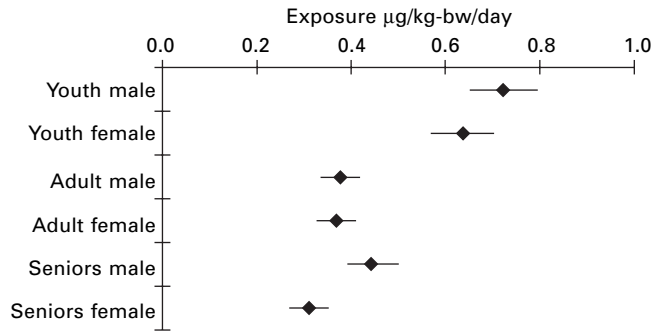

Fig. 6.3 97.5th percentile exposure estimate (with a 95% confidence range) for the three age groups for BADGE using the Food Standards Agency, Food Surveillance Information Sheet 9, November 2000. Median dietary exposure estimate 0.04 µg/kg bw/day (0.03–0.053 µg/kg bw/day) (Holmes *et al*. 2005).

data are low, the foodstuffs are consumed in much greater quantities than others. In some cases identifying the foodstuffs which contribute the major part of the exposure may help mitigate the exposure by, for example that particular packaging being substituted. In other cases, revisiting the model may enable the estimate of exposure to be reduced by refining some of the assumptions used. For example, reducing the LOD for BADGE in beverages substantially reduced the estimated exposure, because the actual levels were still below the reduced LOD. On the other hand, canned meat which had measurable levels of BADGE had only a minor contribution to the exposure due to the relatively low consumption of canned meat. Consult Holmes *et al*. (2005) and Oldring *et al*. (2006) for further information.

Knowledge of the impact of the major sources of uncertainty in input data on the estimate of exposure is essential. Correlation coefficients and scatter

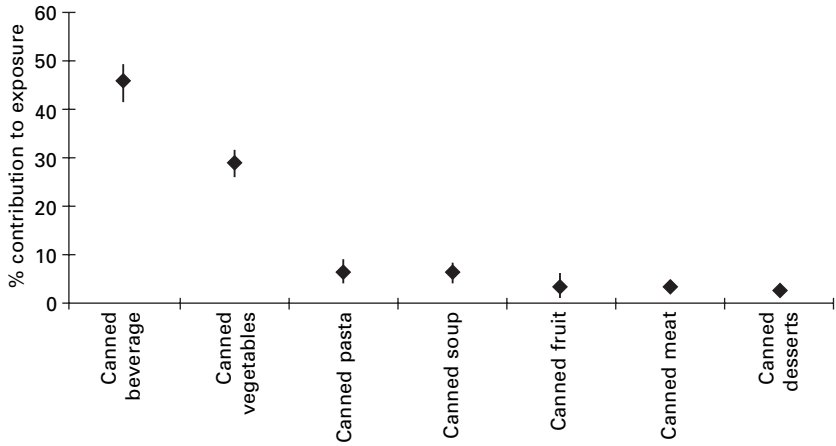

Fig. 6.4 The % contribution of major food groups (with 95% confidence range) toward the overall exposure for a high level basket set up for BADGE using the Food Standards Agency, Food Surveillance Information Sheet 9, November 2000. The data shown is for all age categories and indicates the effect of the uncertainties in the model run (Holmes *et al*. 2005, Oldring *et al*. 2006).

graphs can be used to identify key sources of uncertainty affecting the exposure estimates. The correlation coefficients and graphs can be calculated for each of the uncertain variables against the mean exposures to determine which are the key sources of the uncertainty. Figure 6.5 shows a simplified scatter plot for the mean exposure (μg/kg bw/day) against the mean of the beverage concentration distribution (ND) used to model the level of BADGE in canned beverages. In this case the Pearson correlation coefficient was 0.609. This approach identifies where the risk assessor should concentrate in order to obtain more data to reduce the uncertainty if the estimated exposures are close to levels of concern or to address the data gaps in order to obtain a more realistic assessment of exposure. This is in contrast when the uncertainty in the concentration data for canned fish in oil is considered. As can be seen from Fig. 6.6, there is no correlation between the uncertainty in the concentration values used and the resulting exposure.

Correlation coefficients and scatter graphs of the exposure against consumption of different groups of foodstuffs may also be analysed and these show the correlation between exposure and the variability within the system. Figure 6.7 shows an example of a scatter plot between the consumption in grams of canned beverages and the average exposure for the BADGE model. This plot indicates how the increasing consumption of certain items is correlated with exposure. By combining the approach of the uncertainties in the concentration data and the effect of the amount consumed on exposure (Figs 6.5 and 6.7) it was possible to determine that the ND value for BADGE in beverages was driving any exposure estimate for BADGE, using the input values for ND.

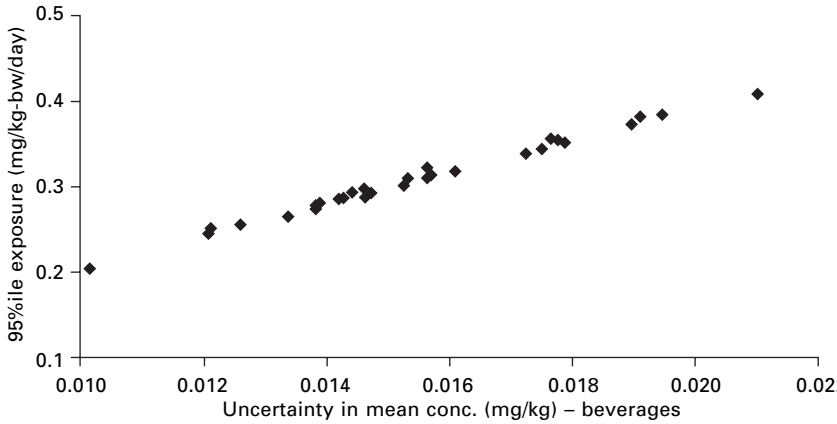

Fig. 6.5 Simplified scatter plot between the average exposure of BADGE with the sampled values used for the mean of the beverage concentration distribution (Holmes *et al*. 2005).

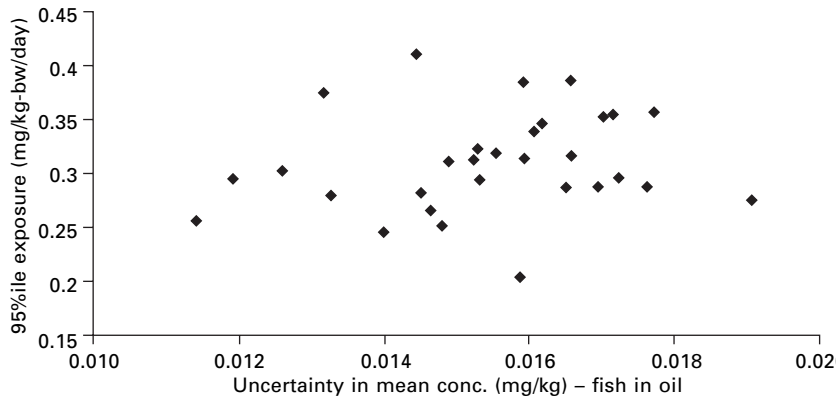

Fig. 6.6 Simplified scatter plot between the average exposure of BADGE with the sampled values used for the mean of the fish in oil concentration distribution.

The advantages and disadvantages of probabilistic approaches can be summarised (Hart A., private communication) as follows.

- Potential advantages of probabilistic approaches include:
  - increased realism, representing real-world variation in factors that influence exposure and replacing or refining worst-case assumptions
  - makes more use of the available data
  - indicates the influence of quantified uncertainties on the assessment outcome
  - helps to increase the cost-effectiveness of further data collection by targeting it on major sources of uncertainty
  - helps in targeting of risk management actions by identifying key contributors to exposure.

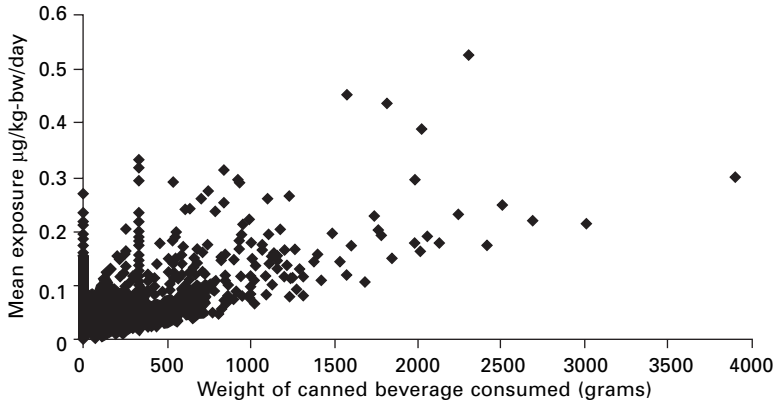

Fig. 6.7 Scatter plot between the total consumed weight (grams) from the canned beverage sub-basket against the average exposure (Holmes *et al*. 2005). Pearson linear correlation = 0.610.

- The main disadvantages of probabilistic approaches are:
  - they are more complex and require more expertise than deterministic approaches
  - the results are more complex than deterministic exposure estimates and can be hard to communicate effectively
  - probabilistic methods – especially those for quantifying uncertainty – are still under development and there is not yet an established consensus on which methods are most appropriate for which purposes
  - probabilistic assessments are not yet readily accepted by regulatory authorities.

It is frequently stated that probabilistic methods require more data than deterministic methods. This is not literally true; it is possible to perform probabilistic calculations with input distributions based on small datasets or expert judgement. It is true that distributions derived from small datasets or expert judgement are likely to be very uncertain. However, if these uncertainties can be adequately represented within the probabilistic assessment, or dealt with by making conservative assumptions for the affected inputs, then probabilistic methods should still provide a useful refinement. Even in those cases where the uncertainties are too great to provide reliable estimates of exposure, probabilistic analysis may still be useful as a form of sensitivity analysis to identify priorities for data collection.

6.8 Conclusions

It is necessary to consider how the shortfall of consumption data with packaging information can be addressed. To this end ILSI are in the process of preparing

a set of guidelines on how to progress with assessing exposure and how to fill the missing gaps. The European Food Safety Authority (EFSA) is initiating a database of food items consumed (Moy 2005), but in the short to medium term packaging of individual food items will not be identified.

As can be seen there is no one method for determining exposure to migrants from food packaging. The availability of the necessary input data and the accuracy of the estimate dictate the methods which can be used. It is strongly recommended that a tiered approach be used for assessing exposure, starting with the simplest and only if the result gives cause for concern should more refined approaches be used. In order for others to understand the approach used for any estimate, all assumptions and sources of data should be clearly spelled out.

Parmar *et al*. (1997) concluded that total diet studies and per capita methods are adequate for looking at average diets of the population. Model diets can be used to look at non-average consumers, but the estimated intake and hence exposure estimate may be exaggerated. Consumption data from dietary surveys when combined with appropriate concentration data are useful when potential intakes by non-average consumers are required. However, it is important that the concentration data are used correctly and the results are interpreted correctly. Duplicate diet studies are the most appropriate for critical groups. They concluded that estimating exposure to consumers to specific chemicals in foodstuffs still requires considerable judgement.

It is believed that the potential offered by probabilistic modelling to overcome the inadequacies in the data will start to be fulfilled in the coming years. The issue could be explaining the use of statistics to resolve a very complex problem.

The need for exposure assessments will increase as concerns about migrants being found increase. It is also of great value for applying the threshold of toxicological concern and demonstration of compliance with the Framework Regulation 2004/1935/EC. In the longer term it should be possible to use such processes for a number of applications including:

- assessment of exposure to an unexpected substance being found
- estimating the most likely exposure to any migrant 'x'
- establishing risk management options for DGSANCO or national authorities
- demonstration of compliance with the Framework Regulation 2004/1935/EC
- supporting dossier submissions to EFSA for new substances.

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7

Toxicology and risk assessment of chemical migrants from food contact materials

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7.1 Introduction

In the US, components of food contact materials are regulated as food additives under the Federal Food, Drug, and Cosmetic Act (FFDCA). The Food and Drug Administration (FDA) has the responsibility for the administration and enforcement of the FFDCA with regard to food contact materials and has published various guidance documents providing background on how FDA performs toxicological evaluations and safety assessments for food additives.

7.2 Regulatory framework for food contact materials in the United States

Within the FDA's Center for Food Safety and Applied Nutrition, the Office of Food Additive Safety administers premarket approval processes for new direct food additives and food additives that are components of food contact materials. Most food contact materials are regulated via the food contact notification process and authorization of new food contact materials is administered by the Division of Food Contact Notifications (see Chapter 2 for further information). The notifier has the primary responsibility to demonstrate the safety of the proposed use of the food contact material. Review scientists within FDA perform a fair evaluation of the data in a food contact notification, as well as other relevant information, to determine if the knowledge base supports the finding with reasonable certainty that no harm will result from the intended use of the food additive. FDA maintains a number of public online listings that include useful information

regarding the safety evaluation of food contact materials (see Chapter 2, Table 2.3).

To understand FDA's current approach to toxicology review and risk assessment for components of food contact materials, it is critical to be aware of FDA's longstanding distinction between food additives and constituents of food additives. Generally, substances added to or present in a food contact material to accomplish a technical effect are considered food additives if they migrate to or are reasonably expected to migrate to food. Examples include polymers, colorants, antioxidants, clarifying agents, and biocides. The additives that are intentionally used, however, are generally not a single chemical but a commercial product that contains several constituents in varying concentrations. Substances that may migrate, or that are reasonably expected to migrate to food may be minor constituents. Examples include monomers, oligomers, catalysts and polymer processing aids whose presence in the final material is not intentional. Many food contact materials are deemed to be food additives because some of their constituents are reasonably expected to migrate to food. Often, minor constituents in food additives are the main concern regarding toxicity. The fact that an additive is typically a mixture is important because the food additive Delaney clause of the FFDCA [21 U.S.C. 348(c)(3)(AA)] (USC, 2005) prohibits FDA from judging a food additive to be safe if it has been shown to be carcinogenic in man or animals. FDA uses carcinogenic risk assessment as a tool to evaluate the safety of individual constituents if the additive itself has not been shown to induce cancer.

7.3 Safety assessment of food additives

As noted above, the FFDCA tasks FDA with determining whether a food contact notification has demonstrated the safety of the proposed use. The food additive Delaney clause of the FFDCA states that 'no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal…'. Therefore, demonstration of carcinogenicity in any animal species is deemed sufficient to prohibit approval as a food additive.

As discussed in FDA's Preparation of Food Contact Notifications for Food Contact Substances: Toxicology Recommendations (FDA, 2002), FDA has set forth minimum testing recommendations for tiered levels of expected consumer exposure. These recommendations are based on the general principle that the potential risk is likely to increase as exposure increases. In addition, submitters are encouraged to discuss the structural similarity of their food contact material or its constituents to known mutagens or carcinogens. This analysis is termed structure-activity relationship (SAR) analysis and is recommended for all exposures (discussed further below). Table 7.1 summarizes

Table 7.1 Toxicology testing recommendations for food contact substances based on dietary concentration (DC) and corresponding estimated daily intake (EDI) values. Note that the cumulative exposures are based on non-biocidal chemicals; biocidal tiers are one-fifth the cumulative dietary concentration (CDC) and cumulative estimated daily intake (CEDI) values expressed

Exposure	Recommendation
DC of ≤ 0.5 μg/kg (EDI of ≤ 1.5 μg/person/day)	• No toxicity testing recommended. • Available information on potential mutagenicity and carcinogenicity, published and unpublished, should be submitted and discussed. • Structural similarity of the substance to known carcinogens or genotoxic chemicals should be discussed, if appropriate.
CDC of > 0.5 μg/kg but ≤ 50 μg/kg (CEDI of > 1.5 μg/person/day but ≤ 150 μg/person/day)	Recommendations for DC of ≤ 0.5 μg/kg and: • Genetic toxicity tests on the substance 1. A test for gene mutations in bacteria 2. An *in vitro* cytogenetic test in mammalian cells or an *in vitro* mouse lymphoma tk± assay.
CDC of > 50 μg/kg but < 1000 μg/kg (CEDI of > 150 μg/person/day but < 3 mg/person/day)	Recommendations for DC of ≤ 0.5 μg/kg and: • Genetic toxicity tests on the substance 1. A test for gene mutations in bacteria 2. An *in vitro* cytogenetic test in mammalian cells or *in vitro* mouse lymphoma tk ± assay. 3. An *in vivo* test for chromosomal damage using rodent hematopoietic cells. • Potential toxicity of the substance should be evaluated by two subchronic (90-day) oral toxicity tests, one in a rodent species and the other in a non-rodent species. • Results from these studies or other available information may trigger the need for longer term (1-year or 2-year) or specialized (e.g. reproductive/developmental toxicity, neurotoxicity, etc.) tests.
CDC of ≥ 1000 μg/kg (EDI of ≥ 3 mg/person/day)	Recommended food additive petition containing the data listed above for lower exposures and: • Two-year carcinogenicity bioassays in two rodent species (one study should include *in utero* phase) • A two-generation reproductive study in rats with a teratology phase. • Other specialized studies, as appropriate.

FDA's recommendations. The regulations for submitting food contact notifications stipulate that all relevant toxicity data available to the notifier be made available to FDA. The rationale and utility of the recommended genetic toxicity tests are discussed in detail by the FDA's Redbook (FDA, 2004).

7.4 Safety assessment for non-carcinogenic endpoints

FDA's recommendations for assessing systemic toxicity endpoints for food contact materials are described in detail elsewhere (Chapter 2; FDA, 2002, 2004). Several key points are now briefly summarized. The notification process places the responsibility upon the notifier for addressing the non-carcinogenic risk of constituent exposure from a proposed use of a food additive. FDA does not generally consider testing for systemic toxicity endpoints necessary to demonstrate the safety of exposures ≤ 150 μg/person/day (discussed further in section 7.5 below). FDA usually recommends *in vivo* animal testing for each exposure greater than 150 μg/person/day (μg/p/d) consisting of one subchronic study in a rodent species and subchronic study in a mammalian non-rodent species (Table 7.1).

For biocides (e.g., materials intended to prevent microbial or fungal growth on food contact materials) and high exposures not normally associated with food contact materials, FDA has additional specific recommendations. When multiple studies are available from which to calculate acceptable daily intake values, traditionally the lowest acceptable daily intake would be chosen as the definitive acceptable daily intake, unless there is scientific rationale not to do so. The acceptable daily intake is based on the no-observed-effect level (NOEL), the highest level for which no treatment-related effects were observed, using appropriate safety factors. In general, FDA considers the use of a safety factor of 1/1000 if NOELs are derived from the results of two subchronic studies in both a rodent and non-rodent species, and 1/100 for NOELs derived from chronic studies to be appropriate. For reproduction and developmental endpoints, FDA considers it appropriate to use a safety factor of 1/1000 if the observed effects are severe or irreversible (e.g., a missing limb or decrease in the number of pups born live); otherwise, FDA recommends a safety factor of 1/100 (see Chapter 2, Table 2.8). Additional adjustments may be appropriate depending on the specific knowledge base available.

7.5 Threshold approaches to safety assessment

Historically, toxicity testing and evaluation schemes have always implicitly included thresholds to prioritize concern or delineate the toxicity testing needed to reach a safety decision. In most cases, such thresholds for testing have been qualitatively based on a general knowledge of a chemical or class of chemicals. Moreover, decisions regarding testing recommendations typically weigh the two main factors of the safety assessment paradigm; the likely consumer exposure to a particular chemical or class of chemicals and the likely inherent toxicity of those chemicals. A larger risk, due either to an expectation of high consumer exposure or greater concern for potential toxicity will ordinarily correspond with a need for greater levels of toxicity testing data to demonstrate the safety of the compound under its intended conditions

of use. Hence, greater amounts of toxicity data are generally needed to demonstrate the safety of bioactive compounds such as drugs, herbicides, and other biocides, and to support the safety of compounds with relatively high consumer exposure such as food ingredients. Less data are ordinarily necessary to demonstrate safety for constituents of food contact materials. As a general principle, starting reactants and reaction byproducts of food contact materials may be expected to be more bioactive and less stable, and therefore more toxic, than the end product. Fortunately, these reactive species tend to be present at relatively low residual levels in end product food contact materials.

The distinction between traditional thresholds used to set specific testing recommendations and the newer approaches of FDA's threshold of regulation and the recently proposed thresholds of toxicological concern is that the latter approaches are based on a more quantitative evaluation of the toxicity of industrial chemicals. Frawley (1967) first proposed a probabilistic analysis of toxicity data to support the establishment of a 300 μg/p/d dietary threshold for toxicity testing for the regulation of food contact materials. Frawley's proposal was based on his review of classical toxic endpoints in a limited number of chronic toxicity studies. In the mid-1980s, the FDA began examining the available scientific literature on toxicity testing, to develop a more quantitative basis for testing recommendations for food contact materials. The advent of larger collections of toxicity data such as the Registry of Toxic Effects of Chemical Substances (NIOSH, 2005), the carcinogenic potency database (CPDB) (Gold and Zeiger, 1997; EPA, 2005b), and others made it possible to perform a more quantitative analysis of the potential risks from consumer exposure to the world of chemicals.

Beginning in the 1980s, Flamm *et al*. (1987) and Rulis (1989) documented FDA's exploration of the use of large databases of toxicity data to address very low exposures to components of food contact materials more efficiently. Flamm *et al*. (1987) performed a probabilistic analysis of carcinogenic potency data in an attempt to discern a dietary level below which no specific toxicity testing data should be considered prerequisite to judge the safety of a compound used in a food contact material.

Continuing the treatment by Flamm *et al*. (1987), Rulis (1989) proposed a range of possible threshold of regulation levels for components of food contact materials, extending consideration to the practical limitations of analytical chemistry and regulatory review. Later, Machuga, *et al*. (1992) reasoned that such practical considerations support a level on the order of 3 μg/p/d. Rulis's (1989) proposed level of 0.15 μg/p/d would eliminate virtually all risk from potential carcinogens as well as other toxins. FDA established a minimum testing recommendation level of 1.5 μg/p/d in its policy on the threshold of regulation (FDA, 1995). This higher threshold was based in part on practical considerations including the ability of analytical chemistry to detect migrants at migration levels related to risk-based dietary thresholds. Although the higher limit of consumer exposure implies a higher potential

risk, in practical terms the ability to identify compounds of concern without testing is substantially the same for all thresholds considered by FDA.

A critical assumption in FDA's development of a threshold of regulation is that carcinogenicity is the most sensitive toxicological endpoint at very low (μg/kg) dietary concentrations. FDA expects that protection against this critical endpoint will also protect against the less severe non-neoplastic toxic effects of food contact materials. Epidemiological data adequate to perform risk assessments for carcinogenicity are very rarely available for food contact materials or their constituents. Therefore, risk assessments for carcinogenic potential are usually based on extrapolations from the results of animal bioassays (relatively high doses) to levels of dietary exposure that may be of negligible or acceptable risk. Historically, upper-bound lifetime cancer risks estimated to be less than one in one million (10^{-6}) have been considered to represent negligible risk. Upper-bound risk estimates in the range of one in a hundred thousand (10^{-5}) have been accepted in specific cases, as the weight-of-evidence data mitigated concern. This extrapolation to negligible carcinogenic risk is tantamount to the application of a safety factor 2–3 orders of magnitude larger than those typically applied to non-neoplastic toxicological endpoints. The work by Munro *et al*. (1996), Cheeseman *et al*. (1999) and Kroes *et al*. (2000, 2004) provide a strong basis of support for the assumption that carcinogenicity is the toxic effect of most concern at the lowest dietary concentrations.

Cheeseman *et al*. (1999) examined the Gold CPDB underlying FDA's threshold of regulation to determine if other, more precise, thresholds could be established based on additional information on the structure or toxicity of food contact materials. They also conducted a more thorough examination of the range of concern levels for specific toxic endpoints other than carcinogenicity. Likewise, attempts by Kroes *et al*. (2000, 2004) to define a toxicological threshold of concern have also included a more careful consideration of the chemicals in the database which underlie FDA's threshold of regulation and the structure-based toxicological thresholds first proposed by Munro (Munro *et al*., 1996, 1999; Munro and Kroes, 1998). In addition, both Cheeseman *et al*. (1999) and Kroes *et al*. (2004) show the value of considering separately the structure activity relationships of the most potent compounds for different toxic endpoints. Both of these treatments demonstrate that toxicity thresholds may be safely established for most compounds or broad classes of compounds without toxicity data specific to the compound of interest. However, implementation of those thresholds should include special considerations for evidence that might identify more potent subsets of compounds.

FDA's threshold of 1.5 μg/p/d is an example of the threshold of toxicological concern approach. Below this threshold level of consumer exposure, FDA does not consider specific testing necessary to identify compounds with significant carcinogenic potential. This threshold of regulation is not meant to be a level below which no chemicals could be harmful. FDA's threshold

of regulation analysis identifies many compounds of potential concern below 1.5 μg/p/d but also concludes that compounds of potential concern may be identified, by SAR analysis, without specific testing data and any necessary testing can be requested. Therefore, this threshold does not represent the level below which data will never be necessary to demonstrate safety. For example, a concern raised by preexisting test data or by structural analysis may be adequately addressable only by additional toxicity testing. It is essential that regulators and industry appropriately apply these caveats to any threshold of toxicological concern that is derived from a probabilistic analysis.

However, when raising such concerns as a regulator or risk manager, it is important to understand the data and assumptions underlying any threshold and the meaning that these data and assumptions give to individual decisions. Only a fraction of the untested chemicals would show evidence of carcinogenicity if actually tested (for obvious practical reasons, testing has been focused on compounds of greater concern). For example, only about 10 percent of known carcinogenic compounds would result in a potential lifetime risk greater than one in one million at the lower proposed threshold of 0.15 μg/p/d. Thus, a decision regarding the safety of an untested substance at this level can be based on an understanding of the likelihood that the substance is as potent as one of the top 10 percent of the most potent carcinogens known. Future testing might verify that this subset represents the top 1 percent of compounds of potential concern in the world of chemicals. Because the carcinogenic potency of each of these chemicals is inherently related to its chemical structure and resulting physical/chemical properties, structural analysis can be an effective approach to determining the safety at a reasonable degree of certainty for low consumer exposures (Cheeseman, 2005; Bailey *et al*., 2005).

As consumer exposures increase, regulators become progressively more concerned about the less potent compounds. As the group of compounds of concern grows to include members of lesser and lesser potency, the scope of chemical structures becomes more diverse and the decision-making process based on distinct structural clues becomes less certain. Although approaches such as the use of SAR analysis software bridge this gap by providing a systematic review tool, at some point consumer exposure and the commensurate risk rises to a level at which specific testing data become necessary to clarify the real likely risk. Whenever such levels of consumer exposure are defined, they can be viewed as thresholds of toxicological concern, above which additional steps are necessary to mitigate risk. As potential risk increases, these thresholds of toxicological concern must trigger requirements for additional testing, implementation of a higher level program of structural analysis, or procedures to prevent unsafe consumer exposure.

Just as a threshold level can be set to address the toxicological concern for carcinogenic risk, other threshold levels for toxicity testing may be established in order to address the likelihood of other toxicological risks. Kroes proposed multiple thresholds of toxicological concern based on Munro's structural

classification of compounds tested for a diverse range of toxicological endpoints (Kroes *et al*., 2000, 2004; Munro *et al*., 1996). Munro used the structural classification scheme of Cramer *et al*. (1978) to segregate a representative data set of compounds into three structural classes. Munro then performed a probabilistic analysis of the range of acceptable daily intakes for each of these groups and proposed a threshold for each group based on the lower 95 percent confidence level for the acceptable daily intakes. As an aside, the threshold of regulation concept is separate from the concept of toxicity thresholds. The thresholds of toxicological concern approach proposed by Munro does not investigate mechanisms of compensation and repair, but rather is a method for prioritization and an efficient approach to risk-safety determination.

Kroes *et al*. (2000) further analyzed the need to specifically consider thresholds for different toxicological endpoints including neurotoxicity, developmental toxicity, immunotoxicity, and developmental neurotoxicity. They also considered the need for a separate threshold for teratogens, allergens, and endocrine-active compounds. Consideration of these specialized endpoints resulted in only a slight change in the originally proposed thresholds of toxicological concern; that being the addition of a consideration of organophosphate compounds as an especially potent subset of neurotoxins.

Collectively, the work by Munro *et al*. (1996) and Kroes *et al*. (2000, 2004) proposed several thresholds of toxicological concern based on toxicological and structural classifications. Table 7.2 summarizes these thresholds, which are cumulative as dietary concentrations increase. These thresholds are based on the analysis of compounds grouped using the so-called Cramer decision tree and on the structural analysis of compounds testing positive for specific toxic endpoints. Maintenance of such a system depends upon maintenance of the decision tree and the ability to continue to discern relationships between toxicity effects and structural information and to then translate those relationships into a decision tree.

Table 7.2 Thresholds of toxicological concern (from Kroes *et al.* 2004)

Threshold exposure	Criteria for safety at threshold
< 0.15 µg/p/d	Verification that compound is not a polyhalogenated dibenzodioxin, dibenzofuran; or biphenyl, aflatoxin-like, azoxy-, or N-nitroso-compound.
< 1.5 µg/p/d	There is no reason to believe the compound is genotoxic.
<90 µg/p/d	The compound is not an organophosphate.
<540 µg/p/d	Compound is not a member of Cramer structural class three (Cramer *et al.*, 1978)
<1800 µg/p/d	Compound is not a member of Cramer structural class two (Cramer *et al.*, 1978).

7.6 Carcinogenicity risk assessment for constituents of food additives

As discussed above, the Delaney clause applies to substances proposed for use as food additives, but does not apply to individual constituents of a food additive. Examples of constituents would include residual monomers or catalysts. The constituents policy, subjected to judicial review in Scott v. FDA, 728 F. 2d 322 (6th cir. 1984), states that FDA may consider the potential risks of constituent exposure under the general safety standards set forth in FFDCA. The notification process places the responsibility upon the notifier for addressing the carcinogenic risk of constituent exposure from a proposed use of a food additive. FDA recommends that notifiers include in their food contact notification a safety narrative that addresses the safety of each carcinogenic constituent at any exposure (in addition to the recommendations listed in Table 7.1). This narrative should include an estimate of the potential human cancer risk from the constituent due to the proposed use of the food contact material (FDA, 2002).

For most food contact materials, a worst-case estimate of the upper bound lifetime cancer risk (LCR)[1] is sufficient to demonstrate safety and allows for the most efficient and complete review process possible. Although such an approach may be overly conservative, this less precise approach allows for a reasonable prioritization of resources without reducing the certainty of safety. The recommended approach for establishing this worst-case upper bound LCR from exposure to a constituent in a food additive is described in more detail below.

First, the highest appropriate unit cancer risk (UCR) is determined from the tumor data from the most sensitive species, strain, sex, and study (FDA, 2002). Tumor incidences not considered treatment related are omitted from analysis; statistical significance is an important tool in evaluating the relationship of treatment to tumor induction. If only one dose was tested and only one type of tumor was induced, then the UCR is defined as the slope of the straight line of tumor incidence versus dose.

$$\text{UCR} = (\text{number of tumors in test group} - \text{number of tumors in controls})/(\text{test dose} - \text{control dose}) \quad 7.1$$

Since the control dose is zero, the denominator in equation 7.1 is simply the test dose. This calculation is based on the worst-case assumption that LCR is linearly proportional to dose, and corrects for the background tumor incidence.

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1. The use of the terms ‘upper bound’ and ‘worst-case’ refer to the expectations that this approach is likely to be highly conservative and will not underestimate potential risk. These terms are not meant to connote that statistical analysis to estimate error bounds would be performed, or that additional safety factors (traditional for extrapolation to acceptable daily intake values for non-carcinogens) would be incorporated into the extrapolation.

When multiple types of treatment-related tumors are observed, the UCR is defined as the sum of the slopes (of tumor incidence versus dose) for each tumor type. This is based on the worst-case assumption that tumors arising at multiple sites may be independent of each other, so that their risks are additive. When multiple doses are tested, the default approach is to consider each tumor type separately and to use the lowest dose at which a statistically significant increase in tumor incidence (compared to controls) is identified to calculate the slope for that tumor type. An example is shown in Table 7.3:

$$\text{UCR} = \text{sum of the slopes of tumor incidence (corrected for background) versus dose} \tag{7.2}$$

$$\text{UCR} = (\text{slope for liver carcinoma}) + (\text{slope for renal carcinoma}) \tag{7.3}$$

$$\begin{aligned} \text{UCR}_{\text{Male rat}} &= [\{(47/50) - (39/50)\} \text{ divided by } 16 \text{ mg/kg bw/d}] \\ &+ [\{(8/50) - (1/50)\} \text{ divided by } 32 \text{ mg/kg bw/d}] \\ &= 0.0100 + 0.0044 = 0.0144 \text{ (mg/kg bw/day)}^{-1} \end{aligned} \tag{7.4}$$

In this example (equation 7.4 and Table 7.3), the incidence of renal carcinoma at the low dose is not used in the UCR calculation since the increase was not statistically significant; instead, the incidence at the high dose is used. For liver carcinomas, the slope is calculated from the low-dose incidence. The sum of the slopes is the UCR value. If data are available for both sexes, multiple species, or multiple bioassays for one species, the worst-case default approach would be to use the most sensitive sex, species, and study to estimate risk.

Several considerations are important in determining how to apply or modify this default UCR approach, including (i) the incidences of benign and malignant tumors, both separately and combined, for each target tissue, (ii) the morphological description of each significant lesion, (iii) tests for statistical trends and of significance between dose and control groups, (iv) time to tumor formation, (v) historical control tumor data from performing laboratories, and (vi) any other potentially related effects, including non-neoplastic and pre-neoplastic findings. The worst-case UCR is then used to determine the worst-case, upper bound lifetime cancer risk (LCR). The LCR is estimated by multiplying the estimated daily intake (EDI) for a constituent expressed in units of mg/kg body weight/day, by the UCR (mg/kg body weight/day)$^{-1}$.

$$\text{UCR} \times \text{EDI} = \text{LCR} \tag{7.5}$$

Table 7.3 Male rat tumor incidence data

Tumor type	Control	16 mg/kg bw/d	32 mg/kg bw/d
Liver carcinoma	39/50	47/50*	50/50*
Renal carcinoma	1/50	3/50	8/50*

*Statistically significant increase ($p < 0.05$).

Thus, the LCR is a unitless number that provides a quantitative upper-bound estimate of the risk to human heath from the ingestion of the constituent under the intended use of the new food contact material (Gaylor *et al*., 1997; Kokoski *et al*., 1990; Lorentzen, 1984).

Historically, the FDA food ingredient program has considered incremental LCR values below 10^{-8} and cumulative LCR values below 10^{-6} to represent a negligible level of risk from exposure to the constituent. The incremental LCR represents the risk resulting from the migration of a potentially carcinogenic constituent from a food contact material to food. Cumulative LCR represents the maximum total risk from a constituent considering its presence in food from all food contact materials and other food additives. Bioassays that use other routes of exposure not directly relatable to food ingestion (e.g., inhalation, dermal, injection) are considered on a case-by-case basis, and adjustments may be applied to extrapolate to an estimation of oral exposure.

The TD_{50} is a conceptual, interpolated value similar to the UCR. The TD_{50} corresponds to the dose that would cause cancer in 50 percent of the treated animals beyond background incidence from control animals. Higher toxicity is indicated by a higher UCR and a lower TD_{50} value. When the same assumptions are used to calculate both, the UCR can be estimated as shown in equation 7.6.

$$UCR = (0.5/TD_{50}) \qquad 7.6$$

This brief description of FDA's default worst-case approach to quantifying the potential carcinogenic risk is not meant to discourage notifiers from presenting alternative approaches. FDA recognizes that modifications to this approach, or the use of other biologically based approaches, may be more appropriate to address safety. FDA performs a proportionally more detailed and comprehensive review in cases for which a more precise estimate would be needed to demonstrate safety. Such reviews are necessarily longer and may involve additional consultations with experts from many disciplines within FDA. In cases where a bioassay exists for a food contact substance that has not been evaluated by FDA and the bioassay is not clearly negative for carcinogenic effects, FDA has authority to reject the food contact notification. This authority helps to ensure that the level of review is appropriate to the potential risk.

Two examples of alternative approaches to cancer risk assessment would be estimations based on threshold-response (EPA, 2005a) and benchmark dose modeling (EPA, 1995, 2000). As a practical matter, if the proposed basis of safety relies on a threshold or mode-of-action characterization to dismiss or mitigate animal tumor data, FDA would recommend that the safety narrative clearly discuss the scientific rationale and present all relevant data for consideration. In the absence of adequate evidence to the contrary, FDA presumes that certain assumptions are appropriately protective of safety, namely that: (i) the induction of tumors in animals is relevant to human

health, (ii) the most sensitive species, strain, and study are the most appropriate basis for risk calculation, (iii) tumors arising in multiple sites may be independent and add to the total risk, and (iv) the dose-response is linear to zero. Data that justify deviation from these default assumptions may support a finding of less (or no) carcinogenic risk from exposure to a constituent of a proposed food additive.

7.7 Structure activity relationship (SAR) analysis in the safety assessment of constituents of food additives

Because of the typically low consumer exposure to constituents of food contact materials, there may be little toxicity testing data publicly available. In such cases, there are a number of methods available to notifiers to address toxicology data gaps, and allow an adequate evaluation of chemicals and the potential risks to a human being exposed to these chemicals. These methods include (i) animal testing, which involves significant time and monetary resources, (ii) *in vitro* testing, which is far less costly but still requires significant investments in time and money and may be of a limited utility, and (iii) SAR analyses, which would need an adequate pre-existing knowledge base.

SAR is a fundamental aspect of toxicology. It is based on observations that the chemical structure and inherent physical/chemical properties of a chemical contribute to and determine the inherent physical and biological properties, including toxicity. Regulatory processes that incorporate SAR analyses include FDA's food contact notification program (Bailey *et al*., 2005; Cheeseman and Machuga, 1997; Cheeseman *et al*., 1999), the Center for Drug Evaluation and Research's (CDER) risk assessments (Matthews *et al*., 2000; Contrera *et al*., 2004, 2005), and Environmental Protection Agency's (EPA's) premanufacture notification (PMN) process (Baumel, 1984; Auer and Gould, 1987; Wagner *et al*., 1995; Woo *et al*., 1995; Nabholz *et al*., 1997). FDA's Toxicology Guidance recommends that for each exposure: 'all available information on the potential carcinogenicity of such substances should be discussed … (e.g., carcinogenicity studies, genetic toxicity studies, or information on structural similarity to known mutagens or carcinogens.' Essentially, this is a recommendation to use SAR analysis, to the extent feasible, to evaluate and demonstrate the safety of food contact materials or their constituents. Currently, systematic guidance is not practical and SAR is weighed with the available data and the exposure estimate on a case-by-case basis. This section represents current thinking and practices, but is not meant to limit the scope of future SAR approaches.

SAR is a relationship of a particular chemical's structure with its physical/chemical properties and its human health effect. Conceptually, these relationships are either qualitative or quantitative in nature. Qualitative SAR

predictions are based on a comparison of physical/chemical data from a subject chemical to a set of similar data from a structurally similar chemical (analog) or group of analogs. If the analyst identifies structurally similar analogs to the food contact material or constituent with appropriate toxicity data (i.e., genetic toxicity or carcinogenicity testing), an initial level of concern can be raised that may trigger additional data recommendations or a quantitative SAR analysis. The results of this type of analysis are described in terms such as 'more toxic', 'less toxic' or 'similar toxicity' to a known compound or class of compounds.

Potential concerns for a constituent of an additive raised by a qualitative SAR analysis may be addressable by a more in-depth, quantitative SAR (QSAR) analysis. The approach to QSAR used in the food contact notification program is to identify the most appropriate specific structural analogs from the pool of chemicals for which adequate carcinogenicity data are available. If, in the expert judgment of FDA reviewers, the analogs can reasonably be considered to be as toxic or more toxic than the compound of concern, these analogs can be used to develop a quantitative estimate of its upper bound LCR.

7.8 Qualitative SAR analysis of food additives and constituents

Based on the available historical data, FDA considers carcinogenicity to be the pivotal endpoint of concern for consumer exposures below 150 μg/p/d, exposure levels typically encountered from food contact material uses. FDA's approach to qualitative SAR is to perform a preliminary 'first look' for structural alerts (SAs) and for close analogy to known carcinogens (Bailey *et al*., 2005). A useful tool for this type of analysis is the Ashby and Tennant (1991) classification scheme for SAs and a related list of functional groups compiled by Munro *et al*. (1996). These schemes assess compounds based on their functional groups. By comparing the SAs for the compound in question to SAs for structural analogs, one can form a qualitative idea of the subject compound's toxicity. Other endpoints that may strengthen the comparison include acute toxicities and physical/chemical properties such as bioavailability, molecular weight and water/octanol partition coefficient.

In addition, several computer programs that predict carcinogenicity based on structure are available to FDA and are used to assist in the qualitative evaluation of food contact materials and their constituents. OncoLogic is an expert system, designed to codify and consistently apply the knowledge of EPA experts. It incorporates SAs and rules regarding mechanisms of action. OncoLogic (EPA, 2005c; Richard, 1998) has reportedly been purchased by EPA, which plans to distribute it free to the public. MULTICASE (MultiCase Incorporated, 2005) is a knowledge-based system. Its designers compiled a relatively diverse database of discrete chemicals for which adequate

carcinogenicity results were available and used this database as a training set to develop a predictive program. Based on statistical and expert analysis of the training set, molecular fragments associated with biological activity, termed 'biophores', and fragments associated with inactivity were identified and weighted. Users of the program's carcinogenicity module can query chemical structures of interest, such as food contact materials, for which the program will predict likely carcinogenic activity. Other predicative modules such as mutagenicity and teratogenicity are also available.

Instead of using structural alerts and weighing substituents, MDL QSAR uses a set of topological descriptors to calculate predictive equations. The descriptors capture atom-type, group-type, individual atom E-states and hydrogen E-state indices, among others (Contrera *et al*., 2005). FDA has access to a carcinogenicity prediction module computed from a training set of approximately 1000 compounds tested for rodent carcinogenicity. The version of MDL QSAR available to FDA gives a probability of the test chemicals being of high or low carcinogenic potential.

7.8.1 Examples of qualitative SAR analysis

For a food contact material with no relevant genotoxicity or carcinogenicity data with an estimated daily intake (EDI) of < 1.5 μg/p/d, FDA would not normally recommend testing. If the food contact material contained SAs, such as the bisfuran polycyclic substructure of aflatoxin B_1 (CASRN 1162-65-8), FDA may recommend additional specific tests due to the potential concern for public safety.

For a constituent of an additive with equivocal (mixed positive and negative) battery of genetic toxicity tests and a EDI of < 150 μg/p/d, SAR analysis for SAs and predictive software such as MDL QSAR (Contrera *et al*., 2005) and MultiCASE's MC4PC (Rosenkranz and Klopman, 1988; Matthews and Contrera, 1998) may be used as part of the 'weight of evidence' approach in assessing the safety of the compound. If a constituent were of potential concern, a quantitative SAR analysis might be feasible to characterize the expected risk.

Within FDA, the Office of Food Additive Safety considers some monomers, such as 1,3-butadiene (CASRN 106-99-0) or tetrafluoroethylene (TFE, CASRN 116-14-3) to be putative carcinogens. The carcinogenic risk for exposure to these monomers from the proposed use of a large butadiene-TFE polymer would be assessed as part of the routine toxicology review (i.e., calculating the LCR from the UCR and the EDI). For a large butadiene-TFE polymer, exposure would not be expected to the polymer itself, but, rather, to the low molecular weight oligomers (LMWO), which is typically < 150 μg/p/d depending on the conditions of use. FDA often considers the toxicity of the monomers as worst-case analogs. For these oligomers, careful consideration of the chemistry and manufacturing process might be needed to understand what, if any, SAs would remain present in the LMWO (see Chapter 2).

7.9 Quantitative SAR (QSAR) analysis in the safety assessment of constituents

If the available genetic toxicity data, or the qualitative SAR analysis, indicate potential concern for the carcinogenicity of a constituent, QSAR may be a feasible approach to safety assessment by estimating a worst-case LCR (Bailey *et al*., 2005). Analog identification is an empirical case-by-case process that uses overlapping approaches to identify structurally and physicochemically related groups of analogs. Historically, analogs have been identified by experience and searching of the toxicology literature. More recently, searches are greatly facilitated by the availability of electronic structure-searchable databases. Publicly available examples are the National Library of Medicine's (NLM) ChemIDPlus (NLM, 2005) and EPA's Distributed Structure-Searchable Toxicity (DSSTox) Public Database Network (EPA, 2005b). FDA also uses internally prepared structure-searchable version of the CPDB and other internal databases.

For transparency and reproducibility, the rules and assumptions used during analog selection should be clearly defined, both for manual analog searches and when substructure/similarity software is used. Usually, decisions to include or omit potential analogs are specific to the context of the relative wealth of candidates and their data.

Analog identification requires careful evaluation by the analyst. Not only is it important to identify an appropriate scaffold (e.g., a common substructure such as a phenanthrene ring system) that contains the same or similar functional groups (SAs) (e.g., nitroso or nitrosamines), but it is also important to consider the positioning of the functional groups on the scaffold and how this might alter toxicity. Examples of positioning differences include the steric hinderance of a SA of the constituent from metabolic activation, or electronic effects (such as conjugation) due to a functional group located within the molecule.

Relatively small differences in substructural features may have a dramatic effect on the metabolism of the constituent or the analog, or even alter the reactivity of the molecules with DNA (genotoxic versus nongenotoxic), thus changing the detoxification pathway or the molecule's mode of action. For example, metabolic activation of N-nitrosamines to potential carcinogenic metabolites is thought to proceed through hydroxylation at the carbon *alpha* to the nitroso group. Hydroxylation is followed by the release of the hydroxyalkyl moiety as an aldehyde and the generation of a primary nitrosamine (Klaassen, 2001). The primary amine ultimately forms a carbonium ion that can interact with DNA. Therefore, the use of nitrosamines containing aliphatic chains (see Fig. 7.1) may not be suitable analogs for N-nitrosodiphenylamine (see Fig. 7.2) since Fig. 7.2 does not contain a carbon *alpha* to the nitroso group that can undergo hydroxylation; thus altering the metabolic detoxification pathway for N-nitrosodiphenylamine compared to compounds in Fig. 7.1. One should also consider the physical properties of the molecule in question and the potential set of analogs. For example, large differences in molecular

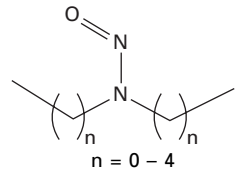


Fig. 7.1 Structures of aliphatic nitrosamines **1-5**.

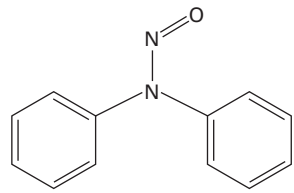


Fig. 7.2 N-nitrosodiphenylamine **6**.

weight, boiling point, pKa, and water/octanol solubility may affect toxicokinetic and toxicodynamic parameters.

7.10 Safety assessment of carcinogenic constituents of food additives

As stated above, identification of the best analog(s) is done on a case-by-case basis. From a pool of potential analogs with available data, the nearest analogs are generally considered the most appropriate. An exception might be to choose a less-near analog with high carcinogenic potency, to be more protective. For low proposed exposures when a rapid assessment would be adequate to demonstrate safety, FDA may summarily review the bioassay data for the analogs. In some cases, the CPDB is useful: the lowest statistically significant TD_{50} value can be converted (eqn 7.6) to identify the lowest UCR. For each appropriate analog, this UCR is then adjusted for molecular weight differences of the untested constituent as compared to the analogs (molar normalization), and then converted to the LCR (eqn 7.5) for risk evaluation. A corresponding safety standard is applied to LCR values calculated by analogy as for LCR values calculated directly from carcinogenicity data. As stated above, FDA has considered incremental LCR values up to 10^{-8} and cumulative LCR values up to 10^{-6} to represent a negligible risk from constituent exposure. However, the analyst should consider whether the analogs are expected to represent adequately the worst-case scenario or if they are likely to underestimate or overestimate risk. Judgments as to the adequacy of the QSAR safety assessment and the need for protective modifiers to the margin of safety can be made only after considering the entire weight of evidence and the expected exposure.

7.10.1 Example of a QSAR analysis

This theoretical example of a QSAR assessment is presented to exhibit FDA's current approach to using SAR as a tool in the safety evaluation of substances proposed for use as food contact materials. If anthrafurin (1,6-dihydroxyanthraquinone; CASRN 117-12-4; Fig. 7.3) were expected to be an impurity in a food contact material, an immediate initial concern would be raised due to reports in the literature of positive results in the bacterial reverse mutation assay and other *in vitro* genetic toxicity tests. A literature search did not identify relevant carcinogenicity data for anthrafurin.

Anthrafurin was evaluated using MultiCASE 4PC version 1.700 carcinogenicity modules (AG1 male rat, AG2 female rat, AG3 male mouse, AG4 female mouse), which identified a biophore associated with carcinogenic activity. Three of the four modules were predicted to be positive, and the overall call (Informatics and Computational Safety Analysis Staff Decision Support Method) was positive for carcinogenicity of anthrafurin. For OncoLogic, no organic subsystem suitable for anthrafurin was identified, and so this compound was not evaluated using OncoLogic.

To provide a worst-case estimate of carcinogenic potency, a search was performed for analogs of anthrafurin using databases internal to FDA's Office of Food Additive Safety as well as publicly available databases such as ChemIDplus (2005). Numerous hydroxy-substituted anthraquinone analogs with genetic toxicity data were identified. Those analogs with adequate bioassay data considered most suitable for QSAR are shown in Table 7.4 with the lowest statistically significant TD_{50} value ($P < 0.05$) reported in the CPDB (Gold and Zeiger, 1997).

In the absence of other relevant data, it may be reasonable to assume that the TD_{50} value for anthrafurin would be near the range of these three analogs. As such, using the most conservative (lowest) TD_{50} value for 1-hydroxyanthraquinone is expected to be adequately conservative, after adjustment for differences in molecular weight (MW).

$$TD_{50\ \text{anthrafurin}} = (TD_{50\ \text{1-hydroxyanthraquinone}}) \times (MW_{\text{anthrafurin}}/MW_{\text{1-hydroxyanthraquinone}}) \quad 7.7$$

$$TD_{50\ \text{anthrafurin}} = (59.2) \times (240.1/224.21) = 63.4\ \text{mg/kg bw/d} \quad 7.8$$

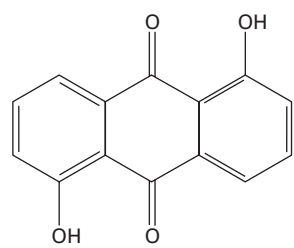
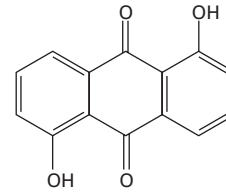
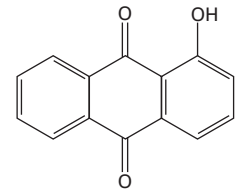
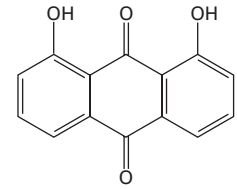
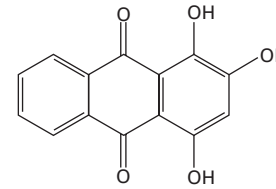


Fig. 7.3 Structure of anthrafurin **7**.

Table 7.4 The structures of anthrafurin and identified analogs suitable for QSAR analysis

Name	Lowest statistically significant TD_{50} (mg/kg bw/d)	Structure
Anthrafurin	Not available	
1-Hydroxyanthraquinone CASRN 129-43-1	59.2	
1,8-Dihydroxyanthraquinone (danthron, chrysazin) CASRN 117-10-2	245	
Purpurin (1,2,4-trihydroxy-9,10-anthracenedione) CASRN 81-54-9	678	

This value corresponds to a UCR of 0.008 (eqn 7.6). For a theoretical exposure of 10 ng/person/day (equivalent to 2×10^{-7} mg/p/d), the LCR would be 1×10^{-9} (eqn 7.5) In such a case, FDA could reasonably conclude that no further information regarding anthrafurin would be necessary to demonstrate safety.

7.11 Future trends

Regulatory programs for food contact materials worldwide are moving toward faster and more efficient review processes. FDA's food contact notification program is a prime example. Relatedly, regulatory bodies worldwide are under increasing scrutiny regarding the need for animal testing and the

suitability of alternative approaches. In order to accommodate such changes safely and appropriately, regulatory bodies need to maximize the use of resources, including available toxicology data on chemicals of similar structure. Pragmatically, this means that reviews of toxicity studies should be captured in such a way as to provide regulatory bodies with efficient access to all relevant toxicity data when making regulatory decisions. It also means that regulatory bodies need to be involved in the development of SAR analysis programs and other predictive tools, to ensure that these tools are effective in regulatory review processes.

FDA's food contact notification program is working to improve its safety assessment process by facilitating a more comprehensive data analysis for individual toxic endpoints. This is being accomplished by mining toxicity data from FDA files and open literature sources and consolidating this information into endpoint specific structure-searchable databases. Such databases have a two-fold value in a regulatory review program. First, they serve as an efficient repository of searchable information that can be used to analyze untested compounds to gauge an initial level of concern for the toxic endpoint of concern. For example, a database of developmental toxicity data can be searched, by structure or keyword, to determine whether data exist for a related compound that would prevent approval or necessitate requesting additional toxicity data. Secondly, such a database will be useful in establishing generally applicable thresholds for requesting specific types of toxicity data. This approach provides for a much simpler organization of toxicological knowledge and permits seamless updates by regulators. Importantly, sharing such databases does not require acceptance of a single interpretation of results. Each user could analyze the data independently and apply appropriate principles to gauge acceptable risk in different regulatory scenarios. Such an approach would help alleviate the maintenance issues associated with the decision tree models discussed above.

As regulators and industry develop these larger databases of toxicity information and make them available to the public, we are poised to make further advances in how we manage risk. This new information might allow refinement of the classification schemes used in the thresholds of toxicological concern and threshold of regulation approaches. Further, these data may allow thresholds to be set for additional toxic endpoints, thereby allowing regulators to ensure the safety of food contact materials while refining their guidance as to the types and quantity of toxicity tests considered necessary to demonstrate safety.

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8

Mathematical modelling of chemical migration from food contact materials

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8.1 Introduction

Food and packaging constitutes an indivisible unit. The most essential requirement for packaging today compared to previous requirements is simultaneous optimisation with respect to several criteria. Such optimisation is always a compromise between different solutions which can lead to the appearance of new problems. Fulfilling, for example, the criterion of packaging minimisation, permeability is increased to the allowable maximum. That may mean that exceeding or falling short of a packaging specification value by even a small amount might lead to a significant change in the quality of a packaged product. In future package development, optimisation from an ecological viewpoint will play an especially important role and minimisation of packaging will help make this possible. One should never forget however, that quality assurance of the packaged food and therefore the guarantee of consumer safety will always have priority and must remain the most important criterion for optimisation. The fulfilment of these requirements assumes complete knowledge of possible interactions between packaging and food during their contact time. In this respect the properties of both parts of package, the packaging material and the food, must be co-ordinated with one another. Here possible interactions between the two parts play an important role in the quality assurance of the food.

Interaction between packaging and food consists of the transfer of substances from the environment as well as from the packaging into the food and vice versa. Chemical reactions inside the packaging or food are also possible. Not only can the quality of the packed food change due to such interactions, but the properties of the packaging may change as well, leading to further loss

of its protective function. Thus the main criterion for an optimal packaging system is, in most cases, minimal interaction.

Worldwide investigations over the last 30 years have demonstrated that interactions between food contact materials and foodstuffs occur as foreseeable physical processes (Figge, 1980; Bieber *et al*., 1985; Till *et al*., 1987; Goydan *et al*., 1990; Castle *et al*., 1991; Vergnaud, 1995/96; Katan, 1996; Begley, 2000). Standardisation of migration measurements is based on this knowledge. In most cases, the mass transfer obeys Fick's laws of diffusion. However, the variety of substances occurring in interaction processes and the necessary time and cost requirements to carry out all the experimental measurements for a complete quality assurance for consumer safety, necessitate additional tools in order to fulfil this task. One such tool is migration modelling, which allows high-speed computer-aided access to migration values independent of analytical limitations. It also manages any given individual food packaging system (geometry, ratio mass/contact area, shelf life etc.).

Modelling is an attractive tool since fast computer systems with high capacities at low costs are available on the market. For such systems corresponding programs that are specifically tailored and user friendly are available. Modelling of potential migration is already used in the USA and EU as an additional tool to help make regulatory decisions or as a quality assurance instrument (Reynier *et al*., 1999; Brandsch *et al*., 2002; Begley *et al*., 2005). However, it must be emphasised that an uncritical application of such programs, without knowledge of the physical and mathematical limitations of them, can lead to serious errors in the evaluation of the packaging quality. In order to avoid such unwanted results it is highly recommended to study the principles behind such models and the corresponding programs. This allows the user of a computer program to understand its limitations and avoid being a simple user of a 'black box'. The aim of this chapter is to give a short overview of these principles (Piringer and Baner, 2000).

8.2 Transport equations

A transport process is understood to be a general movement of mass, energy or other quantity from one location to another. An example of mass transport in packed liquid products is the convection that occurs during the heating or shaking of the package. Macroscopic regions of the liquid move with different speeds relative to one another and cause mixing to occur. With heating, a simultaneous transport of heat takes place along with mass transport. The convection of mass and energy takes place in liquid products during distribution of the packaging from the manufacturer to its final storage destination and during heating and cooling of the package.

Mixing by convection in viscous and solid packed products have very little or no practical significance. A special case is the mixing of particulate products by shaking, which gives results similar to convection. The most

important transport processes in solid, viscous and liquid filled products during the storage period are diffusion and thermal conductance. Mass transport by diffusion and energy transport by conductance have a common molecular basis. They are both affected by the unordered movement of molecules in the medium in which transport takes place. It is the vibration of atoms and groups of atoms, transmitted to neighbouring atoms which is responsible for conductance in solids. Unordered collisions between the mobile molecules of a liquid or gas are also a source of mass transport by diffusion. A further example of energy transport through packaging into the filled product is electromagnetic radiation. This radiation in the form of light can start chemical reactions or, in the case of microwaves, be transformed into heat and then further distributed through the packaging system by conduction or convection.

In addition to mass and energy, other quantities can also experience transfer. Flowing layers with different flow rates in a convection stream can influence one another. The slower flowing layer acts as a brake on the faster layer, while at the same time the faster layer acts to accelerate the slower one. The cause of this behaviour is the inner friction of the liquid appearing as a viscosity difference, which is a consequence of the attractive forces between the molecules. Viscosity can be explained as the transport of momentum. The viscosity of different media can be very different and thus plays an important role in transport processes.

For the mathematical description and understanding of transport processes, it is advantageous for their descriptions to have several common characteristics, regardless of the nature of the transport quantity, to allow them to be treated in a similar manner. Without knowledge of their fundamental causes at the molecular level, which corresponds to their historical development, transport processes can be described with help from quantities that can be quantitatively measured on a macroscopic level. One such quantity is that of flux.

Flux **J** is understood to be the amount of a quantity transported per unit time through a unit surface area. Flux is a vector for which a direction must be specified in addition to the quantity or contribution J. This is accomplished with the help of the unit vector **e** giving:

$$\mathbf{J} = J\mathbf{e} = \mathbf{J}_x + \mathbf{J}_y + \mathbf{J}_z = J_x\mathbf{i} + J_y\mathbf{j} + J_z\mathbf{k} \qquad 8.1$$

$\mathbf{J}_x$, $\mathbf{J}_y$, $\mathbf{J}_z$ are the vector components in the x, y and z axis directions of the coordinate system, J_x, J_y, J_z are their contributions and **i**, **j** and **k** are the corresponding unit vectors. Given a mass quantity m that is transported during time t through an area A, then let J represent the contribution of the mass flux. For energy transport, then J is the contribution of the energy flux with the dimensions J/m^{2}s (where J = joule).

In a very general sense, the flux of a quantity q is proportional at a given location to the gradient of the scalar field, $a(x, y, z)$, produced by the flux. Mathematically, one obtains the contributions of the three flux components with the gradient of $a(x, y, z)$ from the partial derivative of a at the coordinates

x, y, z. The gradient of $a(x, y, z)$ is a vector labelled ∇a (or del a). For the flux q results:

$$\mathbf{J}(q) = -b\nabla a = -b\left(\frac{\partial a}{\partial x}\,\mathbf{i} + \frac{\partial a}{\partial y}\mathbf{j} + \frac{\partial a}{\partial z}\mathbf{k}\right) \qquad 8.2$$

The location independent proportionality factor is designated b. The minus sign in eqn 8.2 shows that the flux goes in the direction of decreasing a-values. This means the quantity q 'flows' down the gradient.

The usefulness of the flow terms as common characteristics for transport processes allows them to illustrate such seemingly diverse processes as convection, momentum transport (viscosity), diffusion and heat conductance. To simplify the written expression, the flux components of the four processes are expressed in eqn 8.3 in the direction of one axis of the coordinate system:

$$\begin{aligned}
&\text{(a)}\quad \mathbf{J}_x\,(\text{mass, convection}) = \rho\frac{\partial x}{\partial t}\mathbf{i}\\
&\text{(b)}\quad \mathbf{J}_z\,(\text{momentum in x-direction}) = -\eta\frac{\partial v_x}{\partial z}\mathbf{k}\\
&\text{(c)}\quad \mathbf{J}_x\,(\text{mass, diffusion}) = -D\frac{\partial c}{\partial x}\mathbf{i}\\
&\text{(d)}\quad \mathbf{J}_x\,(\text{energy, conduction}) = -\kappa\frac{\partial T}{\partial x}\mathbf{i}
\end{aligned} \qquad 8.3$$

In eqn 8.3(a) ρ and $\partial x/\partial t$ are the contributions of the density and the velocity of the liquid in the x-direction. The material specific constants η, D and κ are for the viscosity, diffusion and thermal conductivity coefficients. The derivatives in the z and x directions, $\partial v_x/\partial z$, $\partial c/\partial x$ and $\partial T/\partial x$ are for the velocity components (in the x-direction), the concentration and temperature. A comparison of the four equations in eqn 8.3 shows the similarities between the expressions. These similarities are of great help in finding solutions for specific applications by using formally identical equations.

With respect to their individual historical development, the four expressions above, eqn 8.3(a) to (d), are quite separate. While the above representation of momentum can be traced back to Newton, the expression for heat conductance was first derived by the mathematician and physicist Fourier at the beginning of the nineteenth century. The physiologist Fick, who was concerned with measuring the transport of oxygen in blood, recognised the analogy of diffusion to heat conductance and published in 1855 the diffusion equation now known as Fick's first law, eqn 8.3(c). The relationships between the different processes at the molecular level was first recognised by Einstein and other physicists and led to quantitative relationships between material specific constants, in particular between D and η, which are important for calculating their respective contributions.

During a diffusion process, e.g., the migration of an additive from a plastic into the atmosphere or into the foodstuff, a change in the concentration

of the diffusing substance takes place at every location throughout the plastic. The mass flux caused by diffusion is represented by a vector quantity **J** whereas the concentration c and its derivative of time t are scalar quantities. The scalar c and the flux vector **J** are mathematically connected with help of the scalar or dot product of the divergence operator labelled ∇ and the gradient ∇a. The consequence of this, according to eqns 8.2 and 8.3(c) is the following equation:

$$\frac{\partial c}{\partial t} = -D\nabla\nabla c = D\nabla^2 c = D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} + \frac{\partial^2 c}{\partial z^2}\right) \qquad 8.4$$

Equation 8.4 is known as Fick's second law of diffuson.

The immediate result of the above discussion is that the diffusion equation can be transformed into the differential equation for heat conduction by substitution of c by T and D by κ. This analogy has the consequence that practically all mathematical solutions of the heat conductance equation are applicable to the diffusion equation. The analogy between diffusion and conductance should be kept in mind in the following discussion although the topic here will be mainly the treatment of the diffusion equation, which represents the most important process of mass transport. If diffusion and convection currents are similar in magnitude then the total transport is the sum of all the individual contributions. While convection currents caused by mild shaking of low viscosity liquids lead to a much faster mixing than by diffusion processes, the influence of convection decreases with increasing viscosity (e.g. in mayonnaise).

A decrease in concentration in addition to physical transport effects can also be the consequence of a chemical reaction taking place. The concentration decrease per unit time caused by chemical reaction is defined as the rate of reaction r and is a function of the concentrations present at the reaction site:

$$r = \frac{\mathrm{d}c}{\mathrm{d}t} = kc^n \qquad 8.5$$

The proportionality factor k is the reaction rate constant. The exponent n, usually 1 or 2, specifies the order of the reaction.

The simultaneous occurrence of reaction and transport processes can be represented by adding the contributions together and, for the total concentration decrease over time at a given point $P(x, y, z)$ in the media considered by the general transport equation one obtains:

$$-\left|\frac{\partial c}{\partial t}\right|_{\text{total}} = -D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} + \frac{\partial^2 c}{\partial z^2}\right)$$

$$+\left(v_x\frac{\partial c}{\partial x} + v_y\frac{\partial c}{\partial y} + v_z\frac{\partial c}{\partial z}\right) + kc^n \qquad 8.6$$

which results as the sum of diffusion, convection and reaction. A typical example of transport and reaction occurring during storage of a package is the spoilage of fat-containing food by oxidation with oxygen transported from the atmosphere through the packaging.

8.3 Solutions of the diffusion equation

For interactions between packaging and product the above descriptions of both material transport processes by diffusion and convection as well as the simultaneous chemical reactions come into consideration. The general transport equation (8.6) is the starting point for solutions of all specific cases occurring in practice. Material loss through poorly sealed regions in the package can be considered as convection currents and/or treated as diffusion in the gas phase.

A solution of the general equation delivers the concentration contribution at every point in time and at every location throughout the volume considered, thus $c = c(x, y, z, t)$. But the general form of the transport equation as a second order partial differential equation has no simple solution. Analytical solutions have been derived however, for numerous special cases. For solutions involving complicated cases, simplifying approximations are used or numerical solutions are carried out. Since eqn 8.6 is composed of the sum of its members, it is logical to consider next the contribution of each individual component. The fastest step in a group of simultaneous overlapping processes is the most important. If the overall process is the result of a series of processes taking place one after another, for example, as a consequence of transport processes through one or more boundary surfaces, then the slowest step of the process determines the rate of the overall process. Mass transport by diffusion is without doubt the most important process throughout the storage of packed products. The discussion of the solution begins then with the diffusion equation 8.4.

The diffusion coefficient D can be assumed to be constant or practically constant for most cases of practical interest. In addition, simplified solutions for diffusion along the x-axis can be used instead of the general solution, except for some particular cases. This greatly simplifies presentation of the problem and the resulting equation for diffusion is:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \qquad 8.7$$

Steady state conditions, Fick's first law

The simplest case to solve is when the concentration stays constant over time in the polymer. Under such steady state conditions, $\partial c/\partial t = 0$, as in the case of permeation, the equation of diffusion (8.4) turns to Fick's first law.

This particular case exists, for example, in the diffusion of a substance

through a film with thickness d if the concentrations c_1 and c_2 at the two surfaces at $x = 0$ and at $x = d$ remain constant (stationary case). Integrating eqn 8.3(c) leads to the amount of the flux J through the film:

$$J = D \cdot \frac{c_1 - c_2}{d} = P \cdot \frac{\Delta p}{d} \qquad 8.8$$

where Δp is the partial pressure difference between both sides of the film, $P = D \cdot S$ is the permeability coefficient and S is the solubility coefficient of the gas in the film.

Concentration is variable with time, Fick's second law
Most interactions involving mass transfer between the packaging and food behave under non-steady state conditions and are referred to as migration. A number of solutions exist by integration of the diffusion equation 8.7 that are dependent on the so-called initial and boundary conditions of special applications. Many solutions are taken from analogous solutions of the heat conductance equation that has been known for many years:

$$\frac{\partial T}{\partial t} = \kappa \frac{\partial^2 T}{\partial x^2} \qquad 8.9$$

which can be directly applied to diffusion problems. The standard reference work on the mathematics of diffusion is by Crank (1975), from which most of the solutions contained in this chapter have been taken. The solutions themselves have their origins in the older and more comprehensive reference work on heat conductance in solids by Carslaw and Jaeger (1959).

8.3.1 Diffusion in a two-phase system

Plastic monolayer in contact with liquid food
One of the most important migration problems occurs if a liquid food or food simulant F with the volume V_F and density ρ_F comes in contact with a plastic layer P of thickness d_P and density ρ_P. The mass transfer takes place across an interface with area A between two different media with different characteristics, e.g., with different diffusion coefficients D_P and D_F of the migrant. If the value of a quantity is desired, for example, the concentration of the substance transported across the interface in one of the two media, then a mass balance must be considered that takes into account the ratio of the contact surface area and the volume of the corresponding medium. The model describing this process is based on the following assumptions:

1. A component distributed homogeneously in the matrix P with an initial concentration $c_{P,0}$ is dissolved in F at the contact interface between P and F and subsequently diffuses into the liquid. It is assumed that there is no boundary resistance for the transfer of the migrant between P and F. In so doing there is a decrease in concentration in the region of the contact

surface which leads to further transport of substance from the matrix P to the contact surface.

2. The mass transfer, controlled mainly by diffusion taking place in the plastic during storage, is several orders of magnitude lower than diffusion in the liquid phase. The difference is even greater when mixing (convection) occurs by shaking, e.g., during transport. It can be assumed that the concentration of the migrating component in F, $c_{F,t}$, is dependent on time t but not on the distance x from the contact surface.
3. It is assumed that the interaction between P and F is negligible and no swelling of P by uptake of F occurs during the migration process.
4. The total amount of the migrant in P and F is assumed constant during the migration process.
5. At equilibrium a constant distribution of the migrant between P and F takes place that is independent of its concentration. For relatively small concentrations (< 1%) this approximate assumption is fulfilled and one defines the partition coefficient $K_{P,F}$ as a constant ratio of the migrant concentration in the packaging material, c_P(w/w), to the concentration in the food, c_F(w/w), multiplied by the density ratio:

$$K_{P,F} = \frac{c_P}{c_F}\frac{\rho_P}{\rho_F} \qquad 8.10$$

   The partition coefficient is one of the key parameters needed for the solution of the diffusion equation.
6. The second important quantity influencing the mass transport is the diffusion coefficient D_P of the migrant in P. For relatively low concentration ranges D_P is assumed to be constant.
7. The mass transport is assumed to occur in the x direction perpendicular to the contact surface. Even though the geometry of the packaging/food system influences the amount of mass transport occurring, it is of minor significance for most practical cases.
8. All above assumptions are valid for mass transfer in the reverse direction as well. This means the migration of component from the food F into the P is also described. By considering the corresponding initial conditions the mathematical solution of the problem results in the same form.

The dimensionless solution of the diffusion equation

One type of solution is in the form of infinite series from which often only few members are used. With the dimensionless quantities α and T:

$$\alpha = \frac{1}{K_{P,F}}\frac{V_F}{V_P} = \frac{1}{K_{P,F}}\frac{d_F}{d_P} \quad \text{and} \quad T = \frac{D_P t}{d_P^2} \qquad 8.11$$

one obtains, for the mass transfer by diffusion of a component from P into a well mixed liquid or migration in the opposite direction, the general expression from Crank:

$$\frac{m_t}{m_\infty} = 1 - \sum_{n=1}^{\infty} \frac{2\alpha(1+\alpha)}{1+\alpha+\alpha^2 q_n^2} \exp(-q_n^2 T) \qquad 8.12$$

Equation 8.12 is a solution of the diffusion equation 8.7 for this model where m_t is the mass diffusing up to time t from P through the boundary surface A into F or in the opposite direction and m_∞ is the amount which has migrated at equilibrium. The parameters q_n in the series are the positive roots of the trigonometric identity $\tan q_n = -\alpha q_n$. Several values of this parameter for various α and n are given in Table 8.1. The values of q_n lie between $n\pi$ (for $\alpha = 0$) and $(n - 1/2)\pi$ (for $\alpha = \infty$). For $\alpha << 1$ then $q_n \cong n\pi/(1+\alpha)$, and for the remaining α values $q_n \cong [n - \alpha/2(1+\alpha)]\pi$. The solutions of eqn 8.12 converge rapidly for long diffusion times, while for short times, e.g., at the beginning of diffusion ($T \cong 0.001$), approximately 50 terms are needed.

Even though the above equation is no obstacle for today's PCs, it is more convenient for short times to use the second type of solution which is based on the error function:

$$\frac{m_t}{m_\infty} = (1+\alpha)[1 - \exp(z^2)\,\mathrm{erfc}\,(z)] \qquad 8.13$$

with:

$$z = \frac{T^{1/2}}{\alpha} = \frac{K}{d_F}(D_P t)^{1/2} \qquad 8.14$$

In Table 8.2 the values for the function contained in brackets in eqn 8.13 are given as:

$$F(z) = 1 - \exp(z)^2\,\mathrm{erfc}\,(z) \qquad 8.15$$

Equation 8.13 is particularly suitable for $T < 1$ and $\alpha < 100$.

Table 8.1 Roots of $\tan q_n = -\alpha q_n$

α	q_1	q_2	q_3	q_4	q_5	q_6
∞	1.5708	4.7124	7.8540	10.9956	14.1372	17.2788
9.0000	1.6385	4.7359	7.8681	11.0057	14.1451	17.2852
4.0000	1.7155	4.7648	7.8857	11.0183	14.1549	17.2933
2.3333	1.8040	4.8014	7.9081	11.0344	14.1674	17.3036
1.5000	1.9071	4.8490	7.9378	11.0558	14.1841	17.3173
1.0000	2.0288	4.9132	7.9787	11.0856	14.2075	17.3364
0.6667	2.1746	5.0037	8.0385	11.1296	14.2421	17.3649
0.4286	2.3521	5.1386	8.1334	11.2010	14.2990	17.4119
0.2500	2.5704	5.3540	8.3029	11.3349	14.4080	17.5034
0.1111	2.8363	5.7172	8.6587	11.6532	14.6870	17.7481
0.000	3.1416	6.2832	9.4248	12.5664	15.7080	18.8496

Table 8.2 Table of different error function forms

z	erf z	erfc z	$F(z)$
0.00	0.000000	1.000000	0.00000
0.05	0.056372	0.943628	0.05401
0.10	0.112463	0.887537	0.10354
0.15	0.167996	0.832004	0.14908
0.20	0.222703	0.777297	0.19098
0.25	0.276326	0.723674	0.22965
0.30	0.328627	0.671373	0.26540
0.35	0.379382	0.620618	0.29850
0.40	0.428392	0.571608	0.32921
0.45	0.475482	0.524518	0.35775
0.50	0.520500	0.479500	0.38431
0.55	0.563323	0.436677	0.40907
0.60	0.603856	0.396144	0.43220
0.65	0.642029	0.357971	0.45382
0.70	0.677801	0.322199	0.47407
0.75	0.711156	0.288844	0.49306
0.80	0.742101	0.257899	0.51090
0.85	0.770668	0.229332	0.52767
0.90	0.796908	0.203092	0.54347
0.95	0.820891	0.179109	0.55836
1.00	0.842701	0.157299	0.57242
1.10	0.880205	0.119795	0.59827
1.20	0.910314	0.089686	0.62146
1.30	0.934008	0.065992	0.64236
1.40	0.952285	0.047715	0.66126
1.50	0.966105	0.033895	0.67841
1.60	0.976348	0.023652	0.69405
1.70	0.983790	0.016210	0.70834
1.80	0.989091	0.010909	0.72144
1.90	0.992790	0.007210	0.73349
2.00	0.995322	0.004678	0.74460
2.10	0.997021	0.002979	0.75488
2.20	0.998137	0.001865	0.76441
2.30	0.998857	0.001143	0.77326
2.40	0.999311	0.000689	0.78150
2.50	0.999593	0.000407	0.78919
2.60	0.999764	0.000236	0.79640
2.70	0.999866	0.000134	0.80310
2.80	0.999925	0.000075	0.80950
2.90	0.999941	0.000041	0.81540
3.00	0.999978	0.000022	0.81540

Solutions taking the mass balance into account

For migration from P into F the total amount $m_{P,0}$ of the migrant is contained in P at time $t = 0$ and the mass balance is expressed as:

$$V_{F,\infty}\, c_{F,\infty} + V_P\, c_{P,\infty} = V_P\, c_{P,0} = m_{P,0} \qquad 8.16$$

The amount of substance transferred into the food at equilibrium, $m_{F,\infty} = V_F \cdot c_{F,\infty}$ is obtained by combining eqns 8.10 and 8.11:

$$m_{F,\infty} = V_P\, c_{P,\infty} = \frac{V_P\, c_{P,0}}{1/\alpha + 1} = m_{P,0}\, \frac{\alpha}{1+\alpha} \tag{8.17}$$

and related to $m_{P,0}$ the fraction of the total amount is given by:

$$\frac{m_{F,\infty}}{m_{P,\infty}} = \frac{\alpha}{1+\alpha} \tag{8.18}$$

The fraction of migrant diffused from F into P up to time t, from $m_{F,0} = V_F c_{F,0}$ and the fraction migrated from P into F up to time t, from $m_{P,0} = V_P c_{P,0}$ are:

$$\frac{m_{P,t}}{m_{F,0}} = \frac{m_{P,t}}{m_{P,\infty}}\, \frac{1}{1+\alpha} \tag{8.19}$$

and

$$\frac{m_{F,t}}{m_{P,0}} = \frac{m_{F,t}}{m_{F,\infty}}\, \frac{\alpha}{1+\alpha} \tag{8.20}$$

With eqns 8.12 and 8.20, taking the mass balance into account, the migrated amount $m_{F,t}$ through the contact surface A during time t can be calculated as follows (Piringer, 2000):

$$\frac{m_{F,t}}{A} = c_{P,0}\rho_P d_P \left(\frac{\alpha}{1+\alpha}\right)\left[1 - \sum_{n=1}^{\infty} \frac{2\alpha(1+\alpha)}{1+\alpha+\alpha^2 q_n^2} \exp\left(-D_P t \frac{q_n^2}{d_P^2}\right)\right] \tag{8.21}$$

Equation 8.22 represents the simplified form of eqn 8.21 for $\alpha >> 1$:

$$\frac{m_{F,t}}{A} = c_{P,0}\rho_P d_P \left[1 - 2\sum_{n=1}^{\infty} \frac{1}{q_n^2} \exp\left(-D_P t \frac{q_n^2}{d_P^2}\right)\right] \tag{8.22}$$

where $q_n = (2n-1)\pi/2$.

Equation 8.23 is an alternative migration equation for small t-values using the error function:

$$\frac{m_{F,t}}{A} = c_{P,0}\rho_P d_P \alpha \left[1 - \exp\left(\frac{D_P t}{d_P^2 \alpha^2}\right) \mathrm{erfc}\left(\frac{\sqrt{D_P t}}{d_P \alpha}\right)\right] \tag{8.23}$$

if $m_{F,t}/m_{F,\infty} \leq 0.5$.

Equation 8.24 is a simplified migration equation for $K_{P,F} \leq 1$ and relatively small t-values, for which an infinite thickness of P can be assumed:

$$\frac{m_{F,t}}{A} = \frac{2}{\sqrt{\pi}} c_{P,0}\rho_P (D_P t)^{1/2} \tag{8.24}$$

The maximum amount of migration derived from the mass balance is:

$$\frac{m_{F,\infty}}{A} = c_{P,0}\rho_P d_P\left(\frac{\alpha}{1+\alpha}\right) \qquad 8.25$$

Two typical examples of food packages with the corresponding values of the required parameters are shown in Table 8.3, together with the results obtained with eqns 8.21–8.24:

A = 600 cm^2, d_P = 0.02 cm, ρ_P = 1 g/cm^3, t = 864000 s (10 d),
$c_{P,0}$ = 1000 mg/kg, D_P = 1.0E–10 cm^2/s, $K_{P,F}$ = 1.

The maximum amounts $m_{F,\infty}/A$ calculated with eqn 8.25 are 1.98 and 1.92 mg/dm^2, respectively. As one can see from this comparison, even eqn 8.24 is very precise for applications under certain conditions. But it is useful also because of its simplicity in many fast estimations, giving at least the correct order of magnitude for the amount of migration.

Equations 8.11–8.25 given above have found applications in several publications and it is a highly recommended exercise to compare their power by solving a set of problems as shown at the end of this section. All examples can be calculated with the help of a pocket calculator and as finally seen, in many cases a very simple and fast calculus gives satisfactory results for practical applications.

Material transport from a liquid assumed to be well mixed, into packaging, and migration from packaging into a liquid, both vary proportionally to the square root of time and the square root of the diffusion coefficient. While in the beginning phase (approximation equation is only valid for small z values, meaning short times) the mass transfer of a compound from F into P is proportional to $K_{P,F}$, but the migration from P into F is independent of $K_{P,F}$. The partition coefficient plays a deciding role in the sorption (solution) of a substance in the packaging layer in contact with the liquid. This leads to the total amount of sorbed material being concentrated in a thin layer of packaging material in contact with the liquid and the transport process in the initial stage is independent of the material thickness.

8.3.2 Plastic monolayer in contact with viscous or solid food

For viscous or solid food the simplifying assumption of a well-mixed liquid is abandoned and finding an analytical solution for this two phase system

Table 8.3 Comparison of the results obtained with different equations

Calculated with equation	V_F = 1000 cm^3, α = 83 $M_{F,t}/A$ (mg/dm^2)	V_F = 300 cm^3, α = 25 $M_{F,t}/A$ (mg/dm^2)
8.21	1.042	1.030
8.22	1.047	1.047
8.23	1.049	1.049
8.24	1.049	1.049

becomes more complicated (Reid *et al*., 1980; Vergnaud, 1991). One must take into account the diffusion coefficient of the migrant in the solid foodstuff, which is often in the same range as in the packaging material. This has been done in a simplified way in the following expression derived from eqn 8.24:

$$\frac{m_{F,t}}{A} = \frac{2}{\sqrt{\pi}} \cdot c_{P,0} \cdot \rho_P \cdot \frac{\beta}{1+\beta} \cdot \sqrt{D_P \cdot t}, \text{ with } \beta = \frac{1}{K_{P,F}} \cdot \sqrt{\frac{D_F}{D_P}} \qquad 8.26$$

For $D_F >> D_P$ and $K_{P,F} \leq 1$ we obtain eqn 8.24. If the diffusion coefficients in the packaging and in the food are approximately equal, the partition coefficient, $K_{P,F}$ determines transport through the system. The packaging determines the rate of the whole process. If the migrant dissolves much better in the food than in the packaging, that means $K_{P,F} \leq 1$ and the food determines the rate of the whole process. But if the migrant dissolves much better in the packaging than in the food, $K_{P,F} >> 1$. If $D_F < D_P$ the mass transport is determined by the diffusion coefficient in the food, D_F and the partition coefficient, $K_{P,F}$. This leads to the build up of a concentration profile in the foodstuff. An exact analytical solution of the differential equation that takes into consideration the diffusion in food and finite values for V_P and V_F is not available and in consequence the application of numerical methods is necessary.

Food/packaging interactions include the uptake of major food components, such as fats and oils or water, by the packaging material. If great enough, such absorption can cause swelling and changes in the properties of the polymer. This swelling can lead to increased migration of additives from the polymer because their diffusion coefficients increase by several orders of magnitude. Other consequences of swelling are structural changes that occur in the polymer, which may weaken the mechanical properties of the packaging. The possibility of swelling is an important consideration in food/packaging compatibility.

8.3.3 Migration from multilayer packaging into food

In the whole of the above discussion an actual practical situation is reduced to some kind of an idealised plastic migrant system in which the plastic material is a single layer structure with a finite thickness and there is a homogeneously distributed concentration of the migrant. That means the initial and boundary conditions for analytical solution of the diffusion equation are fulfilling the assumptions for eqn 8.21. On the other side, a monolayer plastic in contact with a solid food is the first example of a multilayer system. In the general case of structures with more then one layer, or variable diffusion coefficients in different regions of the matrix, only numerical mathematics leads to the desired result. Basically, these imply restricting the solution of the diffusion problem to a set of grid points, conveniently distributed

within the integration domain, and approximating the derivatives involved by discrete schemes. Such an approach leads to a system of linear equations, having as unknowns the solution values at the grid points. The linear system can be solved in principle by any classical method, even though, for the sake of computational efficiency, more specialised methods are recommended. Such numerical discretisation methods affect the essence of the physical model much less than analytical approximations do, allowing for much more complex diffusion problems to be treated.

In a multilayer polymer system with n layers each layer $k = 1, 2, \ldots n$ has its diffusion coefficient D_k, density ρ_k, thicknes d_k and the laminate is in contact with a foodstuff medium of mass m_F and density ρ_F. In addition to the partition coefficient, $K_{P,F}$, of the migrant between the plastic layer in contact with food F, the $n - 1$ partition coefficients, $K_{k,k+1}$, of the migrant between two adjacent layers must also be considered. The migration of a compound is governed in each layer by the partial differential equation 8.7 with its corresponding D_k. Solving this problem is possible only with adequate computer programs.

In the following section a simple treatment will be given for the case of a packaging material made of two plastic layers P_A and P_B. The migrant is initially solved in P_A with a high D_P-value. The second layer P_B is between P_A and the food F. In P_B the migrant diffuses with a much smaller D_P-value, $D_{PB} << D_{PA}$. Steady state permeation which follows Fick's first law has been previously described in eqn 8.8. But assuming at the beginning a constant value $c_{P,1}$ of the migrant at the outer surface ($x = 0$) of the food contact layer P_B and the value $c_{P,0} = 0$ at $t = 0$ inside of this layer P_B, then a non-steady state of diffusion will take place leading to a change in the concentration $c_{P,t}$ within the food contact layer P_B. The resulting amount of mass diffusing through P_B up to time t is then given as:

$$m_t = A\, d_P\, C_{P,1} \left(\frac{D_P z}{d_P^2} - \frac{1}{6} - \frac{2}{\pi^2} \sum_{n=1}^{\infty} \left[\frac{(-1)^n}{n^2} \exp(-D_P n^2 \pi^2 t / d_P^2) \right] \right) \qquad 8.27$$

This equation becomes asymptotic to the straight line:

$$m_t = \frac{A D_P c_{P,1}}{d_P} \left(t - \frac{d_P^2}{6 D_P} \right) \qquad 8.28$$

as $t \rightarrow \infty$. The intersection of this straight line with the t-axis at location Θ is:

$$\Theta = \frac{d_P^2}{6 D_P} \qquad 8.29$$

This is the time lag equation which was used by Barrer for determining the diffusion coefficient using permeation measurements. The steady state permeation flux is given by the slope of the straight line, eqn 8.28:

$$J = \frac{m_t}{A\,t} = D_{\mathrm{P}}\,\frac{c_{\mathrm{P,l}}}{d_{\mathrm{P}}} \qquad 8.30$$

This expression is identical to eqn 8.8 for $c_{P,2} = 0$.

Diffusion through a barrier layer is a special case of diffusion through a laminate composed of several layers with different thicknesses and diffusion coefficients. Mathematical treatment of the non-steady state case is complicated. But the steady state permeation case allows the overall transport to be simply treated. Let n films with thickness d_{P1}, d_{P2}, ..., d_{Pn} with corresponding diffusion coefficients D_{P1}, D_{P2}, ..., D_{Pn} be bound together in a laminate. Because in steady state, the flux J of the diffusing substance is the same through each individual layer of the laminate, one obtains an expression for the concentration gradient:

$$\Delta \mathrm{C} = \frac{J\,d_{\mathrm{P,l}}}{D_{\mathrm{P,l}}} + \frac{J\,d_{\mathrm{P,2}}}{D_{\mathrm{P,2}}} + \ldots + \frac{J\,d_{\mathrm{P},n}}{D_{\mathrm{P},n}} = (R_1 + R_2 + \ldots R_n)\,J \qquad 8.31$$

with the resistance $R_1 = d_{P1}/D_{P1}$ etc. The total resistance related to the diffusion is then the sum of the individual resistances and the total flux is practically determined by the layer with the smallest diffusion coefficient. Therefore the presence of a thin barrier layer with low D_P can determine the permeation characteristics of the whole multilayer structure.

In many cases one layer in a laminate is selectively permeable to some substances, e.g., organic compounds, and impermeable to metals, salts and other electrolytes. A typical example is packaging made of paper or board coated with polyethylene for contact with foods. The polyethylene layer is then designated as a functional barrier for metals and electrolytes.

8.3.4 Diffusion plus reaction

When a first-order irreversible chemical reaction (e.g. oxygen absorption and oxidation) takes place simultaneously with diffusion in food, then one obtains the following expression from the general mass transfer equation 8.6:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} - kc \qquad 8.32$$

where k is the reaction rate constant. If the reaction takes place in a relatively thin layer of F near P, then one can consider F as a half open medium (infinitely thick). This leads to a considerable simplification of the mathematical treatment. Furthermore, letting $c_{F,0}$ be a constant surface concentration one obtains the reacted amount $m_{F,t}$ up to time t:

$$m_{\mathrm{F},t} = Ac_{\mathrm{F},0}\,(D_{\mathrm{F}}/k)^{1/2}\left[\left(k\,t + \frac{1}{2}\right)\mathrm{erf}\,(k\,t)^{1/2} + (kt/\pi)^{1/2}\,e^{-\mathrm{kt}}\right] \qquad 8.33$$

For large $k{\cdot}t$ values the erf $(k{\cdot}t)^{1/2}$ goes to one and:

$$m_{\mathrm{F},t} \rightarrow Ac_{\mathrm{F},0}\,(D_{\mathrm{F}}/k)^{1/2}\left(t + \frac{1}{2k}\right) \qquad 8.34$$

which means $m_{F,t}$ increases linearly with t. For very small values of $k \cdot t$ one obtains:

$$m_{F,t} = Ac_{F,0}\,(D_F/k)^{1/2}\left(1 + \frac{1}{2}kt\right)(D_F t/\pi)^{1/2}$$

$$\cong Ac_{F,0}\,(D_F/k)^{1/2}\left(1 + \frac{1}{2}kt\right)(D_F t)^{1/2} \qquad 8.35$$

When $k \to 0$ only diffusion without reaction takes place:

$$m_{F,t} \cong Ac_{F,0}(D_F t)^{1/2} \qquad 8.36$$

Because the diffusion process and the reaction occur in the same medium F the ratio of A/V_F does not come into consideration.

8.3.5 Non-Fickian processes

The preceding discussions hold true only if the diffusion and partition coefficients are constants. However, in some cases D_P and $K_{P,F}$ can be functions of a concentration gradient in the polymer and can vary with time. If the migrant causes extensive swelling, diffusion can no longer be described by the concentration dependence from Fick's second law. At very low migrant concentrations in the polymer, the migration rate may no longer be proportional to its concentration in the polymer. For example, active sites within the polymer matrix may tend to bind a migrant, thus decreasing the possibility of its transfer from the polymer to the food contacting phase. In many cases, the observed transfer of additives is due not to migration but to removal of material from the polymer surface in contact with the food. During manufacturing of the packaging material, some of the additives are forced to the surface of the polymer. Subsequent contact with food, often in the initial period of contact (e.g. pasteurisation), removes this surface layer of additives. After removal of this layer, a much slower, diffusion-controlled migration occurs. In the case of paper and board the transfer of migrants to foods is controlled by sorption isotherms and diffusion. Nevertheless, one can determine apparent diffusion coefficients, which are comparable to those in polyolefins.

8.4 The diffusion coefficient

In order to use eqn 8.21 in practical cases the availability of data for two fundamental constants is needed: (i) the partition coefficient, $K_{P,F}$, of the migrating compound between the polymer P and the foodstuff or simulating liquid F and (ii) the diffusion coefficient, D_P, of the migrant in P. So far upper limits for migration amounts are needed from regulatory standpoints, predictions of 'worst case' scenarios can start with the assumption of good solubility of the migrant in F and consequently $K_{P,F} = 1$ can be used. Much

more complicated is the prediction of an adequate value for D_P. Whereas the diffusion coefficients in liquid foods lie in a relative narrow range between 10^{-5} to 10^{-6} cm^2/s, the D_P-values scatter between many orders of magnitude below 10^{-6} cm^2/s.

Much work has been done in correlating polymer structure with migrant structure to predict migrant diffusion in the polymer. From a practical viewpoint, most of this work has limited value in predicting the diffusion behaviour of substances in food packaging systems because of the complex nature of the system (Mercea, 2000). Thus, at present, the only practicable way to use modelling for quality assurance is to start with much simpler migration estimation procedures. With this in mind a first solution for the estimation of D_P was to correlate in a very simple manner this coefficient with the relative molecular mass, M_r, of the migrant, with a polymer matrix specific parameter and with the absolute temperature T. This approach has already been used (Piringer, 1994; Limm and Hollifield, 1996). To pursue the goal of obtaining a simple formula for the estimation of D_P, which does not rely on experimental diffusion and/or migration data, an equation for D_P in a reference amorphous polyolefin material was developed (Brandsch *et al.*, 2000). Following this approach the following equation resulted:

$$D_P = D_0 \exp\left(A_P - 0.1351\, M_r^{2/3} + 0.003\, M_r - \frac{10454\, R}{RT} \right) \qquad 8.37$$

with

$$A_P = A'_P - \tau/T \qquad 8.38$$

where $D_0 = 1$ m^2/s $= 10^4$ cm^2/s. M_r, T and R are the relative molar mass of the migrant, the temperature in kelvin and the gas constant, respectively. The dimensionless parameter A_P has the role of a 'conductance' of the polymer matrix towards the diffusion of the migrant. Higher values of A_P in such polymers as polyethylene lead to increased D_P values, while in stiff chain polymers, such as polyesters and polystyrene, lower A_P values account for smaller diffusion coefficients for the same migrant. This equation can be used for $M_r \leq 4000$ daltons.

The polymer specific term A_P can also be a function of temperature, as shown in eqn 8.38. A'_P is an athermal term. The constant τ, together with the constant 10454 in eqn 8.37, both with the formal dimension of temperature, account for the diffusion activation energy, E_A. The term $10454R = 10454 \times 8.31451 = 86.9$ kJ/mol $= E_A$ is the reference activation energy of diffusion, which resulted for amorphous polyethylene. By taking into account many diffusion coefficients for a variety of migrants and polymer matrices it is concluded that $\tau = 0$ and the reference activation energy represents a great many plastics, for example, low density polyethylene (LDPE). For other important groups of plastics relevant to food packaging, e.g., high density polyethylene (HDPE), polypropylene (PP) and polyethylene terephthalate (PET), a higher activation energy is generally observed. A good mean value

for these matrices is obtained with $E_A = (10454 + 1577)R = 100$ kJ mol^{-1}, which requires $\tau = 1577$.

In order to calculate migration rates with a sufficient safety margin from the regulatory standpoint it is possible to match the parameter A_P in eqn 8.37, as mentioned above, to yield a 'worst case' value, A_P*, which leads to a corresponding D_P* instead of the real D_P. Due to the scatter of experimental values, the use of $D_P^* \geq D_P$ can avoid underestimations with a certain statistical degree of assurance. The greater the scatter, the higher the upper limit for D_P* must be set. This statistical assurance is a matter of convention and can be established from a regulatory point of view. A consequence of the above consideration is a periodic change of A_P* values depending on available data collections. In Table 8.4 values of A'_P and τ, as well as upper limits, A'_P*, are given for different polymers. In order to work only with a minimum number of specific variables, τ was fixed in a first approximation at $\tau = 0$ and $\tau = 1577$ which give corresponding activation energies of E_A = 87 and 100 kJ/mol, respectively. Although each migrant may have a small specific contribution to the A'_P-and E_A-value, the main contribution to these values comes from the specific structure of the polymer matrix (Brandsch *et al.*, 2002; Begley *et al.*, 2005).

For polyolefins another semi-empirical diffusion model has been developed, by Limm and Hollifield (1996). From their studies it is possible to arrive at the following relationship:

$$D_P = D_0 \cdot \exp\left(\alpha \cdot M_r^{1/2} - K \cdot \frac{M_r^{1/3}}{T} \right) \qquad 8.39$$

D_0, α and K are empirical constants determined from experimental diffusion data. These values for polyolefins are given in Table 8.5. The constant ln D_0

Table 8.4 Mean values of A'_P and 'worst-case' values A'_P*

Polymer	A'_P	A'_P*	τ
LDPE	10.0	11.7	0
HDPE	10.0	13.2	1577
PP	9.4	12.4	1577
PET	2.2	6.35	1577
PEN	–0.34	3.7	1577
PS	–2.8	–0.7	0
HIPS	–2.7	0.1	0
PA (6,6)	–1.54	1.9	0

Table 8.5 Empirical constants for the diffusion model of Limm and Hollifield (1996)

Polymer	K	α	ln D_0
PP	1335.7	0.597	–2.10
HDPE	1760.7	0.819	0.90
LDPE	1140.5	0.555	–4.16

is a polymer-specific term, similar to the A_P-value in eqn 8.37. The main limitation in estimating migration for legislative purpose is underestimation in some cases.

8.5 The partition coefficient

Most additives from packaging materials for which modelling is applicable are organic substances with low solubility in water and aqueous food/simulants, but good solubility in fat and fatty food/simulants. The consequences of this behaviour are partition coefficients, $K_{P,F} \leq 1$ for fatty foods in contact with polymers. In many cases the food contact layer is made of a non-polar polyolefin (PO) and the partition coefficient of an organic migrant between PO and an organic solvent or fat is $K_{P,F} < 1$. With increasing polarity of the liquid food or simulant, the partition coefficient increases until extreme values for pure water, where $K_{P,F} >> 1000$. The typical range for partition coefficients between PO and actual food is $1 \leq K_{P,F} \leq 1000$. This explains why $K_{P,F} = 1$ and $K_{P,F} = 1000$ have been proposed as 'worst case' values for migration modelling if upper limits are needed for safety. There are many approaches to predicting partition coefficients, but even a summary description of them is beyond the limits of this chapter (Baner, 2000).

8.6 Possibilities and limitations of migration modelling

Migration modelling is already allowed to be used as an additional tool for verification of compliance with the specific migration limits, as shown in the European Commission Directive 2002/72/EC. Detailed instructions, together with limitations of the applicability, are given in the European Commission Practical Guide (2004). For practical applications of modelling specifically tailored and user-friendly computer programs are available on the market (MIGRATEST Lite (FABES GmbH, Munich, Germany) (http://wwwfabes-onlinede); MIGRAPAS (Specialchem S. A., Paris, France) – online version of MIGRATEST (http://www.specialchem.com); MULTITEMP and MULTIWISE (INRA, Reims, France) available as freeware (http://www.inra-fra/internet/Produits/securite-emballage/pagefr.htm#4.%20multi); EXDIF (Office Fédéral de la Santé Publique, Bern, Switzerland) (http://www.bag.admin.ch/verbrau/gebrauch/info//f/exdif.htm); SML (AKTS AG, Switzerland) (http://www.akts.com)). Actual modelling of migration from plastic monolayers into liquid food/simulants, based on the analytical solution of the diffusion equation 8.21, is recognised as an official tool for compliance checking (Directive 2002/72/EC) within the application range shown in the EU Practical Guide, referred to above. But for the many further applications of modelling for multilayers made of different materials, in contact with all

types of food, including solids, computer programs are also available. Their general official recognition as additional tools is a process which will be achieved step by step in the future. The underlying physical principles summarised in this chapter emphasise that all such migration phenomena are predictable.

8.7 Exercises

Example 1 Ten 4 cm diameter circular 200 μm thick plastic film pieces are mounted on a stainless steel wire and placed in a glass vial containing 100 ml solvent. What percentage of the additives initially contained in the plastic migrate into the liquid over the 24 hour period (D_P = 2.10E-10 cm^2/s)? Note that the plastic additives are readily soluble in the solvent, the solvent has low viscosity and the solvent does not swell the plastic. Because the additives are readily soluble in the solvent $K_{P,F} \cong 1$ can be assumed in eqn 8.10. The volume of the plastic is:

$$V_P = 10 \cdot \pi \cdot r^2 \cdot h = 10 \cdot \pi \cdot 2^2 \text{ cm}^2 \cdot 0.02 \text{ cm} = 2.51 \text{ cm}^3$$

Using eqn 8.11 one gets:

$$\alpha = \frac{1}{K} \cdot \frac{V_F}{V_P} = \frac{1}{1} \cdot \frac{100}{2.51} = 39.8$$

Given the two sided contact of the liquid with the plastic 0.5 d_P = 0.5·0.02 cm = 0.01 cm and thus with eqn 8.11 one gets for T:

$$T = \frac{D_P \cdot t}{d_P^2} = \frac{2.1\text{E-}10 \text{ cm}^2/\text{s} \cdot (24 \cdot 60 \cdot 60 \text{ s})}{(0.01 \text{ cm})^2} = 0.181$$

With $\alpha = 39.8$ one uses the values for α equal to infinity (∞) in Table 8.1 for the roots of tan $q_n = -\alpha \cdot q_n$. Carrying out calculations with eqn 8.12 for the fraction of additive migrating at time t to what would migrate at $t = \infty$:

$$\frac{m_t}{m_\infty} = 1 - \sum_{n=1}^{\infty} \frac{2\alpha(1+\alpha)}{1+\alpha+\alpha^2 q_n^2} \exp(-q_n^2 T)$$

$$= 1 - \frac{2 \cdot 39.8(1+39.8)}{1+39.8+39.8^2 1.5708^2} \exp(-1.5708^2 \cdot 0.181)$$

$$- \frac{2.39.8(1+39.8)}{1+39.8+39.8^2 4.7124^2} \exp(-4.7124^2 \cdot 0.181)$$

$$= 1 - 0.65544 - 0.001657 = 0.473$$

Note that for the summation the second term is quite small. Because the mass balance for migration out of plastic into a liquid (eqn 8.17) shows $m_{F,\infty} = m_{P,0}$:

$$m_{F,\infty} = m_{P,0}\frac{\alpha}{1+\alpha} = m_{P,0}\frac{39.8}{1+39.8},\ \therefore m_{F,\infty} \cong m_{P,0}$$

Therefore, the percentage of additive that has migrated from the polymer in 24 hours according to eqn 8.19 is 46.1%:

$$\frac{m_{F,t}}{m_{F,\infty}} \cdot \frac{\alpha}{1+\alpha} = 0.473 \cdot \frac{39.8}{1+39.8} = 0.461$$

Example 2 Solve Example 1 using eqn 8.13 and compare the two results. Starting with $\alpha = 39.8$ and $T = 0.181$ from Example 1 calculate the value for using eqn 8.14:

$$z = \frac{T^{1/2}}{\alpha} = \frac{0.181^{1/2}}{39.8} = 0.01069$$

Entering this value for z in eqn 8.13 one can solve for m_t/m_∞:

$$\begin{aligned}\frac{m_t}{m_\infty} &= (1+\alpha)[1 - \exp(z^2)\mathrm{erfc}(z)] \\ &= (1+39.8)[1 - \exp(0.01069^2)\ \mathrm{erfc}\ (0.01069)] \\ &= (1+39.8)[1 - \exp(0.01069^2) \cdot (0.98795)] = 0.487\end{aligned}$$

Then calculating the fraction migrated using the mass balance equation:

$$\frac{m_{F,t}}{m_{F,\infty}} \cdot \frac{\alpha}{1+\alpha} = 0.487 \cdot \frac{39.8}{1+39.8} = 0.475$$

Thus 47.5% of the additive in the polymer migrates in 24 hours which is very close and within experimental error to the result in Example 1 of 46.1%. Note the values of erfc(0.01069) are estimated from Table 8.2 values by linear interpolation.

Example 3 Edible oil is stored in a plastic bottle with an external diameter of 10 cm and with a wall thickness of 2 mm. What percentage of the antioxidant contained in the plastic bottle migrates after (i) 100 days and (ii) two years into the oil when the antioxidant has a diffusion coefficient of D_P = 1E-11 cm^2/s and is soluble in oil?
(i) Calculating α, T and z:

$$\alpha = \frac{1}{K_{P,F}} \cdot \frac{V_F}{V_P} = \frac{1}{K_{P,F}}\frac{d_F}{d_P} = \frac{1}{1} \cdot \frac{4.8}{0.2} = 24$$

$$T = \frac{D_P \cdot t}{d_P^2} = \frac{1\text{E-}11\ \mathrm{cm}^2/\mathrm{s} \cdot (100 \cdot 24 \cdot 60 \cdot 60\ \mathrm{s})}{(0.2\ \mathrm{cm})^2} = 0.00216$$

$$z = \frac{T^{1/2}}{\alpha} = \frac{0.00216^{1/2}}{24} = 0.00194$$

For short times one can use eqn 8.13 and performing linear interpolation on the z values between 1 and 0.05 in Table 8.2:

$$\frac{m_t}{m_\infty} = (1 + \alpha)[1 - \exp(z^2)\mathrm{erfc}(z)]$$
$$= (1 + 24)[1 - \exp(0.00194^2)\ \mathrm{erfc}\ (0.00194)]$$
$$= (1 + 24)[1 - \exp(0.00194^2) \cdot (0.997813)] = 0.0546$$
$$\frac{m_{\mathrm{F},t}}{m_{\mathrm{F},\infty}} \cdot \frac{\alpha}{1 + \alpha} = 0.0546 \cdot \frac{24}{1 + 24} = 0.0524$$

Thus $100 \cdot m_t/m_\infty = 5.24\%$ migrates.

(ii) Using eqn 8.13:

$$T = \frac{D_\mathrm{P} \cdot t}{d_\mathrm{P}^2} = \frac{1\mathrm{E}\text{-}11\ \mathrm{cm}^2/\mathrm{s} \cdot (2 \cdot 365 \cdot 24 \cdot 60 \cdot 60\ \mathrm{s})}{(0.2\ \mathrm{cm})^2} = 0.01577$$
$$z = \frac{T^{1/2}}{\alpha} = \frac{0.01577^{1/2}}{24} = 0.005232$$

Using the same eqn 8.13 and performing a linear interpolation on the erfc values for z between 0.05 and 1.0 in Table 8.2:

$$\frac{m_t}{m_\infty} = (1 + \alpha)[1 - \exp(z^2)\mathrm{erfc}(z)]$$
$$= (1 + 24)[1 - \exp(0.00523^2)\ \mathrm{erfc}\ (0.00523)]$$
$$= (1 + 24)[1 - \exp(0.00523^2) \cdot (0.994104)] = 0.1467$$
$$\frac{m_{\mathrm{F},t}}{m_{\mathrm{F},\infty}} \cdot \frac{\alpha}{1 + \alpha} = 0.1467 \cdot \frac{24}{1 + 24} = 0.141$$

Thus $100 \cdot m_t/m_\infty = 14.1\%$. Note that the additional migration from the bottom of the bottle has been neglected.

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Part III

Chemical migration from particular food contact materials

9

Recycled plastics and chemical migration into food

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9.1 Introduction

Glass, metal and paper packaging materials have been recycled and reused in the packaging area for several decades. In contrast, plastic packaging materials were recycled only in the non-food area. One reason was the unclear regulatory position for the reuse of packaging plastics. On the other hand the lack of suitable recycling processes with a high decontamination potential, and the lack of knowledge of the art and concentration of potential contaminants, restricted the use of recycled plastics in the sensitive area of food contact. Within the last two decades recycling processes have developed or been optimised due to their cleaning efficiency. In addition, equipment for the sorting of the different plastic materials has been developed. Sorting of the input material is the first and crucial step for the successful recycling of post-consumer plastics. As a consequence of this development, plants for the recycling of post-consumer plastics were built up on an industrial scale. On the scientific side knowledge of the diffusion behaviour and the contamination increased. Regarding plastics recycling, the driving force was the polymer polyethylene terephthalate (PET). Today post-consumer recycled (PCR) PET has the highest market share in the packaging sector and the 'super-clean' recycling capacity for PCR PET is increasing year by year.[1] Also polymers like high-density polyethylene (HDPE),[2] polypropylene (PP)[3] or polycarbonate (PC) are more and more interesting for commercial recycling processes. Increasing oil and virgin polymer prices make packaging materials with a certain amount of PCR polymer interesting for economical and environmental reasons.

Today several recycling technologies are on the market. Most decontamination processes are based on sophisticated washing procedures

and thermal treatment under vacuum. Some of the processes add chemical surfactants, detergents or aggressive chemicals towards the polymer surface into the washing solution. In addition re-extrusion steps with stripping gases or vacuum degassing systems further deep-cleanse the polymer material. Modern recycling and decontamination technology is, in some cases, able to reduce the post-consumer contaminants in polymers to levels below analytical detection limits. On the other hand, the deep-cleansing step might also reduce typical polymer by-products. Therefore the migration potential of recyclate-containing packaging materials is in several cases similar or lower than for virgin packaging materials.

In this chapter the technical as well as legislative aspects of mechanical (secondary) recycling of post-consumer plastics will be described. For packaging materials containing a certain amount of PCR plastics the most important point is the migration of the suspicious compounds from the polymer.

9.2 Legislative aspects

In the United States the US Food and Drug Administration (US FDA) has been discussing the use of post-consumer plastics in food applications since the late 1980s. The US Code of Federal Regulations allows in principle the use of recycled plastics in food contact. However, the US FDA published guidelines for the formal approval of recycled plastics in direct food contact. Their concern is that the consumer may use the packaging materials for storing household, garden and automotive chemicals before discarding the container into the post-consumer plastics feedstream. Because it is not known which chemicals the consumer might put in the container, traditional approaches like specific migration testing are not suitable for assessing the PCR polymers. The FDA therefore gave recommendations for simulating the misuse of the packaging materials. A major part of the FDA guidance was exposing plastics with a cocktail of chemical compounds, so-called surrogates, and then processing the material to establish the capabilities of the process to remove contaminates below a certain threshold level. The end threshold limits for the migration of the surrogates are given by the US FDA Threshold of Regulation concept with a general migration limit of 0.5 ppb per surrogate. The general migration limit is increased for the different polymer types with their individual diffusion behaviour by using consumption factors (CF). For example, polyolefins have a market share of about 33%, which increase the migration limit according to the Threshold of Regulation concept up to about 1.5 ppb. The consumption factor for recycled PET is 0.05, which increases the migration limit up to 10 ppb.

In Europe, industry has pressed for harmonised EU contols on recycling since the early 1990s. However, till now no such recycling directive exists, which means that the individual Member States of the European Union are responsible for any laws within their territories. For PET bottles, multilayer

applications with a functional barrier of virgin polymer and monolayer applications with direct contact using super-clean recycling processes have been given clearance or approval by a number of the European countries. Multilayers have received clearance, for example, in Austria, Belgium, Finland, France, Norway and Sweden. The monolayer direct contact approach has received clearance for use in Austria, Belgium, France, Germany, The Netherlands, Norway, Sweden and Switzerland. The heterogeneity in Europe is most clearly indicated by the fact that in some countries, such as Italy or Spain, plastics recycling into direct food packaging application is currently still prohibited. However, experts from industry, governments and research institutes are still discussing the topic and European harmonised measures are being developed. In the meantime two guidelines have been published. An expert group of the International Life Science Institute ILSI[4] and the excerpt of an European project on recycling[5] gave practical instruction and help for companies. In addition, the German plastics commission of the Bundesinstitut für Risikobewertung (BfR) has published recommendations for the safe recycling of post-consumer PET.[6]

In summary, European Guidelines and US FDA recommendations have a different basis for the evaluation of the suitability of the investigated recycling processes. US FDA guidelines based their end point on the concept of the Threshold of Regulation, whereas the European evaluation (ILSI and BfR guidelines as well as the conclusions of the EU project) focus on an end point of demonstrating no detectable migration at the limit of detection of analytical methodology. However, regarding PET as the favourite candidate for closed loop recycling, the final end point in both instances, i.e., the Threshold of Regulation of the US authorities and the non-detectable migration limit in the European view, are in fact the same value of 10 ppb. Post-consumer compounds from recyclate containing PET packaging materials should not exceed that migration limit. It should be noted here that the same migration should not be exceeded by unknown impurities of virgin polymers if the polymer is used in direct food contact.

9.3 Special considerations for using recycled materials as food contact materials

It is well known from diffusion theory that different types of polymers have different diffusion behaviours. For example, the polyester type polymers like poly(ethylene terephthalate) (PET), poly(ethylene naphthalate) (PEN) and polycarbonate (PC) as well as rigid poly(vinyl chloride) (PVC), which have a high glass transition temperature, are low diffusive polymers. The migration of potential contaminants in these polymers will result in low migration values. In contrast, polyolefins like high density polyethylene (HDPE), polypropylene (PP) or low density polyethylene (LDPE), which

are amorphous polymers, are much higher diffusive polymers. Post-consumer contaminants with a certain concentration in the packaging material will therefore result in a higher concentration in the foodstuff for polyolefins than for polyesters, PC or rigid PVC. In general, the higher diffusivity of the polyolefin polymers lead to a higher sorption of post-consumer compounds into the polymer materials. In addition, if the post-consumer compounds are not completely removed during the recycling process the re-migration of these compounds is also higher. As a consequence, regarding the evaluation of food law compliance, the input material for polyolefin recycling processes has to be much more under control than for a low diffusive polymer like PET. Post-consumer PET, for example, can have a certain amount of non-food packaging material without influencing the food law compliance of the output material.[7]

One crucial parameter for the evaluation of a super-clean recycling process producing a recyclate suitable for food contact is the contamination level of the input material. Due to the fact that diffusion is a reversible process, the higher diffusive polymer types should have higher input levels of post-consumer contaminants. The first step in the evaluation of PCR polymer should therefore be the determination of the input concentrations of post-consumer compounds in the polymer materials. For a review of concentration of post-consumer compounds in packaging materials intended for recycling see ref. 8.

Regarding the application of post-consumer polymers in packaging applications, the contact conditions have also to be taken into account. If recycled polymers are used for fruit trays for agricultural products which were peeled or washed before eating (e.g. bananas, citrus fruits), migration from the packaging could be neglected. Therefore the content of post-consumer compounds in these packaging materials plays a minor role. However, the regulations for food contact articles are still valid. On the other hand, PET bottles for edible oil with a shelf life of several months will result in a much higher migration. In this case the migration from, as well as the residual concentrations of, post-consumer compounds in the packaging materials should be determined. In this case the low diffusivity of the PET polymer material has a positive influence on the result. However, higher diffusivity polymers like HDPE are not excluded from closed loop recycling. If the recyclate containing high diffusive packaging material has only a low surface area, like closures for soft-drinks bottles, the application of recycled materials is less critical than for applications with high surface areas. On the other hand, the storage and shelf life conditions also have an influence on the migration of potential post-consumer compounds. For example, typically a soft drink bottled in PET has a shelf life of about one year whereas fresh bottled milk has only a few days under refrigerated storage conditions. Even if the HDPE material typically used for fresh milk bottles has a higher diffusivity than PET, the application of post-consumer HDPE for such an application is possible.[9]

9.4 Assessing the safety of recycled food contact materials

9.4.1 Source control

Source control is one of the most important steps for closed loop recycling of packaging plastics. As mentioned before, especially for the high diffusive polymers, the source control plays the major role because only non-contaminated packages previously used for food packaging should be introduced into the recycling process. In general, feedstock materials for recycling processes can be divided into the four quality classes:

Class 1: materials remaining from production by the manufacturing or converting industry where their history is well known. These materials typically are always under the control of the processor. Provided that good manufacturing practice is followed and contamination can be excluded, this material is as suitable for direct contact with foodstuffs as new material. Class 1 material can be defined as 'post-industrial recycled polymers' and corresponds to US FDA's primary recycling (pre-consumer scrap).
Class 2: PCR material which had been used for food packaging for well-known applications and re-collected pure-grade by the recycler, for instance, via a deposit system. This material typically contains only post-consumer food packaging materials. Due to its post-consumer character, the recycler usually does not have complete control of the plastics material over the time period from its first use up to its return.
Class 3: impurified PCR material and possibly mixed plastics which have been used for certain applications outside the food packaging area that enters the recycling feedstream via mixed plastics collection. This material could include packaging materials from non-food packaging applications.
Class 4: any class 1 to 3 material which had been chemically reprocessed by depolymerisation into monomers or oligomers from which, after purification, a new polymer has been regenerated.

Classes 2 and 3 correspond to US FDA's category 'Physical reprocessing: Secondary Recycling'. Class 4 corresponds to US FDA's category 'Chemical Reprocessing: Tertiary Recycling'.

Closed loop recycling materials from class 1 and class 4 can be considered to be safe and in compliance with the legal requirements due to the absence of contamination or the high purification effect of the de- and re-polymerisation steps. The materials from class 2 and 3 should have been sorted to a polymer purity of about 99%, which means also that materials from non-food packaging should also be separated. However, for the special case of PET, the FDA also allows non-food PET as an input material as long as the polymer is in compliance with 21 CFR 177.1630.

9.4.2 Challenge test

The cleaning efficiency of a recycling process should be tested with a so-

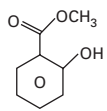
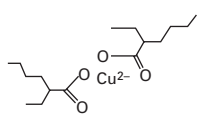
called 'challenge test'. Deliberately contaminated material with several surrogates is introduced in the recycling process. After the recycling process the residual concentrations of the surrogates are determined. The difference between the input and the output concentration represents the cleaning efficiency of the investigated recycling process in relation to the individual surrogate. Typically, a set of several surrogates is applied which represents the general four categories of compounds: volatile and non-polar, volatile and polar, non-volatile and non-polar and non-volatile and polar. In addition, several chemical functional groups are introduced, i.e., alcohols, esters, aromatic rings or chloro-organic compounds. Table 9.1 summarises some surrogates used for challenge tests.

A general recommendation for which chemical compounds should be applied in the challenge tests is difficult and depends in the end on the polymer type and on the recycling process being investigated. However, the surrogates should be stable during the recycling process and it should be possible to analyse the output material for the residual concentrations of the surrogates. For example, the metal organic compound copper-II ethylhexanoate was used in some challenge tests described in the literature. The cleaning efficiency of the investigated recycling processes was reduced due to the fact that the metal organic compound reacts with copper oxide (CuO), which could not be removed any more. In this case the cleaning efficiency was determined to be lower than in reality. On the other hand dimethylsulfoxide (DMSO) was discussed as a water soluble surrogate. During the high temperature typically used for recycling, DMSO is oxidised to dimethylsulfate. Therefore the determined cleaning efficiency for DMSO is higher than in reality with serious consequences regarding food law compliance evaluation.

The applied surrogates should also be non-toxic compounds. During recycling, high temperatures are applied which result in a volatilisation of the surrogates and this represents a hazardous risk to the recycling plant staff. In addition, if the challenge test is performed on a production line of the investigated recycling process, the use of hazardous compounds as surrogates leads to a contamination of the production line. Chemicals like lindane should therefore be substituted with other, non-hazardous compounds. In general, practical instructions and recommendations for challenge tests are given in refs 5 and 10.

Regarding the contamination conditions and the initial concentrations of the surrogates, there are some different procedures recommended. The US FDA[10] recommends a soaking procedure using contact conditions of 14 days at 40 °C. The surrogates should be dissolved in the solvents heptane and *iso*-propanol. The material, which should be contaminated, is totally immersed with this solution. A 100% feedstock of contaminated material is then recycled with the investigated recycling process. The initial concentrations are in the range of 49 ppm for, e.g., benzophenone, to 1100 ppm for trichloroanisol and up to 4860 ppm for the solvents chloroform and diethyl ketone.[7] In Europe

Table 9.1 Examples of chemicals to be used as surrogates in a challenge test

Surrogate	Formula (MW in g mol^{-1})	Functional group	Properties	Comments
Toluene	C_7H_8 (92.1)	Aromatic hydrocarbon	Volatile, non-polar, liquid	
Chlorobenzene	C_6H_5Cl (112.6)	Halogenated aromatic hydrocarbon	Volatile, medium-polar, liquid, aggressive to PET	
Chloroform	$CHCl_3$ (119.4)	Halogenated hydrocarbon	Volatile, medium-polar, liquid, aggressive to PET	
1,1,1-Trichloroethane	CH_3CCl_3 (133.4)	Halogenated hydrocarbon	Volatile, medium-polar, liquid, aggressive to PET	Environmentally hazardous compound, restricted use in Europe, should be substituted
Methyl salicylate	 (152.2)	Ester	Non-volatile, polar, liquid	
Tetracosane	$C_{24}H_{50}$ (338.7)	Hydrocarbon	Non-volatile, non-polar, solid	
Phenyl cyclohexane	$C_{12}H_{16}$ (160.3)	Aromatic hydrocarbon	Non-volatile, non-polar, liquid	Surrogate for limonene
Benzophenone	$C_{13}H_{10}O$ (182.2)	Aromatic ketone	Non-volatile, polar, solid	
Methyl stearate	$C_{19}H_{38}O_2$ (298.5)	Aliphatic ester	Non-volatile, polar, solid	
Lindane	$C_6H_6Cl_6$ (290.8)	Halogenated hydrocarbon	Non-volatile, medium-polar, solid	Hazardous compound, should be substituted
Copper-II-ethylhexanoate		Metal organic compound	Non-volatile, solid	Not stable during recycling

a solventless contamination procedure is recommended using contact conditions of seven days at 50 °C;[5] 100% of contaminated feedstock in form of flakes (or bottles) should be used. The initial concentrations of feedstock material range from 350 ppm to 500 ppm (which are understood to be the concentrations of contaminants after a conventional recycling treatment). When comparing these surrogate concentration ranges with contamination levels of post-consumer contaminants found in PET[11] safety factors 18 to 25 (e.g. for flavour compounds such as limonene) or 120 to 170 for unknown compounds, can be discussed.[5] It should be noted that these safety factors do not include the effect of the super-clean process which reduces the contamination concentrations to non-detectable levels.

In conclusion, science and practice have demonstrated that both the US FDA soaking procedure (14 days at 40 °C) and the solventless contamination procedure (seven days at 50 °C) are suitable to evaluate decontamination technologies with respect to their potential for producing regulatory compliant food grade recycled PET. The preferred procedure may be selected case by case according to the particular requirements of the technological process and the end user (customer).

9.4.3 Migration estimation

For several of the super-clean recycling processes cleaning efficiency data or residual surrogate concentrations can be found in the literature. However, the recycling company normally do not know how much recyclate will be applied in the packaging material. In addition the packaging dimensions (volume, surface area) are not known. Therefore a general estimation of the migration on the basis only of the cleaning efficiency is not possible, which means that every application should be experimentally tested. In the pre-market or pilot plant phases such a procedure is not feasible.

Migration models can be used for estimating the maximum migration of organic compounds out of the packaging materials into contact media. A generally recognised migration model based on diffusion coefficient estimation or organic chemical substances in polymers has been validated within a European project.[12] For migration estimation of surrogates from PET, this migration model is applicable and provides estimated migration values on a 95% probability level. For PET such a migration calculation is illustrated by Fig. 9.1, which models the migration from PET after ten days at 40 °C depending on the molecular weight of a migrating PET constituent or contaminant and its residual concentration of the compound in the PET bottle wall ($C_{P,0}$). The migration model applied for this calculation is described in ref. 12. Figure 9.1 shows that the higher the molecular weight of a compound the lower is the migration into a contact media. According to Fig. 9.1 and assuming that $C_{P,0}$ = 10 ppm for any potential migrant of a PET constituent, toluene (molecular weight MW = 92) as a surrogate would give a migration value of approximately 7 ppb whereas methyl stearate (MW = 298) migrates

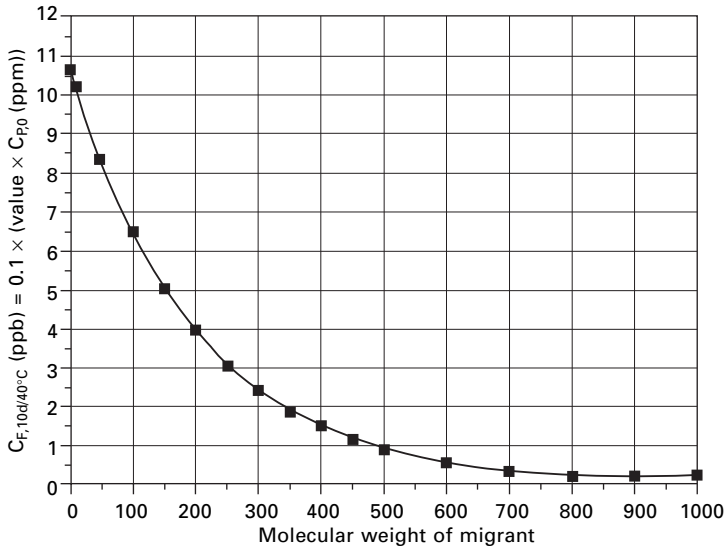


Fig. 9.1 Molecular weight dependent relationship between residual content $C_{P,0}$ of an organic chemical compound in PET and its migration after ten days at 40 °C into a food simulant or food with high solubility for the substance. For a substance with MW = 200, for instance, a $C_{P,0}$ of 10 ppm corresponds to a migration of 4 ppb.

at approximately 2.4 ppb only. Or, when defining the maximum initial concentration (MIC in ppm) of a surrogate in PET which would correspond to a migration value of 10 ppb in food or food simulant then the ratios of MIC values given in Table 9.2 can be derived for contact conditions of ten days at 40 °C. It should be noted that these MIC values are still conservative due to the applied migration model.

9.4.4 Quality assurance and compliance testing

Analytical determination of contaminants

Suitable analytical monitoring programmes are recommended to ensure continued product quality as will have been demonstrated by the challenge test. Useful, and in practice feasible, approaches have been developed and published in the literature. Possible methods and techniques include sniffing devices for returned used bottles as well as instrumental analysis techniques such as headspace or thermodesorption gas chromatography coupled to flame ionisation (FID) or mass spectrometry (MS) detectors.[7,9,11,13–17] Other suitable methods may also be established. These analytical methods can be comfortably implemented into the production process for checking either the input quality to allow early sorting out of any inconvenient post-consumer qualities from conventional recycling as well as for super-clean product control.

Table 9.2 Surrogate-dependent MIC values (in ppm) corresponding to a migration value of 10 ppb

Surrogate (mol. weight)	MIC (ppm)
Toluene (92)	12
Chlorobenzene (113)	13
Phenyl cyclohexane (160)	19
Benzophenone (182)	22
Methyl stearate (298)	44
fictive substance (400)	72
fictive substance (500)	112
fictive substance (750)	310

Migration determination

To enable migration testing as the most direct evaluation step, a model food contact article should be manufactured from the particular challenge test product. The model article should be manufactured as close as possible to the real industry scale conditions. However, technical difficulties may occur due to relatively high contamination levels and also mechanical adverse effects, or optical impairments may be observed on the final model articles for the same reasons. Nevertheless, these articles can be used for migration testing since they rather generate a worse case concerning the diffusion of surrogates. Similarly, when different types and geometries of food contact articles are likely, it is recommended that the type which is expected to have the highest diffusion rate should be manufactured. For instance, amorphous sheets have higher diffusion rates than bottles.

Migration testing is generally recommended but not always necessary. Instead of verification of the assessment criteria by migration testing, this requirement can be checked via determination of residual surrogate content in the recycling product (recycled PET pellets or bottles and other articles) or in the surrogate article, in connection with a scientifically recognised method for migration estimation. If the concentrations of the surrogates in the output material (e.g. pellets) are such that under the assumption that 100% migration of the whole surrogate amount will not lead to concentrations above 10 ppb in the foodstuff, no migration testing is necessary. The foodstuff/PET relation and the amount of recyclates in the bottle wall (e.g. 25% recycled material and 75% virgin PET or other ratios) should be taken into account.

In any case where the challenge test product fails the above-mentioned criteria, or in cases of doubt, migration testing is obligatory and needs to be carried out according to the provisions laid down in EU Directives 97/48/EC and 85/572/EEC and their amendments. The conditions of foreseeable use of the PCR PET containing article do influence the extent of possible migration into food. The migration rate determining parameters are contact time and temperature as well as the nature of the real filled product respectively, and the corresponding test conditions according to the above mentioned EU Directives. With regard to the conditions of use it also has to be considered

whether the recycled PET is in direct contact with the foodstuff or separated by a functional barrier. In cases of doubt, it must be guaranteed that migration testing is carried out under worst-case conditions.

The assessment criterion to decide whether the challenge test has passed the crucial requirement of efficient removal of potential contaminants is defined by a maximum migration rate leading to a concentration of 10 ppb (μg l^{-1}) in the food simulant. It must be noted that initial surrogate concentrations introduced by a challenge test into a super-clean process range several orders of magnitude higher compared to what can be found in reality. Therefore, reduction of these initially high concentrations to such low levels in the challenge test product, or in the model food contact article, which correspond with or lead to migration values smaller than or equal to 10 ppb, demonstrates the deep-cleansing efficiency of the technology and is not connected to any consumer exposure considerations.

Sensorial evaluation

To comply with the general requirements of Article 3 of the EU Regulation 1935/2004[18] sufficient sensory inertness of the PCR PET products as food contact articles needs to be assured. Therefore appropriate sensory testing of food contact articles made from super-clean products is recommended. As worse case test conditions for this purpose, storage of the article in direct contact with water for ten days at 40 °C have been generally accepted. However, depending on the particular application, modified tests may be more suitable.

9.5 Use of functional barriers

Instead of using 'super-clean' recycling technologies which remove, or reduce substantially, the amount of post-consumer compounds and contaminants in the polymer down to similar levels to those in virgin polymers, so-called functional barrier packaging systems can also be efficiently applied to achieve the same effect. No or only negligibly low migration levels of any unwanted foreign compounds can be achieved.

A functional barrier can be generally defined as a package construction that limits the extent of migration of a component from the package to food or a food simulant in amounts below a threshold value.[19] This value is usually established by regulatory institutions and is generally derived from toxicological evaluations. In the case of unknown contaminants as potential migrants from recycled materials US FDA's Threshold of Regulation concept may be applied where there is some certainty that the legal authorities will accept the application of the principle. It applies a general dietary concentration of 0.5 ppb (μg kg^{-1}) as the threshold which is derived from toxicological data on oral feeding studies.[20–22] According to this concept the migration of

any non-carcinogenic compound leading to dietary concentrations equal or lower than the threshold is not considered a significant health risk.

From recent investigations on the nature and quantities of typical post-consumer contaminants[5,7,8,11,23] the presence or influence of carcinogenic principles can be largely excluded. Therefore, a package construction containing recycled plastics material which is usually achieved by a multi-layer structure (e.g. a sandwich structure where the food contact layer consists of virgin material) is compliant with US FDA's food packaging regulations as long as the threshold is not exceeded. Lacking such a concept in Europe, this approach is very useful to demonstrate or justify compliance with the general requirements of Article 3 of the European Framework Regulation 1935/2004/EC[24] according to which the food contact materials and articles should not endanger human health.

It is generally known[25] that only a very limited number of packaging materials such as glass or metal provide absolute protection properties concerning the penetration of chemical compounds from layers behind or from the environment. In the case of multi-layers with plastics materials as functional barriers there occurs, in most cases to a certain extent, an unavoidable mass transfer from the plastics layers into the product. This must be understood as a functional quantity which, however, must comply with food regulations. Therefore it is necessary firstly to understand functional barrier characteristics and mechanisms and, secondly, to define the functional barrier efficiency in relation to food safety and to establish appropriate test methods. This is especially important with those food packaging applications where recycled plastics are covered by plastics functional barriers.

Over the last decade numerous publications have dealt with the functional barrier concept from different points of view and with different scientific and pragmatic intentions.[19,26–44] Many of these papers have discussed and proposed theoretical treatments and approaches to this issue and developed diffusion theory based mathematical models to describe the mass transfer processes and the developing concentration profiles in the packaging system. In the first theoretical treatments of the functional barrier one important point was not, or not sufficiently, taken into account. It was assumed that the functional barrier layer made from virgin materials was free of contaminants just after manufacture of the package. However, since multi-layer plastic structures are mostly manufactured under coextrusion conditions, where extreme temperatures far above the melting point of the plastic are applied, a significant inter-diffusion between the *in-situ* formed polymer layers occurs in reality.

Taking co-extrusion temperatures up to 280 °C into account, it can be estimated, in relation to the polymer type and thickness, that middle layer contaminants are penetrating the functional barrier layer partially or completely within a time range of seconds down to fractions of one second. As a consequence, more or less significant contamination of a 'virgin' functional barrier layer is likely to occur during manufacture. This compromises the

originally designed functional barrier efficiency to a reduced efficiency and could even result in the possibility of complete penetration, with the consequence of having direct food contact with the contaminants originating from the middle layer at the start of migration, i.e., after the time when the foodstuff is filled into the packaging. Other papers have investigated this question experimentally and taken the *in-situ* contamination into account for their modelling approach. Any mathematical model which does not consider this physical process of *in-situ* contamination would underestimate the actual amount of migration. It should be noted that the same effect, i.e., a reduction of the functional barrier efficiency, could occur when multi-layer packaging sheets are stored for long periods before they are used to pack food.

As a consequence, three principally different situations for a functional barrier packaging system can be assumed as depicted in Fig. 9.2. The corresponding kinetic migration characteristics are outlined in Fig. 9.3 which categorises the kinetic migration behaviour possibilities for a migrant at time t = 0 (for instance the time of package fill) into three typical cases:

1. Clean functional barrier: full lag time of the functional barrier takes effect.
2. Contamination functional barrier: depending on the degree of contamination of the functional barrier, only reduced lag time available.
3. Fully contaminated functional barrier: direct contact and no lag time.

As opposed to absolute barriers such as an aluminium layer of at least 6 to 7 µm, the effectiveness of functional barrier systems is related to a 'functional' quantity in terms of mass transfer, which is dependent on the technological and application-related parameters of the respective food-package system.[45] These parameters are:

- manufacture conditions of the package (e.g. high temperatures applied)
- type of functional barrier plastic

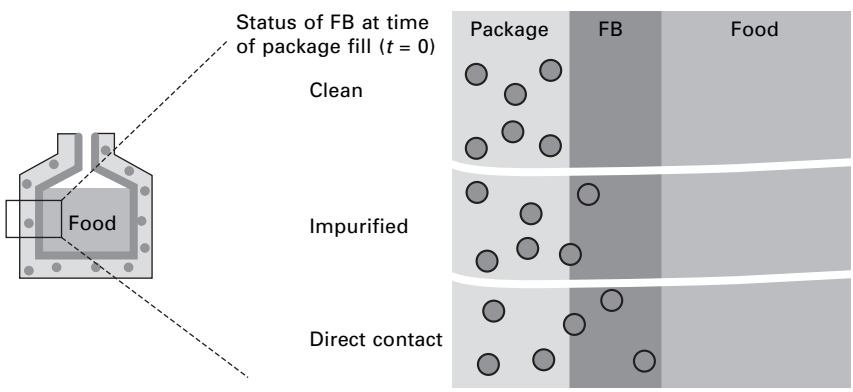


Fig. 9.2 Possible levels of contamination of functional barrier packaging structures at time of package fill (t = 0).

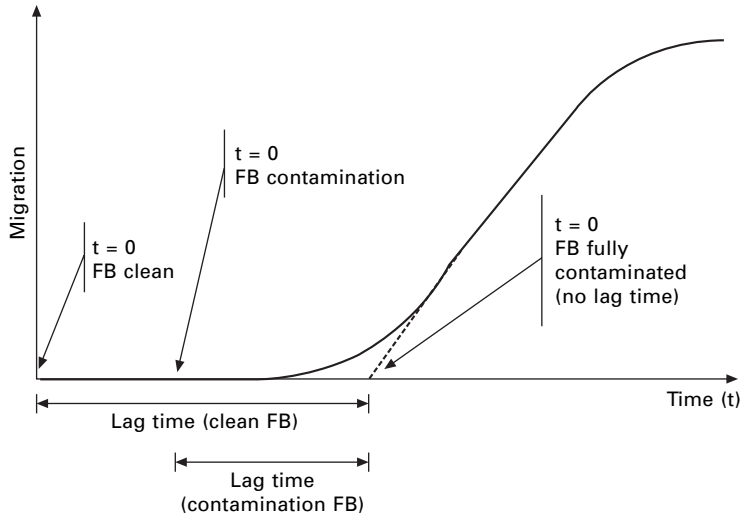


Fig. 9.3 Possible migration behaviour characteristics of migrants from functional barrier packaging structures dependent on status of FB at time of package fill (t = 0).

- thickness of the functional barrier layer
- molecular weight and chemical structure of contaminants
- concentration and mobility of contaminants in the matrix behind the functional barrier
- time between manufacture of package and filling
- type of foodstuff, i.e., fat content, polarity etc.
- filling conditions and storage (time, temperature) of the packed foodstuffs.

Within a European project FAIR-CT98-4318 'Recyclability'[5,33] a comprehensive work programme has been carried out to systematically study determinants in most of these functional barriers. One major aim of this project was to develop screening procedures of barrier properties of polymers to evaluate whether they are likely to behave as functional barriers and to elaborate testing procedures for functional barriers and multilayer materials. Another aim was to provide tools based on predictive, validated approaches, thus allowing optimisation of the functional barrier packaging structures and reduction of the need for testing to a minimised extent. To establish the necessary experimental data sets with respect to diffusivities of numerous packaging plastics from storage up to extrusion conditions, suitable chemical compounds have been used as surrogates to test general functional barrier behaviour.

The results of these comprehensive studies have been recently published in two papers.[43,44] To study functional barrier contamination effects taking place during manufacture when multi-layers are produced at high temperatures, and when the molten polymer layers are put in contact together, methods were elaborated to determine diffusion coefficients in molten polymers. It

was found that diffusion in the melt of (at ambient temperature) glassy polymers is much slower than in (at ambient temperature) rubbery polymers. Intrinsic diffusion coefficients in normal storage and service conditions were measured using Moisan type tests[46] for which a particular three-layer test with solid-solid plastics contact was designed. It was found that interface effects, (e.g. associated to a poor solubility of a migrant in the (liquid) food simulant) can strongly influence both the lag time and migration. For migration into aqueous media, an increase in the hydrophobic character of migrants results in a decrease of migration at equilibrium and an increase of the apparent lag time.

Finally, for the simulation of migration, a numerical model was developed. This model takes into account a stepwise migration, first during processing at high temperatures (programme 'multitemp'), then during storage of the empty package or after filling (programme 'multiwise'). A database of diffusion coefficients was proposed for a broad range of polymers. Since other parameters such as partition coefficients K (understood as the ratio at equilibrium of the migrants concentration in food simulant and the concentration in polymer) and the mass transfer coefficient at the food-polymer interface H needed for the calculation are not always available, so it is recommended to work with default parameters (K infinite, H infinite) because this leads to an overestimated predicted value, which favours consumer protection. Based on determined activation energies for diffusion other quick tools for functional barrier efficiency testing, such as accelerated tests with time-temperature correlated acceleration factors (manufacture process and storage), have also been proposed.

Another study on the migration behaviour in flexible thin multi-layer structures has recently been carried out and results have been presented.[47] One of the essential findings was that testing of thin multi-layer films with current recognised and accepted alternative fat simulating liquids such as 95% ethanol and *iso*-octane, lead in many cases to too strong interactions which can cause swelling effects within the packaging structures and lead to increased diffusion. One example is shown in Fig. 9.4 where the migration kinetics of an organic migrant from a PET-PA-PE film is shown for three different temperatures.

The migrant was initially used as an additive in the adhesive between the PET and PA layer and the migration test was carried such that the PE layer was in contact with the food simulant, 95% ethanol. In this case, the efficiency of the PA layer as a functional barrier was investigated. This situation is totally analogous to the hypothetical case that PCR PET was used and the test migrant was a contaminant in the PCR PET. Therefore the investigations on this multi-layer can be considered as very instructive in relation to the question, 'how should functional barrier efficiency tests on recycled plastics packaging applications be conducted?'. In Fig. 9.4 it can be recognised that at room temperature the PA layer acts as a very efficient FB whereas at 40 °C a lag time phase is observed with reduced functional barrier efficiency and

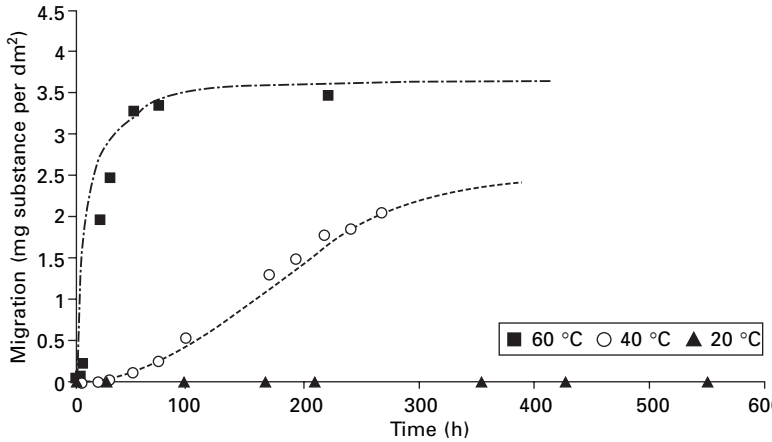


Fig. 9.4 Kinetic migration behaviour of an organic substance (initially used in the adhesive between the PET and PA layer) from a PET-PA-PE multi-layer structure into 95% ethanol in contact with the PE layer at different temperatures (20 °C, 40 °C and 60 °C).

at 60 °C the functional barrier effect is completely lost. The reason for this accelerated and exaggerated migration behaviour at 60 °C is due to interactions between the food simulant and the PA layer. With regard to the practical use for functional barrier efficiency testing it can be stated that with known relationships between the migration kinetics at the three applied test temperatures one can derive a very quick test at exaggerated conditions, for instance, at 60 °C or at 40 °C, to conclude whether or not the functional barrier efficiency is adequate under package storage and service conditions and in relation to a certain acceptable specific migration limit relevant for the migrant of interest.

As another test approach to meet any delays in migration due to functional barrier effects, the artificial ageing of a multi-layer structure was considered. The motivation for this idea was to replicate potential migration processes which would take place after the manufacture of a functional barrier package until the time of filling. Following ageing, the functional barrier structure could then be tested using the usually applied conventional migration test conditions according to relevant EU directives. To investigate this test strategy, in the study mentioned, the same test film as described above and shown in Fig. 9.4 was stored for 21 months at room temperature and tested again. In addition, this test film was finally artificially aged by a one week 60 °C conditioning. In all cases the migration behaviour at 40 °C was measured to compare if at all, and how, the effects of the 'dry' storage and hot treatment of the test film would behave. The results are shown in Fig. 9.5. It can be recognised that all tests provided the same kinetic lag time behaviour. This can be explained only by the understanding that the test film was already, after the manufacturing process (where high temperatures had been applied), in the thermodynamically preferred equilibrium situation which did not change

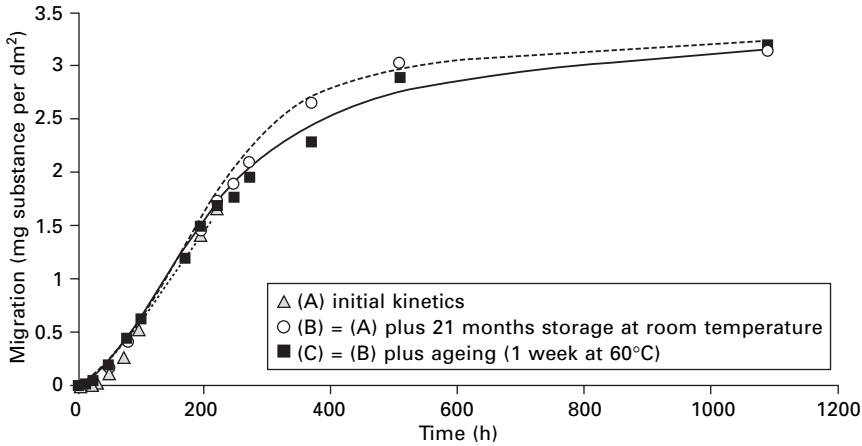


Fig. 9.5 Influence of 21 months room temperature storage (B) and artificial ageing for one week at 60 °C (C) on the kinetic migration behaviour of a PET-PA-PE multi-layer film as depicted in Fig. 9.4 at 40 °C (A).

again after long-term storage or even short treatment at elevated temperature (60 °C). This and other results that were obtained showed that the partitioning effects that occur during manufacture under coextrusion conditions overwhelm any sequential effects by a later ageing of the test film. It was concluded that, at least for the usual thin flexible multi-layer structures, ageing appears to be unnecessary.

Finally, the current available elaborated knowledge and the proposed test methodologies are suitable to serve for national or federal authorities and industry as a basis for safety evaluation, establishing criteria and guidelines for the appropriate functional barrier protection design of recycled plastics for food packaging.

9.6 Sources of further information and advice

9.6.1 European ILSI document

An expert group under the aegis of ILSI Europe has proposed specific guidelines on the re-use of recycle plastics in food packaging. These guidelines[4] are based on the results obtained from the European 'Recycle Re-use' project. The document gives recommendations for recycling or packaging companies that want to use post-consumer plastics in food contact applications. The ILSI guidelines contain eight key recommendations.

9.6.2 German BfR recommendations

The German BfR (former BgVV) published recommendations on the mechanical recycling of post-consumer PET for direct food contact

applications.[6] The BfR document gives recommendations for source control, challenge test and for the quality assurance of post-consumer PET intended to come into direct food contact. In comparison to the above-mentioned ILSI guidelines this statement introduces additionally two interesting novelties: (i) the concept of analytical quality assurance connected with the requirement that PCR PET products must not be disadvantageously distinguishable from virgin material and (ii) the 10 ppb migration limit for surrogates as a technical cleaning efficiency criterion for evaluation of the super-clean process capability and not understood as a toxicology-based end parameter.

9.6.3 US FDA points to consider

The FDA published two guidelines for industry dealing with post-consumer plastics for direct food contact applications.[10,48,49] These guidelines provide recommendations about testing of the cleaning efficiency of the investigated recycling process and the maximum content of post-consumer substances in recyclate containing packaging materials as well as threshold limits for migration. The FDA also provides information about all 'non-objection letters' on their internet homepage.[50,51]

9.6.4 EU report

Based on the results of the European Project FAIR CT98-4318[52] proposals for the forthcoming legislation are given and filed to the European Commission.[5] Based on the results of the Europe-wide screening of post-consumer PET flakes and on migration considerations the document gives detailed recommendations for performing the challenge test, migration testing and for quality assurance of recyclate containing PET articles.

9.7 Glossary

Bold text within an entry indicates a glossary definition for that word or phrase.

Adventitious contaminants Any unwanted substance that inadvertently comes into contact with the packaging material before it is collected for recycling and that therefore may contaminate the plastic and negatively influence the quality of the product filled by a recycled packaging material.

Challenge test A test of the effectiveness of a **super-clean recycling** process to remove chemical contamination from materials or articles. The test involves introduction of exaggerated levels of **surrogates** and includes as an end parameter the migration evaluation of these surrogates from a model food contact article.

Consumption factor (CF) Generally, CFs are used to correct migration test results (measured concentration in food simulant) into an exposure value (average uptake by the consumer with the diet). Specifically, the US

FDA defines CF as the plastic packaging usage factor which is CF = 0.13 for HDPE, CF = 0.12 for LDPE, CF = 0.35 for polyolefins in general, CF = 0.16 for virgin PET and CF = 0.05 for recycled PET.[51] In Europe, the system of packaging usage factors has not yet been established. However, the concept of fat consumption factors has recently been adopted with the consequence that a fat (consumption) reduction factor (FRF) is currently being introduced into European legislation (expected to be published by the next amendment of EU Directive 2002/72/EEC).

'Conventional' recycling processes A recycling procedure using process steps, grinding, washing and surface drying of collected plastics. The output material of conventional recycling processes is flakes customarily used for non-food or for the core layer of multi-layer applications. Conventional recycled polymers are usually used as input material for **super-clean recycling** processes.

Extraction Quantitative dissolution of constituents from a plastic into a solvent and based on a strong interaction between plastic and solvent.

Feedstock/feed stream Post-consumer plastics used as raw materials for recycling.

Food grade polymers For Europe – polymers of a suitable standard for food contact manufactured in compliance with EU Directive 2002/72/EEC (and amendments). For the USA – the polymers must be compliant with the relevant requirements according to US FDA's Code of Federal Regulations (21 CFR 177 series).

Functional barrier A package construction or barrier layer which limits the extent of migration of a component from the package to the food or food simulant in amounts below a threshold value: see **threshold of no concern** or **migration limits**.

Lag time The time that a substance needs under given conditions to cross a functional barrier package construction and to reach the food contact surface. The migration kinetics of a functional barrier system are in general characterised by an initial time lag phase.

Migration Diffusion- and/or partitioning-controlled mass transfer from a packaging material or article into food or a food simulant. Classically, migration is experimentally determined by standardised tests using food simulants. Due to the scientific progress in this field, migration can also be mathematically modelled and conservatively predicted.

Migration limits Food regulatory maximum concentrations of migrants in food simulants or foodstuffs resulting from a migration process. With respect to the sensitive area of recycled food packaging materials and articles, the legally prescribed overall migration is of much lower relevance and importance than specific migration limits as, for instance, defined by a **threshold of no concern**.

Post-consumer polymers Polymer resins that have been converted into bottles/containers, distributed and used by the consumer. Discarded plastic material becomes the **feedstock** for recycling processes.

Post-industrial polymers Industrial in-house plant scrap generated during

the manufacturing process, which may be re-used in the production of new containers.

'**Super-clean' recycling** In most instances the process uses as a source the output material from **conventional recycling**, for example, washed and surface-dried flakes, and includes one or more additional cleaning steps. The output of the 'super-clean' process may be used for packaging applications in direct contact with the foodstuff provided it meets the appropriate regulatory guidelines or legal requirements.

Surrogates Organic compounds (also known as 'model contaminants') of a wide range of chemical types and physical properties representing exaggerated contamination to challenge the safety of recycled materials and articles (see **challenge test**). Possible application may be as individuals or as a test mixture.

Threshold of no concern The concentration of a migrant in a foodstuff that, from a toxicological point of view, is considered to pose no health risk to the consumer, even when the chemical structure of the migrant is unknown. Using the threshold-of-regulation concept as a basis (see US FDA 21 CFR 170.39), the US FDA has determined that exposure to contaminants from recycled food-contact articles of the order of 0.5 ppb dietary concentration or less generally is of negligible risk. In Europe, this concept is under discussion but a general threshold value has not yet been adopted. However, specifically for evaluation of the safety of the **super-clean recycling** processes the purely technical cleaning efficiency criterion is applicable. A JECFA task force of FAO/WHO has adopted the use of a threshold of toxicological concern concept for the evaluation of flavouring substances in food. The proposed no-concern level was 1.5 μg per person per day.[53,54]

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10

Plastics and chemical migration into food

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10.1 Introduction

Plastics are the most versatile and popular materials used in the manufacture of food packaging and other food contact materials (FCMs) with approximately 50% of all Europe's food packaged in plastics. This has come about through the ready availability of a variety of plastics with different permutations of properties, so that the ideal materials (or combination of materials) can be selected to satisfy most applications, particularly with the increasing performance demands in recent years. Section 10.3 of this chapter briefly discusses the different plastics used in the manufacturing of FCMs, their key attributes and properties, composition and manufacture.

Food packaging has the prime function to protect food from contamination until it is consumed and to help keep the food fresh, but it also fulfils other requirements, such as to convey information about the foodstuff and present it in an appealing manner. Moreover, there are a host of other requirements for food contact materials, such as physical properties with advantages in being robust and light in weight. Plastics are able to fulfil a wide range of functional requirements and offer unparalleled advantages compared to other materials. However, it is also important that the FCM is inert and does not contaminate the foodstuff through migration or transfer of substances used in its manufacture.

This chapter is primarily devoted to assessing the safety of FCMs with the next section discussing in depth the requirements of EU Plastics Directives and how compliance with the legislation is demonstrated (see also Chapters 3 and 5). Section 10.4 reviews degradation products, whilst sections 10.5 and 10.6 are concerned with future trends in plastics materials and sources of further information.

10.2 Testing plastics materials for compliance with EU directives

EU legislation covering plastics food contact materials is well advanced with a positive list for monomers complete and a positive list for additives near completion. Decisions on how other substances used in plastics, such as aids to polymerisation and colourants are to be regulated, if at all, have yet to be made. Plastics used in contact with food must comply with the Framework Regulation,[1] which lays down the basic rules:

> Materials and articles in contact with food shall be manufactured in compliance with good manufacturing practice so that, under normal or foreseeable conditions of use, they do not transfer their constituents to food in quantities which could:
>
> - endanger human health
> - bring about an unacceptable change in the composition of the food
> - bring about a deterioration of the organoleptic characteristics thereof.

Plastics food contact materials and articles should comply with Directive 2002/72/EC[2] and its amendments that include:

- an overall migration limit (OML)
- specific migration limits (SMLs) on monomers
- specific migration limits (SMLs) on additives
- compositional limits (QMs) on some monomers.

Demonstration of compliance with any of these restrictions, where applicable, is the main responsibility of the converter who makes the finished plastics article. However, the food packer or retailer who is at the 'sharp end' of any enforcement and the polymer manufacturer, who should ensure that the polymer granules comprise only authorised substances, also have responsibilities to fulfil. The British Plastics Federation 'Guide'[3] provides extensive guidance on the responsibilities of each link in the chain and other related issues such as Good Manufacturing Practice and frequency of retesting. The 'Guide' proposes that if the test result is between 0–33% of the limit then annual retesting is sufficient. If the results are between 33–66% of the limit then an immediate retest should be carried out to ensure that the results are repeatedly within the band or lower. If confirmed then annual retesting may be sufficient. If the test result is greater than 66% of the limit then there should be an immediate retest twice on different samples followed by sufficient testing to ensure that the results are repeatedly lower than the limit. Consideration should be given to batch-by-batch testing to build up a statistical case for compliance. In the UK it is important to demonstrate due diligence and not rely entirely on warranty and statements from suppliers. Figure 10.1 illustrates the main responsibilities.

Demonstration of compliance with specific migration limits may be accomplished by two simple procedures that should be considered first before any testing is conducted.

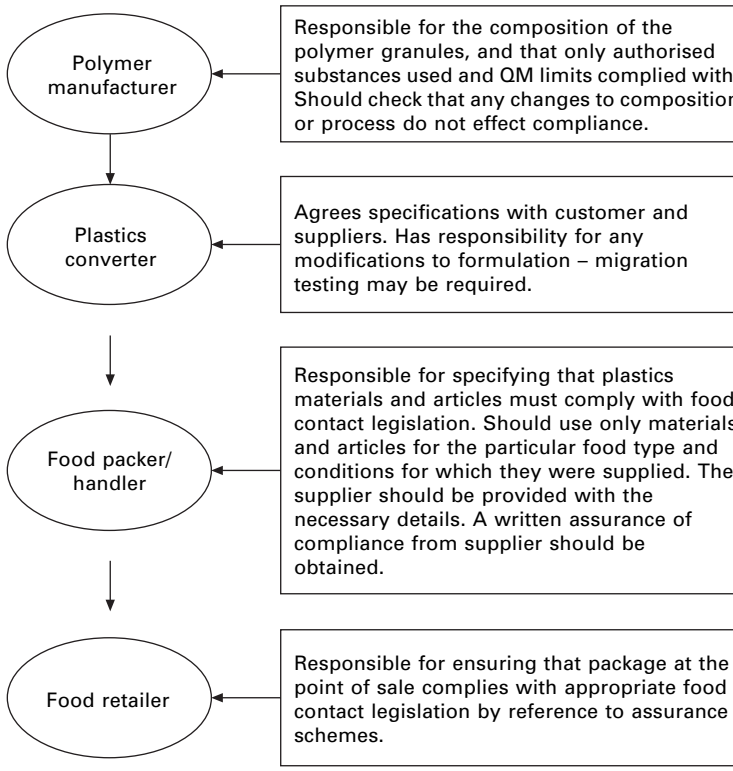

Fig. 10.1 Summary of responsibilities of food packaging supply chain.

1. Determination of levels of residual substances and calculation of 100% mass transfer to food. Measurement of levels is usually needed for monomers, but in the case of additives this can be the level added to the polymer.
2. Use of a 'generally recognised' migration model based upon diffusion theory, such as MIGRATEST Lite® (see Chapter 8). There are some cases where migration cannot be predicted by this approach including substances that are ionic, or those that bloom to the surface of the polymer or are not homogeneously distributed, or some polymers such as plasticised PVC.

However, where these simple approaches are not appropriate, or the calculated values exceed SMLs then migration tests are conducted, normally using food simulants (see Chapter 5).

10.2.1 Test conditions

The migration tests that are performed on food contact materials need to be done using appropriate test conditions that properly cover the conditions of

use (see also Chapter 5). This is most important and needs knowledge about how the food is packed, processed and stored. Selection of the correct temperature for a test is particularly important. The relationship between temperature and migration of a substance generally can be described by the Arrhenius equation. In some cases the temperature in use is not precisely known. For example for PVC stretch film for home use compliance tests are usually carried out for ten days at 20 °C with fat. This is a reasonable compromise between ten days at 40 °C (shelf storage) which is judged to be too severe and ten days at 5 °C (refrigerated storage) which is not severe enough. The test conditions for evaluation of compliance against food contact legislation are laid out in Directive 97/48/EC and amendments.[4]

Where storage under ambient or chilled temperatures is intended for the foodstuff, accelerated tests are carried out. For example, ten days at 40 °C covers ambient storage. For a combination of time and temperatures a combination of test conditions is used. In some cases carrying out only the most severe test is allowed. For example two hours at 175 °C to cover oven cooking would also cover ambient storage. To cover all anticipated conditions of use, test conditions of two hours at 175 °C with olive oil, and reflux conditions for four hours are used with aqueous simulants. Some examples of test conditions are given in Table 10.1.

It should be noted that items intended for repeated use, such as the spatula and beer mug, should be tested according to the guidelines given in the Directive 2002/72/EC where the test is repeated three times on the same test piece, using fresh simulant on each occasion. Compliance is then judged based upon the result obtained on the third test. When the temperature of the food is not known or cannot be judged, for example, with microwaveable

Table 10.1 Selection of test conditions

Food contact material	Processing/conditions of use	Test conditions
PET bottle	Aseptic filling and shelf storage	10 days at 40 °C
PP pouch	Retort sterilisation plus shelf storage	2 h at 121 °C plus 10 days at 40°C
PET ovenable tray	Refrigerated storage plus cooking in a conventional oven	1 h at 175 °C (fat) 4 h reflux (aqueous)
PS vending cup	'Hot fill'	2 hours at 70 °C
Polycarbonate beer mug	Short exposure at room temperature	30 minutes at 40 °C or 30 minutes at 20 °C
Spatula	Mixing/dispensing hot food	30 min at 175 °C (fat) 2 h at reflux (aqueous)
VC/VA copolymer sandwich pack	Storage 1 day ambient	24 hours at 40 °C
Soup pouch	Refrigerated storage plus microwave reheat	30 min at 130 °C (fat) 30 min at 100 °C (aqueous)
Glass jar with twist-off cap	Sterilised plus ambient storage	2 h at 121 °C plus 10 days at 40 °C

food, the temperature of the food/plastic interface can be measured by use of thermocouples or infra-red thermography.

10.2.2 Overall migration testing

The EU overall migration limit was originally introduced to minimise the number of SMLs, so that substances with a Tolerable or Acceptable Daily Intake of 1 mg/kg bodyweight or greater need not be given a SML because they would automatically exceed the Overall Migration Limit (60 mg/kg or 10 mg/dm^2). In practice, this does not hold true for volatile substances as these are lost in the overall migration test procedures. Tests are carried out using food simulants and the test methods are EN Standards 1186 Materials and articles in contact with foodstuffs – Plastics – Parts 1–15, shown below. They are available in the UK from the British Standards Institution, 389 Chiswick High Rd, London W4 4AL.

Part 1 Guide to selection of conditions and test methods for overall migration.
Part 2 Test methods for overall migration into olive oil by total immersion.
Part 3 Test methods for overall migration into aqueous food simulants by total immersion.
Part 4 Test methods for overall migration into olive oil by cell.
Part 5 Test methods for overall migration into aqueous food simulants by cell.
Part 6 Test methods for overall migration into olive oil using a pouch.
Part 7 Test methods for overall migration into aqueous food simulants using a pouch.
Part 8 Test methods for overall migration into olive oil by article filling.
Part 9 Test methods for overall migration into aqueous food simulants by article filling.
Part 10 Test methods for overall migration into olive oil (modified method for use in cases where incomplete extraction of olive oil occurs).
Part 11 Test methods for overall migration into mixtures of ^{14}C-labelled synthetic triglycerides.
Part 12 Test methods for overall migration at low temperatures.
Part 13 Test methods for overall migration at high temperatures.
Part 14 Test methods for 'substitute tests' for overall migration from plastics intended to come into contact with fatty foodstuffs using test media iso-octane and 95% ethanol.
Part 15 Alternative test methods for migration into fatty food simulants by rapid extraction into iso-octane and 95% ethanol.

Part 1 of EN1186 describes the basic rules for the following: choosing the most appropriate mode of test; how the plastic specimen is brought into contact with the food simulant (e.g. by total immersion, in a cell or pouch, filling a plastic article); the most appropriate test conditions to use. After

exposing test specimens to food simulants, the solvent and aqueous-based food simulants are evaporated to dryness and the residue accurately weighed. The aqueous Overall Migration (OM) test methods have been ring-trialled and a reproducibility of better than 2 mg/dm^2 or 12 mg/kg achieved. Results are expressed in units of mg/dm^2 except for containers and articles that can be filled with a volume less than 500 ml or greater than ten litres. Generally, very few plastics exceed the OM limit with aqueous food simulants, except for some biodegradable polymers. Occasionally formulations containing calcium carbonate as a filler will give rise to high values using 3% acetic acid.

With the OM test with olive oil, or an alternative fat simulant, such as sunflower oil or HB307, it is the weight loss on the plastic test pieces that is measured. To take into account the quantity of fat absorbed by the test pieces during the exposure, the fat is extracted using a solvent and determined separately by gas chromatography. In ring trials a reproducibility of better than 3 mg/dm^2 or 18 mg/kg was achieved. Instances when plastics exceed the OM test limit with olive oil are mainly older formulation PVC 'stretch films' that contain plasticisers, or polyolefins tested at temperatures around their maximum useful temperature. In the case of PVC stretch films, these have been largely reformulated replacing a significant percentage of the monomeric plasticiser, di-(2-ethylhexyl) adipate (DEHA), with polymeric adipates that have less propensity for migration. Even the newer style PVC films are not suited to wrapping pure fats and oils or margarine where the reduction factor of 1 or 2 will not bring down the olive oil test result to below the OM limit of 10 mg/dm^2.

10.2.3 Specific migration testing

Directive 2002/72/EC contains a positive list of monomers, therefore food contact plastics can be made using only listed substances. Some substances are subject to limitations in the form of specific migration limits (SMLs) or restrictions on the maximum permitted residual concentration of a substance in the finished product (QM or QMA) (see also Chapter 5). To test for compliance with SMLs, migration tests can be carried out using food simulants or foods. The test methods that have been validated for food simulants are EN Standards 13130 Parts 1–8. Part 1 of EN 13130 describes ways of conducting the specific migration test by total immersion, cell, article fill or pouch. Specific migration tests for volatile substances require the use of a sealed cell to mimic the worst-case situation. A typical cell is shown in Fig. 10.2. Listed below are the parts of EN 13130*:* Monomer test methods for plastics materials and articles intended to come into contact with foodstuffs. They are available in the UK from the British Standards Institution, 389 Chiswick High Rd, London W4 4AL.

Part 1 Guide to the test methods for specific migration of substances from plastics into foods and food simulants and the determination of

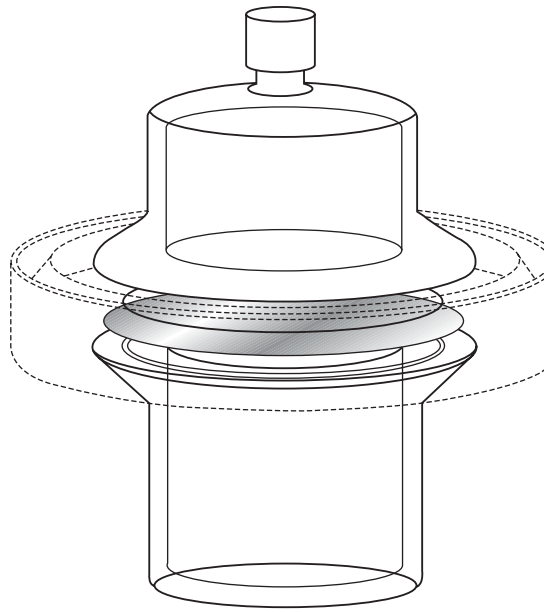

Fig. 10.2 Glass migration cell for one-sided contact (courtesy FABES, Munich).

substances in plastics and the selection of conditions of exposure to food simulants.

Part 2 Determination of terephthalic acid in food simulants (SML = 7.5 mg/kg).

Part 3 Determination of acrylonitrile in food and food simulants (SML = not detectable, DL = 0.02 mg/kg).

Part 4 Determination of 1,3-butadiene in plastics (QM = 1 mg/kg).

Part 5 Determination of vinylidene chloride in food simulants (SML = not detectable, DL = 0.05 mg/kg).

Part 6 Determination of vinylidene chloride in plastics (QM = 5 mg/kg).

Part 7 Determination of monoethylene glycol and diethylene glycol food simulants (SML(T) = 30 mg/kg).

Part 8 Determination of isocyanates in plastics (QM = 1 mg/kg).

SML = specific migration limit in food or food simulant.
QM = maximum permitted quantity of the 'residual' substance in the material or article.
DL = detection limit of the method of analysis.

A further 20 monomer test methods were developed in the EU funded BCR Project.[5] The number of monomer test methods published in the report was 35. This was reduced to 20 for the new work items by removing a method for BADGE (bisphenol A diglycidyl ether). This was covered separately by Task/Working Group 8. The number was also reduced by consolidating similar methods. The substances covered by the 20 methods are given below.

They were published as Technical Specifications (TS) in February 2005. As Technical Specifications these methods will be required to be reviewed every two years.

1. acetic acid, vinyl ester (vinyl acetate).
2. acrylamide.
3. 11-aminoundecanoic acid.
4. 1,3-benzenedimethaneamine.
5. 2,2-bis(4-hydroxyphenyl) propane.
6. 3,3-bis(3-methyl-4-hydroxyphenyl)-2-indolinone.
7. butadiene.
8. caprolactam and caprolactam salt.
9. carbonyl chloride.
10. 1,2-dihydroxybenzene, 1,3-dihydroxybenzene, 1,4-dihydroxybenzene, 4,4′-dihydroxybenzophenone and 4,4′-dihydroxybiphenyl.
11. dimethylaminoethanol.
12. epichlorohydrin.
13. ethylenediamine and hexamethylenediamine.
14. ethylene oxide and propylene oxide.
15. formaldehyde and hexamethylenetetramine.
16. maleic acid and maleic anhydride.
17. 4-methyl-pentene.
18. 1-octene and tetrahydrofuran.
19. 2,4,6-triamino-1,3,5-triazine.
20. 1,1,1-trimethylopropane.

There is no analytical method available for many substances and in these cases it is necessary to develop a method with 'acceptable performance'. In the first instance, where no information exists on the stability of the substance to be measured, then it is a good idea to carry out a recovery test. This is done by adding the substance at an appropriate level to the food simulants and measuring the amount of substance remaining after the proposed test conditions have been applied. It is best carried out in the same cell as the proposed migration tests. A poor recovery of, say, < 50% indicates the substance may be degrading or lost from the cell. In this situation it may be necessary to use a different cell or a different test medium to improve the recovery by use of a substitute test, for example, instead of olive oil. In some cases it may not be possible to improve the recovery and consideration should be given to measurement of the level in the polymer and migration modelling or measurement of the decomposition products.

For borderline cases where recoveries are outside of the analytical tolerance, at say 50–70%, it is arguable whether correction of the concentrations found in the migration test for the recovery is justified. But it can be viewed to be a 'worst case' and so in principle it is recommended. Losses may also occur due to insolubility of the substance in the food simulant or adsorption onto glass/metal surfaces and this should be investigated by rinsing the cell with a suitable solvent.

The document 'Note for Guidance'[6] available on website www.efsa.eu.int provides guidance on provision of migration (and other) data for the authorisation of new substances for food contact application. In particular, method performance should be adequate at the given SML with data obtained on the precision and the limits of detection and quantitation. In the event that the SML is exceeded then confirmation of the level present is essential, preferably using mass spectrometry.

10.3 Properties and composition of plastic FCMs

Plastics can be placed into two main categories, thermoplastic and thermoset. Thermoset plastics are irreversibly formed into a permanent shape often by applying heat. Thermosets cannot be softened and remoulded on heating and have few applications in food packaging, except for the inner linings used for can coatings and many adhesives, as used, for example, in multilayer materials. A limited range of food contact materials is made from thermosets, predominantly melamine resins and unsaturated polyesters used in tableware and utensils.

Thermoplastics can be softened repeatedly by heating and are more easily recyclable. These plastics are used most often in food contact applications and will be considered in most detail in this chapter. Cellophane, an important material used for packaging of sweets and pies, made from cellulose, is strictly not considered to be a true plastic. Its versatility has been increased by the additions of softeners and polymeric coatings. Food packaging materials tend to be grouped into two categories in market research, flexible and rigid. The main types of plastics and other materials used as substrates in flexible packaging applications are given in Fig. 10.3. For rigid packaging materials, a significantly higher proportion of PET, as used in beverage bottles, and polystyrene, used for expanded polystyrene food trays and high impact polystyrene cups, and pots is used.

The criteria for selection of the most appropriate polymeric materials for food contact applications are generally based upon:

- cost
- physical properties at different humidities and temperatures (–18 °C for frozen foods to 200 °C+ for ovenable foods), including dimensional stability
- inertness to foods under given use/storage/processing/cooking temperatures
- ease of conversion
- clarity, visual appeal and printability.

Further factors sometimes come into play for food packaging:

- flexibility
- sealability

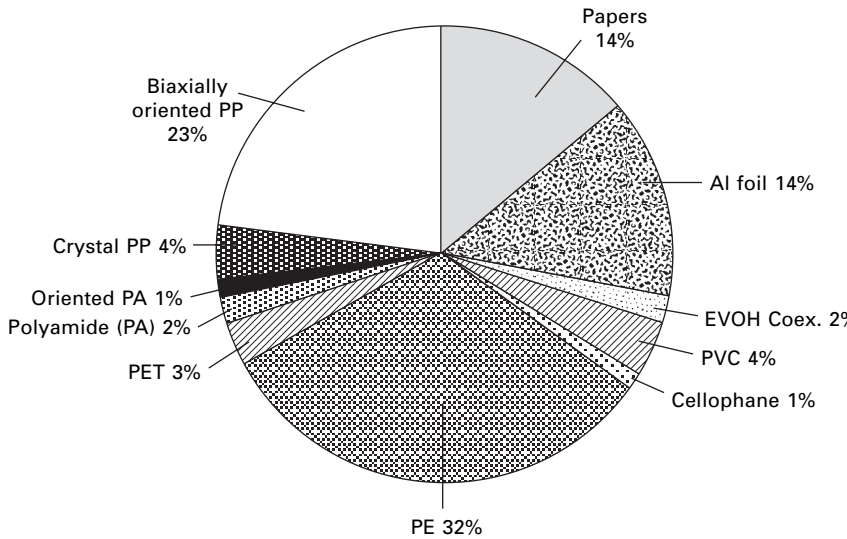

Fig. 10.3 Flexible packaging substrate use 2003 (reproduced with permission from Research Information Ltd).

- barrier properties to oxygen and water (in some cases also carbon dioxide and ethylene).

These criteria are not in any particular order and some may conflict with one another. Fortunately for food packaging, in cases where no single plastics monolayer can satisfy all the functional requirements, recently applied technologies such as co-extrusion and lamination can provide complete solutions. The most commonly used plastics for the manufacture of FCMs are given below.

10.3.1 Low density polyethylene (LDPE)

This type of plastic is used frequently for food bags, which are produced by blowing a film. As LDPE is very flexible it is also used to make lids for food storage containers, produced by injection moulding techniques. The polymer is relatively cheap with good water vapour and moisture resistance, but has poor barrier properties to gases and low molecular weight organic chemicals. 'Stretch films' used for wrapping food contain a few percent of a polybutadiene additive to provide a degree of 'cling' property. LDPE is often used as a film or coating on other materials, such as paper and aluminium foils to provide flexibility and heat sealability.

Ethylene may be copolymerised with vinyl acetate to make ethyl-vinyl acetate, offering high seal integrity and clarity for frozen food applications where a high degree of toughness is required. Ethylene copolymers with other olefins such as propylene, 1-hexene and 1-octene allow a range of properties to be achieved. Linear low density polyethylene (LLDPE) has a

linear structure when compared to LDPE which has a high degree of branching. Frozen food, for example, for meat and poultry, must maintain strength at very low temperatures. LLDPE is one material that meets this requirement, although a traditional disadvantage of LLDPE has been its lower clarity than LDPE. This has largely been overcome by metallocene-catalysed grades which also offer greater strength and better oxygen barrier properties. Copolymers with acrylates produce ionomers which have superior heat sealability and are increasingly used in laminated films.

Polyethylenes are susceptible to oxidative degradation at processing temperatures, therefore antioxidants are added. Silica is sometimes added to LDPE as an antiblock to prevent films sticking and N,N-bis(2-hydroxyethyl)alkyl(C8-C18) amine (BEA) as an additive to reduce a build up of static charge (antistat). Table 10.2 gives commonly used substances in polyethylenes.

10.3.2 High density polyethylene (HDPE)

HDPE is used in similar applications to LDPE, but has better barrier properties than LDPE and a greater rigidity. So HDPE is also used for blow-moulded bottles for milk and other drinks, and in food storage containers. HDPE has a higher usable temperature than LDPE (up to about 100–120 °C) making it suitable for 'hot fill' and pasteurisation applications. HDPE is used for meat and poultry packaging because of its greater strength and puncture resistance at thinner gauges. Another increasing market for HDPE is in closures for

Table 10.2 Commonly used substances in polyethylene materials

Substance name	PM ref. no.	Function	Restriction SML
Ethylene	16950	Monomer	
Propylene	23980	Comonomer	
4-methylpentene	22150	Comonomer	0.05 mg/kg
1-hexene	18820	Comonomer	3 mg/kg
1-butene	13870	Comonomer	
1-octene	22660	Comonomer	15 mg/kg
Pentaerythritol tetrakis[3-(3,5-di-tertbutyl-4-hydroxyphenyl)propionate]	71680	Antioxidant	
Phosphorous acid, tris(2,4-di-tert-butylphenyl)ester	74240	Antioxidant	
Octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	68320	Antioxidant	6 mg/kg
Erucamide, oleamide, stearamide	52720, 68960, 88960	Slip additives	
N,N-bis(2-hydroxyethyl)alkyl (C8-C18) amine	39090	Antistatic	(T) 1.2 mg/kg
Glycerol stearate	57520	Antiblock	
Silica (silicon dioxide)	86240	Antiblock	

(T) = total migration of two or more moieties.

beverages. The monomers and additives used in HDPE formulations are similar to those in LDPE. A typical formulation for a HDPE bottle would be: HDPE 100 parts per hundred (pph); octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate 0.05 pph; phosphorous acid, tris(2,4-di-tert-butylphenyl)ester 0.1 pph.

10.3.3 Polypropylene (PP)

The market for polypropylene polymers and copolymers is generally increasing owing to their excellent versatility in a range of food processing conditions. Generally, PP is stiffer than LDPE or HDPE and has superior tensile strength, good clarity and grease resistance. Co-polymerisation of propylene with ethylene and other olefins yields materials with greater flexibility and impact strength, fulfilling requirements for low temperature applications. PP can be converted by a range of procedures to make films, pouches, closures, containers, bottles and injection moulded containers and articles that can withstand retorting and microwave reheating. Similar conversion methods are used as with other polyolefins, but with the addition of thermoforming to make, for example, trays for cakes and pots for yoghurts.

A typical formulation for a polypropylene (PP) film used for wrapping biscuits would be: PP 100 pph; pentaerythritol tetrakis[3-(3,5-di-tertbutyl-4-hydroxyphenyl) propionate] 0.1 pph; phosphorous acid, tris(2,4-di-tert-butylphenyl)ester 0.1 pph; erucamide 0.05 pph. Nucleators, such as substituted benzylidene sorbitols, can be added to improve the clarity of PP and LDPE (see Fig. 10.4). Oriented polypropylene (OPP) films are also available where a higher transparency is required with improved strength.

10.3.4 Polystyrene (PS)

Polystyrene homopolymer, often referred to as general purpose polystyrene (GPPS) or 'crystal' polystyrene, is a hard, fairly brittle polymer with excellent transparency. GPPS is used for making disposable tableware and plastic glasses. Styrene polymers and copolymers with butadiene and acrylonitrile, to a lesser extent, are used in a range of food contact applications including tableware, wine/beer glasses, yoghurt pots, coffee cups, and thermoformed trays for meat and fish. Although GPPS is hard it is rather brittle and lacks strength, therefore impact modifiers and/or copolymerisation with 1,3-

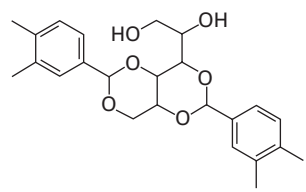

Fig. 10.4 Structure of bis(3,4-dimethylbenzylidene)sorbitol PM ref. no. 38879.

butadiene, to varying degrees, provide increased flexibility and strength. Oriented polystyrene (OPS) retains the clarity but increases the strength of the material and is better suited to making transparent films.

Expanded polystyrene (EPS) articles are made using high impact polystyrene formulations with incorporation of a blowing agent (this is usually a volatile solvent such as pentane). Often, EPS containers will have a crystal polystyrene skin applied to the food contact surface to act as a barrier between food and container. Applications of EPS include thermoformed packaging for eggs, meat, fish and fast food trays. Substances typically used in the manufacture of polystyrene are given in Table 10.3.

10.3.5 Polyvinyl chloride (PVC)

Vinyl chloride can be polymerised to form polyvinyl chloride (PVC) which is fairly brittle and unsuitable for food contact applications, so it is mixed with plasticisers to soften the polymer and impart flexibility. Plasticised PVC may contain about 30% of plasticisers and is used to make stretch films and flexible PVC. Flexible PVC used for tubing and gaskets may contain di(2-ethylhexyl)phthalate, and stretch films will probably contain di(2-ethylhexyl)adipate and a polymeric adipate plasticiser. 'Rigid' PVC may

Table 10.3 Substances commonly used in the manufacture of PS

Substance name	PM ref. no.	Function	Restriction SML
Styrene	24610	Monomer	
1,3-Butadiene	13630	Comonomer	QM 1 mg/kg SM = ND, DL = 0.02 mg/kg
Acrylonitrile	12100	Comonomer	SM = ND, DL = 0.02 mg/kg
'White' mineral oil	95883	Extender	Specification
Pentaerythritol tetrakis[3-(3,5-di-tertbutyl-4-hydroxyphenyl)propionate]	71680	Antioxidant	
Phosphorous acid, tris(2,4-di-tert-butylphenyl)ester	74240	Antioxidant	
Octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	68320	Antioxidant	6 mg/kg
Erucamide, oleamide, stearamide	52720, 68960, 88960	Slip additive	
N,N-bis(2-hydroxyethyl) alkyl(C8-C18) amine	39090	Antistatic	(T) 1.2 mg/kg
Thiodipropanoic acid, didodecyl ester (DLTDP)	93120	Antioxidant	(T) 5 mg/kg
Thiodipropanoic acid, dioctadecyl ester (DSTDP)	93280	Antioxidant	(T) 5 mg/kg
Alkyl (C8-C22) sulphonic acids	34230	Antistatic	6 mg/kg

(T) = total migration of two or more moieties.

contain low levels of plasticiser and is used to make trays for fresh meat having good clarity and water bottles. PVC compounds are calendared – the resin is forced between rollers to form a sheet that can then be thermoformed to produce trays or pots. PVC bottles are blown in a similar way to HDPE.

PVC tends to degrade slowly at processing temperatures to release hydrogen chloride (HCl) which can impair the performance of the plastic. Therefore HCl scavengers are added to the PVC compound. ESBO (epoxidised soybean oil) acts as both an HCl scavenger and a plasticiser, and is used in both stretch films (with other plasticisers) and in cap gaskets. In rigid PVC formulations, tin stabilisers are often added, to scavenge HCl, in conjunction with calcium/zinc stearates. One limitation of rigid PVC is that its maximum use temperature is about 70 °C, above which it begins to deform. Copolymerisation of vinyl chloride with vinylidene chloride increases this temperature so that a film suitable for microwaveable reheating is produced. Polyvinylidene chloride (PVDC) film is commonly plasticised using a plasticiser such as tri-*n*-butyl acetyl citrate (ATBC). Vinyl chloride monomer (VCM) is the subject of three directives: 78/142/EEC, 80/766/EEC and 81/432/EEC where the limits for VCM are given together with analytical methodology. Table 10.4 lists commonly used substances in PVC.

10.3.6 Polyethylene terephthalate (PET)

PET is made by polymerising ethylene glycol with terephthalic acid or transesterification with dimethyl terephthalate, commonly using an antimony trioxide catalyst. Other monomers such as isophthalic acid are used to make copolymers for some bottle formulations. The use of PET plastics has increased significantly over the last ten years replacing glass and, to some extent PVC, in applications for water and soft drinks. PET bottles are made in a two-stage process, initially a preform is made which is then blow moulded. PET is also thermoformed to make trays and pots used for cooking and heating foods in both conventional and microwave ovens. The PET used in high-temperature applications has a higher crystallinity and is opaque compared to the transparent amorphous material used to make bottles. Greater crystallinity is achieved by heating and/or addition of crystallisation aids. By-products of polymerising or processing the components of PET are diethylene glycol and acetaldehyde, although acetaldehyde scavengers, such as anthranalamide (2-aminobenzamide), can be used to reduce the level of acetaldehyde which can cause taint/odour problems.

Polyethylene naphthalate (PEN) polyesters are made from 2,6-naphthalene dicarboxylic acid or 2,6-naphthalene dicarboxylic acid, dimethyl ester. They have higher temperature resistance than amorphous PET and are increasingly used in applications requiring heat sterilisation of the food/drink, although PEN at the moment is significantly more expensive. Table 10.5 lists commonly used substances in polyesters.

Table 10.4 Substances commonly used in the manufacture of PVC

Substance name	PM ref. no.	Function	Restriction SML
Vinyl chloride	26050	Monomer	QM = 1 mg/kg or SML = ND (DL = 0.01 mg/kg)
Acetic acid, vinyl ester	10120	Comonomer	12 mg/kg)
Vinylidene chloride (for PVDC)	26110	Comonomer	QM = 5 mg/kg or SML = ND (DL = 0.05 mg/kg)
Methacrylate/butadiene/styrene (MBS)		Impact modifier	See Table 10.3
Acrylic polymer		Process aid	
Octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	68320	Antioxidant	6 mg/kg
Erucamide, oleamide, stearamide	52720, 68960, 88960	Slip additive	
N,N-bis(2-hydroxyethyl)alkyl (C8-C18) amine	39090	Antistatic	1.2 mg/kg
Soybean oil, epoxidised (ESBO)	88640	Stabiliser	60 mg/kg 30 mg/kg (infants) Specification
Adipic acid, bis(2-ethylhexyl)ester (DEHA)	31920	Plasticiser	18 mg/kg
Phthalic acid, bis(2-ethylhexyl)ester	74640	Plasticiser	3 mg/kg under review
Polyester of 1,2-propanediol and/or 1,3- or 1,4-butanediol	76866	Plasticiser	30 mg/kg
Calcium/zinc stearate or laurate		Stabiliser	
Di-*n*-octyl-tin compounds		Stabiliser	SML (T) 0.006 mg/kg as total tin
Mono-*n*-octyl-tin compounds		Stabiliser	SML (T) 1.2 mg/kg as total tin
Methyl tin compounds		Stabiliser	SML (T) 0.18 mg/kg as total tin
Glycerol stearate	56585	Lubricant	

(T) = total migration of two or more moieties.

10.4 Degradation products and impurities

Other substances may be present in food contact plastics that were not originally intended to be present in the finished material or article, but arise from reactions during polymerisation or processing. Or they may be present as

Table 10.5 Substances commonly used in the manufacture of PET/PEN

Substance name	PM ref. no.	Function	Restriction SML
Ethylene glycol	53650	Monomer	(T) 30 mg/kg
Diethylene glycol	47680	By-product	(T) 30 mg/kg
Isophthalic acid	19150	Comonomer	5 mg/kg
Terephthalic acid	24910	Monomer	7.5 mg/kg
2,6-naphthalene dicarboxylic acid, dimethyl ester	22390	Monomer	0.05 mg/kg
2,6-naphthalene dicarboxylic acid	22360	Monomer	5 mg/kg
Acetaldehyde	10060	Degradant	(T) 6 mg/kg
Adipic acid, bis(2-ethylhexyl)ester	31920	Carrier for colourants	18 mg/kg
2-aminobenzamide	34895	Acetaldehyde scavenger	0.05 mg/kg
1,4-Cyclohexanedimethanol	13390	Monomer	
Erucamide	52720	Lubricant	
Antimony trioxide	35760	Catalyst	0.04 mg/kg as Sb

(T) = total migration of two or more moieties.

impurities in one of the starting substances or additives. In Europe when a new additive or monomer has been developed for use in food contact applications, and it is not already positively listed or listed nationally, a dossier must be submitted to the European Food Safety Authority (EFSA) before it can be used. The dossier should contain sufficient information on the manufacture, uses and properties of the substance for EFSA to be able to make a safety evaluation (risk assessment). In particular, information on the migration of the substance into foods and/or food simulants needs to be provided. The level of migration will usually dictate the amount of toxicological testing required and as toxicological testing can be a costly exercise, migration testing is normally the first step.

When dossiers for new plastics' additives are submitted to EFSA for evaluation, it is a requirement for the petitioner to provide information on the technical effect of the additive in the polymer and any impurities that may be present and degradation products that arise in use (Note for Guidance, reference 6). The resulting SML may be a combination of those for the starting additive plus its degradation products. An example of this is 2,4,6-tris(tert-butyl)phenyl-2-butyl-2-ethyl-1,3-propanediol phosphite (PM ref. no. 95270) with an SML of 2 mg/kg that is the sum of the phosphite, phosphate and phenol individual migration values. Substances evaluated a long time ago may not have had such a thorough evaluation because degradation products and some impurities were not considered. It is also possible that a new substance will degrade partly or completely during a migration test and in this case a 'substitute test' may be more appropriate. In considering the migration of a new substance into food and food simulants, it is important to consider any impurities and degradation products.

Many of the reaction products derived from stabilisers can be predicted because they are added to react with free radicals or chemicals released during processing of the polymer. Many plastics will react with oxygen during processing and if additives are not present to reduce this autoxidation, the polymer will undergo 'ageing' reactions that have detrimental effects on their properties, such as discolouration, surface cracking and poorer physical properties such as impact strength. The most important primary antioxidants used in food contact polymers are usually based on hindered phenols. These react by interfering with the chain propagation reactions, where oxygen reacts with an alkyl free radical in the polymer chain ($P^{\cdot}$) to form a peroxy radical ($PO_2^{\cdot}$). These propagation reactions tend to occur when the polymer is at high temperature (for example during processing) or under stress and where a certain amount of oxygen is available.

A simple primary antioxidant is BHT (2,6-di-tert-butyl-*p*-cresol, PM ref. no. 46640). However, its use in food contact applications has declined somewhat recently as it has a low SML of 3 mg/kg and a relatively high migration into fatty food compared to some of its higher molecular weight rivals. Figure 10.5 illustrates the reaction of BHT with a free radical that in this example is designated $PO_2^{\cdot}$, that is responsible for propagation reactions in the polymer giving oxidation products. Figure 10.6 illustrates the structure of octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate, a more commonly used hindered phenol antioxidant used in polyolefins and polystyrene. Secondary antioxidants decompose hydroperoxides and remove peroxide radicals as they are formed, without producing free radical intermediates, and prevent chain branching occurring. Phosphites such as tris(t-butylphenyl)phosphite (Fig. 10.7) are oxidised to form phosphates. Phosphites also react with water to form phenols. Therefore in tests carried out to assess the migration of a phosphite stabiliser, measurements of the corresponding phosphate and phenol should be included.

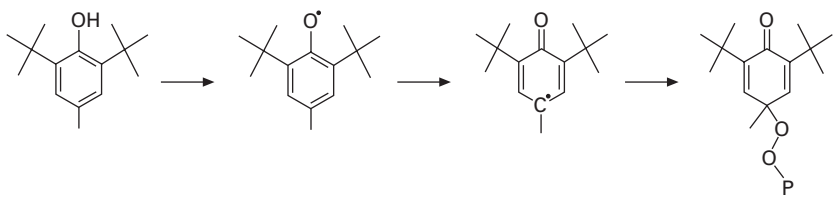

Fig. 10.5 BHT reaction with free radical $PO_2^{\cdot}$ (P = polymer).

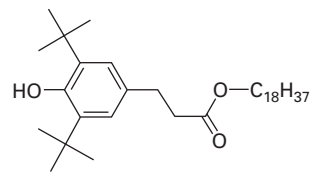

Fig. 10.6 Structure of octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate.

When screening polyolefin food packaging for additives by GC/MS, it is common to see two peaks, one for tris(t-butylphenyl)phosphite, base ion m/e 441, and the other for the corresponding phosphate, base ion m/e 316. Some secondary antioxidants are a mixture of compounds, such as tetrakis(2,4-di-tert-butylphenyl)[1,1-biphenyl]-4,4′diylbisphosphonite (P-EPQ), PM ref. no. 83595, one of six reaction products[7] of di-tert-butylphosphonite with biphenyl. Where there are a number of potential degradation products, although it is more convenient to concentrate on the major components, a minor component might be the most likely to migrate. Amongst reaction products of di-tert-butylphosphonite with biphenyl, the minor product 2,4-di-tertbutylphenol will have a higher migration rate into food because of its significantly lower molecular weight.

Another class of secondary antioxidants used in food contact plastics is thioether. The most common examples used in polypropylene, polystyrene and PVC are thiodipropanoic acid, didodecyl ester (DLTDP) and thiodipropanoic acid, dioctadecyl ester (DSTDP). Thioethers react with hydroperoxides to form sulphoxides as shown in Fig. 10.8.

Use of both primary and secondary antioxidants usually provides a synergistic effect, where the combined effect of two or more stabilisers is greater than the sum of the effects of the individual stabilisers. It is common practice to include both a phosphite, such as tris(t-butylphenyl)phosphite and a hindered phenol, such as octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate to provide improved heat stabilisation in polyolefin formulations.

Synergistic systems are also widely used in PVC formulations where additives are present to react with labile chlorine atoms in the polymer chain and scavenge hydrogen chloride that may be generated due to thermal degradation during processing. The resulting small concentrations of HCl, if left to remain would cause further HCl ‘unzipping’ degradation reactions of

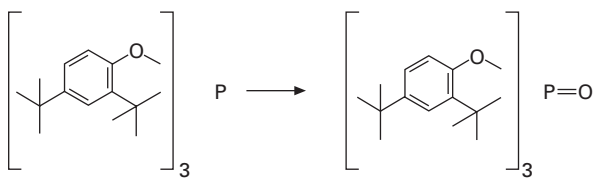

Fig. 10.7 Oxidation of tris(t-butylphenyl)phosphite to tris(t-butylphenyl)phosphate.

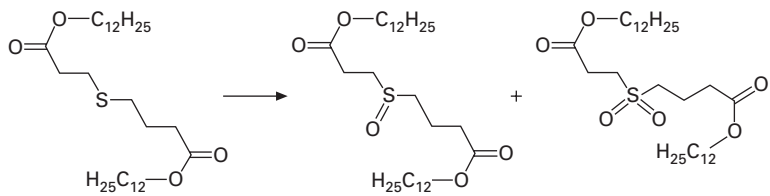

Fig. 10.8 Reaction of DLTDP with hydroperoxides.

the polymer (autocatalytic chain reactions). Epoxides are one group of chemicals that react rapidly with HCl to form chlorohydrins. Epoxidised soybean oil (ESBO) is a common plastics additive useful for this purpose. It is often present at levels of about 5% in PVC compounds. In some applications, such as 'Press to seal, twist to open' (PT™) closures for glass jars, ESBO is present at much higher levels (~ 35%) as it also acts as a plasticiser.

Calcium/zinc stearates are very effective stabilisers and can be used in conjunction with ESBO. They react with HCl to form calcium and zinc monochlorides Ca(OCOR)Cl with HCl. Other HCl scavengers used in PVC include tin stabilisers, although these are not used in plasticised PVC formulations. Typical tin stabilisers are based upon dioctyl- or dimethyl-tins and degrade to form a range of products with HCl. Most tin stabilisers have very low SMLs, as low as 0.006 mg/kg, expressed as total tin. Salts of 2-ethylhexanoic acid are also used as heat stabilisers in PVC compounds and can degrade to give 2-ethylhexanoic acid which has been shown to migrate from sealing compounds into fruit juices and baby food.[8] Use of these stabilisers is being phased out owing to suspected undesirable toxicological properties of the substance.

Impurities in polymers generally originate from the starting substances used in synthesising monomers or additives. It is clear from the EU 'Practical Guide'[9] that impurities in authorised substances themselves do not require specific authorisation, but they should comply with the general provisions of the EU Framework Regulation.[1] In some cases impurities are specified with restrictions as it is possible that they accumulate in the polymer and do not get bound into the polymer structure. Therefore they may easily migrate, especially if they have a low molecular weight. For example, ethylbenzene, the precursor for manufacture of styrene is an impurity that often remains in finished polystyrene at levels around 10 mg/kg. Other impurities can be present in antioxidants and plasticisers and would probably arise from their precursors.

Other impurities may arise from additives that are not covered yet by the plastics legislation or are not evaluated by EFSA, such as polymerisation production aids and solvents. Although these substances are not intended to remain in the finished plastics, low levels may be detected when looking at sub-parts per million levels.

Oligomers is another class of substances that does not need to be separately authorised, if the monomers are already authorised. In the 'Note for Guidance', EFSA request that oligomers with a molecular weight below 1000 daltons be characterised, although identification may not be required. In most cases it is assumed that oligomers tend to be less toxic that the starting monomer(s). However, it is commonplace that concentrations in the polymer are correspondingly higher. This is certainly the case for PET, where the cyclic trimer can be present at 1–2% levels in the polymer.[10] Indeed, styrene dimer and trimer are usually present at significantly higher levels than styrene in

polystyrene materials. Some work has also been carried out on the measurement of caprolactam and laurolactam oligomers in nylons.[11,12]

The migration of oligomers will decrease with increasing molecular weight, Fig. 10.9 illustrates the correlation of migrant molecular weight against migration into food from polypropylene at 40 °C for ten days. In this example it is assumed that the migrant is highly soluble in the food and that the initial concentration of the fictive substance in the polymer is 0.2%.

Catalysts are currently not covered specifically by EU directives on food contact plastics. They tend to decompose during the polymerisation process. Again, the degradation products are often predictable and may sometimes be found in the finished food contact material. However, catalysts are usually present at low levels and the degradation products are often volatile. For example, the common catalyst t-butyl perbenzoate may decompose to give benzene when used in some thermoset polymers.[13] Tert-butyl peroxide is used as a catalyst in certain polymers and will decompose to give tert-butanol.

The blowing agent azodicarbonamide (PM ref. no. 36640) acts by releasing nitrogen gas during the blowing process. During the decomposition of azodicarbonamide, semicarbazide (SEM) can also be released and can migrate into foods. Highest concentrations (up to 25 ppb) were found in some baby foods packed in glass jars with PVC gaskets and, owing to the considerable unknowns relating to SEM's toxicological properties and exposure, it was judged by EFSA to be undesirable in baby food. Directive 2004/1/EC prohibited the use of azodicarbonamide in food contact materials from August 2005. It is also prohibited as a food additive in the EU following doubts about its several degradation products.

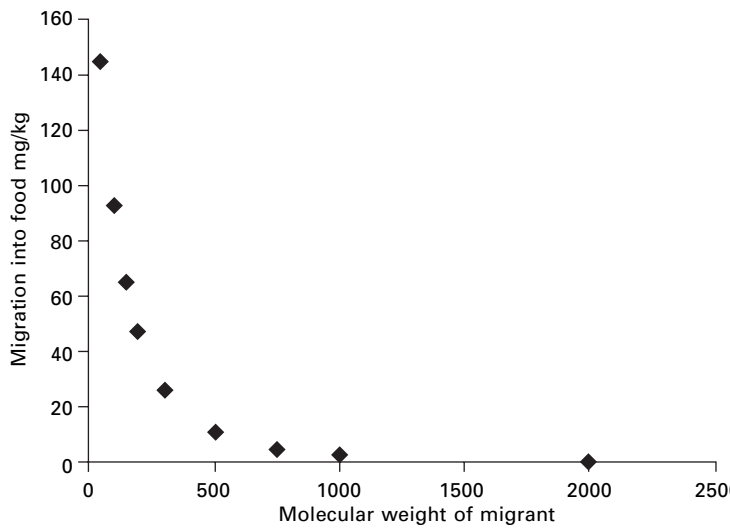

Fig. 10.9 Correlation of migrant molecular weight and migration.

10.5 Future trends

Future trends in food contact plastics are most likely to be directed at developing more environmentally friendly or sustainable materials, such as those that are biodegradeable and plant derived, to reduce the negative environmental impacts created by landfill and incineration of plastics.[14] The driving force here is EU Directive 2004/12/EC, which amends Directive 94/62/EC on packaging and packaging waste, and approximately doubles packaging recycling targets and strengthens the target for recovery. There is also an ever increasing trend in the development and use of active and intelligent packaging with the associated benefits of increased food safety for the consumer. In particular, the availability of oxygen scavengers that can be incorporated into inner layers has been a key element in the design of new PET beer bottles.

In the field of antimicrobial food packaging, technology suppliers are developing systems to target bacteria on the surface of food.[15] An antimicrobial chemical is intended to be immobilised in the packaging film and so not migrate into food (bread or cheese for example), but prevent any bacterial growth on food particles trapped in microscopic fissures in the surface contact layer. Only those antimicrobials on a positive biocides list for food contact will be permitted for use, provided also that they are effective in this particular type of application. Appropriate labelling of biocide-containing food packaging will also be required to communicate usage. EFSA will be assessing any risk of these biocides using the additional considerations outlined in 'Note for Guidance' – in particular evidence should be provided showing that:

- any migration into food is not intentional but only incidental
- its use does not exert any preservative effect on the food
- its use does not allow the selection of non-sensitive organisms on the food contact materials
- it does not allow the development of biocide resistance in sensitive micro-organisms.

In addition, the petitioner should provide evidence that the substance is not used to replace the normal hygienic measures required in handling foodstuffs.

At present, nanotechnology is being applied in plastics packaging to a limited degree to improve the properties of materials and increase the efficiency of making packaging.[16] Potential benefits include improved barrier properties (delivering longer shelf life or allowing material substitution) and better temperature performance using titanium, zinc, aluminium and iron oxides. Applications are also being developed in areas of active and antimicrobial food packaging. Nanotechnology is expected to be a major growth area in coming years in all food contact materials, and there is a major EU funded project in this area, 'SustainPack', with a budget of €36m of which €19m is being provided by the EU's Sixth Framework Research Programme. However, at present little is known about the toxicity or migration of nanoparticulates and substances used in the manufacture of nanocomposites.

10.6 Sources of further information and advice

More information on the role of plastics additives can be found in ref. 17, and refs 18 and 19 provide information on packaging materials. More information on the methods and research projects conducted in the field of food contact safety and legislation can be found on the following websites:

http://cpf.jrc.it/webpack/ – this website provides links to the European Commission, ILSI, EFSA, CEN and Council of Europe websites. There is also a satellite website http://cpf.jrc.it/smt/ which gives details of analytical methods and spectroscopic information on certain monomers and additives.
http://www.efsa.eu.int/
http://www.foodstandards.gov.uk/science/research/
http://europa.eu.int/comm/food/food/chemicalsafety/foodcontact/eu_legisl_en.htm
http://www.cfsan.fda.gov/~dms/opa-notf.html
http://www.packaginglaw.com/

Reference 20 provides a review on research carried out on food contact materials. On the following websites more information can be obtained about plastics:
http://www.bpf.co.uk/
http://www.plasticseurope.org/Content/Default.asp

Reference 21 is a valuable resource on migration from food contact materials.

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11

Metal packaging and chemical migration into food

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11.1 Introduction

Metal food contact materials (FCMs) cover a very diverse range of products from metal tanks, pipes and components in food manufacturing machinery, through cutlery, bowls and work surfaces (commercial or domestic) to metal packaging for foodstuffs (either food or drink). Only metal foodstuff packaging will be dealt with here. For guidance on the wider application of metal FCMs the Council of Europe (CoE) Guidelines on Metals and Alloys Used as Food Contact Materials (CoE 2001) provides a useful reference. Metal foodstuff packaging itself covers a wide range of packaging types including food and beverage cans and ends, closures, tubes, trays, drums and pails. The focus of this chapter will be on metal cans, ends and closures.

Although metal is the defining component of these packages providing strength and integrity, the additional materials required to make a functional package are more often the primary food contact materials in the package and much of this chapter covers these materials. As for all FCMs, consumer safety is of prime importance and is assured through a combination of regulatory compliance and industry risk assessment. In the USA coated metal packaging is specifically regulated, but there is currently no EU harmonised legislation covering this sector beyond the Framework Regulation (1935/2004) and certain substance specific legislation. Some EU national member state legislation exists and is used in demonstrating compliance with the Framework Regulation, but this provides only limited help.

For this reason harmonised EU legislation that includes metal foodstuff packaging is needed. Extension of the existing harmonised legislation on plastics materials and articles is not appropriate without significant

modifications due to the particular nature of metal packaging and the filling and subsequent processing operations specific to this sector. These differences are particularly significant for those food cans that do not have an internal protective coating, and these packages will also be covered in this chapter, as will other areas of special consideration.

11.1.1 Scope of metal packaging for food and beverage

A common factor of metal foodstuff packaging is that it provides long term ambient stable storage with excellent abuse resistance and protection from environmental contamination ensuring food safety and quality retention with extended shelf life. Flexible packaging which is covered elsewhere in this book may also use thin layers of metal either as discrete foil layers or as metallised plastic or paper layers for improved barrier properties, but the main structural components are non-metallic and so are not covered here.

The metals used to manufacture cans, ends and closures are either steel (tin plated or chromium passivated) or aluminium. In most cases they are coated on the food contact surface with a resinous or polymeric protective coating to avoid interaction between the foodstuff and the metal. However, there is a well defined sector of the tinplate food packaging market where no protective organic coating is needed or used.

Cans may either be 'three piece' consisting of a body made up of a welded cylinder with one end seamed in place which is then closed with a second end, or 'two piece' consisting of a body formed from a single piece of metal closed with an end (see Fig. 11.1). Aluminium cans are always 'two piece' whereas steel cans may be either 'three piece' or 'two piece'. The end or ends are seamed onto the can body which involves the forming of a 'double seam' of folded metal (see Fig. 11.2). A hermetic seal (a key element of metal food and beverage packaging) is ensured by the incorporation of a

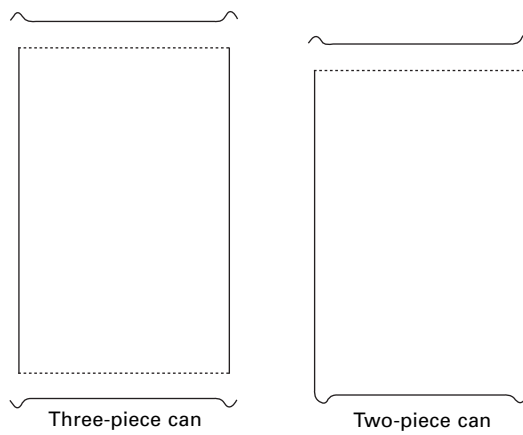

Fig. 11.1 Major can technologies.

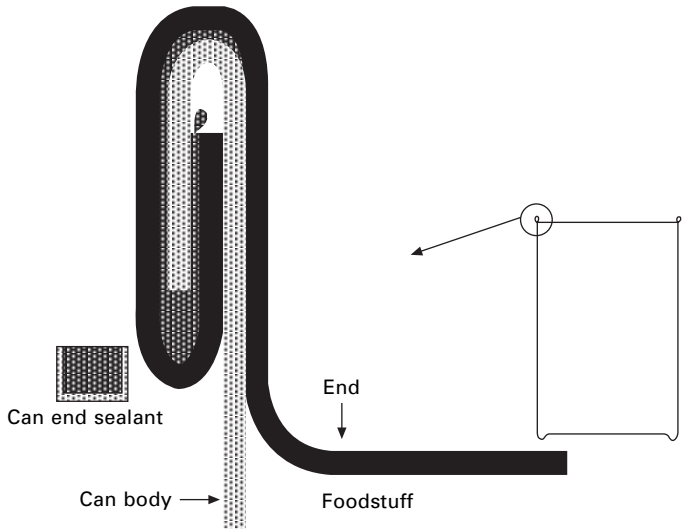

Fig. 11.2 Can double seam.

very thin layer of rubber based compound buried within the seam. Metal closures always incorporate some form of sealing gasket to ensure that an effective seal is maintained. These various elements of the construction of metal packaging mean that a number of different material types have to be considered in the assessment of the safety and regulatory compliance of the finished package:

- metals, from uncoated packaging and from failure of the internal coating
- internal protective coatings
- can end sealants (buried within the double seam)
- gaskets for metal closures
- residual lubricants, etc., from the package manufacturing process
- adventitious contamination from the manufacturing process.

These last two categories, which are common to most packaging manufacturing processes, could be considered as 'non-intentionally added substances' if they contaminate the foodstuff.

11.1.2 Particular features of metal packaging influencing migration

Metal packaging for food and beverage has particular features that differentiate it from other food packaging materials and which also influence the management of overall food safety and regulatory compliance. These features differ in some aspects between food and beverage packaging.

Food packaging

Foods packaged using metal packaging are almost always ambient stable

and have long shelf lives of between one and five years. Other than with dried foods and some intrinsically microbiologically stable foods this is achieved by a heat sterilisation or pasteurisation process of the foodstuff after sealing into the packaging. Long-term microbiological stability of the foodstuff is then assured by eliminating post-process contamination. Maintenance of the integrity of the structure and seal of the package is therefore critical to the safety of the foodstuff. It also plays a vital role in retaining the food quality, nutrition and wholesomeness by excluding oxygen ingress that would lead to product deterioration. This latter feature can also be important for those intrinsically stable foods which do not rely on the seal integrity for microbiological safety. The integrity of the metal packaging must be retained throughout the life of the product. This includes withstanding damage and abuse during distribution, retail and consumer handling. This puts significant demands on the performance of the can end sealants, closure sealing gaskets and internal protective coatings and constrains the potential choice of these materials. The thermal sterilisation process, which may be at temperatures in excess of 130 °C, puts significant demands on the packaging material with regard both to migration and material performance and sets particular challenges to compliance testing which will be covered later in this chapter.

Beverage packaging
Depending on the nature of the beverage, the cans or bottles may either be heat processed post-filling (beer and cider, fruit juices, tea, coffee and milk based drinks) or ambient filled where the product formulation and pH ensure microbiological stability. Although post-filling contamination of the non-heat-processed products is less critical, it remains important in retaining product quality. Exclusion of oxygen and retention of carbonation are also important in ensuring long-term product quality and consumer acceptability.

11.1.3 Internal protective coatings, sealants and gaskets

Internal protective coatings
These coatings, typically 2–20 micrometres (μm) thick, protect the metal package surface from the corrosive properties of the foodstuffs throughout filling, long-term storage, and in some cases, consumer heating. This role requires very high performance, as the coating must survive without any loss of integrity during metal forming operations and high temperature food processing, as well as abuse during distribution and retailing. The coatings need to have very good substrate adhesion combined with flexibility, temperature resistance, food product resistance and inertness. To achieve this level of performance for the wide range of foodstuffs, package styles and manufacturing routes, many different coating formulations are needed, used either as a single coating or for some critical applications in combination

in multi-coat systems. Although most coatings belong to a small number of basic chemistries, a typical metal packaging manufacturer may use a range of over 100 different coating formulations which adds to the complexity of managing food safety and regulatory compliance. Most coatings are thermoset systems and are formulated from resins, cross-linkers and additives. These are generally dispersed in solvent mixtures which are driven off in the early stages of the thermal stoving sequence leading to the highly cross-linked, impervious, inert finished coating film. Powder coatings which are usually thermoplastics with some thermoset modification, may be used as a side stripe to protect the welded side seam of cans. In addition, increasing use is being made of thermoplastic polymer coated metal, either extrusion coated onto the substrate or laminated as a film. Difficulties in welding polymer coated metal limit its use currently to 'two piece' can technology and end/closure manufacture and the market share of this material is still low. A summary of coating chemistries with their typical applications and properties is given in Table 11.1.

Can end sealants

As already described, the ends on food and beverage cans are mechanically seamed onto the can bodies. Although the 'double seam' gives a very tight, strong seal, a thin layer of rubber based sealant is incorporated, buried within the seam, to ensure a hermetic seal. This seal must accommodate the differential expansion and contraction of the can components during the heating and cooling of the sterilisation process as well as withstand the abuse that distribution and storage entails. Although the potential for contact between the foodstuff and the sealant is limited by the positioning of the sealant, it still needs to be considered in the management of the food safety and regulatory compliance of canned foodstuffs. These sealants are generally dispersions of rubber or latex either in an organic solvent or in aqueous dispersion which are applied to the curl of the end and allowed to dry at ambient or elevated temperatures before seaming onto the can. Control of sealant application and end seaming ensures the correct placement in the finished seam.

Closure gaskets

There are a large variety of metal closures for glass, plastic or metal containers which may be used for thermally processed foods, ambient stable foods, dry foods, still and carbonated beverages, etc. A common requirement for all these closures is an effective seal, in much the same way as with can ends. For thermally sterilised or pasteurised foods this seal is responsible for preventing post-process microbiological contamination of the foodstuff and its performance is critical to the safety of the finished product. In a similar way to can ends, the performance of the seal also ensures retention of the quality of the foodstuff though control of oxygen ingress and, for carbonated products, retention of carbonation. The range of materials that have the required properties is very limited with plasticised polyvinyl chloride (PVC)

Table 11.1 Typical protective coatings used for metal foodstuff packaging

	Coating chemistry	Flexibility	Pack/process resistance	Applications
Epoxy-phenolic	High molecular weight epoxy resins cross-linked with phenolic resole resins	Good	Very good	Most widely used system Universal gold lacquer for three piece cans Shallow drawn cans
Epoxy-amino and epoxy-acrylate	High molecular weight epoxy resins cross-linked with amino or acrylate resins Water reducible for reduced environmental impact	Good	Limited	Universal lacquer for beer and beverage cans (water reducible) Side seam stripes Some food systems
Organosol	PVC dispersed in an appropriate varnish and conventionally stabilised with a low molecular weight epoxy , resin or epoxidised bean/seed oils	Very good	Very good	Drawn cans Easy-open ends* Closures* *Often used over epoxy-phenolic basecoat
Epoxy-anhydride	High molecular weight epoxy resins cross-linked with anhydride hardeners	Good	Very good	Internal white for three piece cans
Thermoset polyester	Polyester resins cross-linked with amino or phenolic resins May contain lower molecular weight epoxy resin	Very good	Pack dependent	May not be suitable for very acidic and aggressive foods
Thermoplastic polymer coated	Extrusion coated or laminated film of thermoplastic polyester, polypropylene, nylon or combinations – high molecular weight	Very good	Good	Shallow drawn cans Easy-open and standard ends Closures

plastisols being used for virtually all food applications and either plasticised PVC (plastisols) or thermoplastic polymers used for beverage applications.

11.1.4 Holistic management of food safety

In most cases, foodstuffs packed in metal packaging make use of its unique properties to provide long-term storage of foods and beverages with retention of food safety, quality and nutrition. This is achieved by maintaining the package integrity, which prevents any post process contamination of the foodstuff. The integrity of metal packaging relies heavily on the properties of the different materials used in its construction, particularly the internal protective coatings, the can end sealants and closure gaskets. As well as providing the long-term integrity of the package, these materials must not themselves contaminate the foodstuff at levels that may be harmful to health and in addition they must not taint the foodstuff in any way. Because of the complex interactions between real foods and metal packaging, only limited use can be made of predictive testing of package performance and long-term pack testing with real foods is invariably required to ensure the safety of the package over the one- to five-year shelf life. The packaging manufacturer and the food packer have responsibility for all aspects of the safety of the packaged food which includes package integrity as well as the potential for migration. It is essential that any restriction of materials available to the packaging manufacturer on the grounds of precaution do not compromise the existing high degree of microbiological as well as chemical safety that metal packaging provides.

11.2 Regulation and use of metals as food contact materials

In general, the existing regulation of metal packaging covers the metallic and non-metallic components of the package separately. In the EU, where there is currently no harmonised specific regulation of metal foodstuff packaging, all components are covered primarily by the Framework Regulation (1935/2004) but it is expected that when harmonised legislation is extended to metal foodstuff packaging, metallic and non-metallic components will be treated separately. In the absence of harmonised EU specific regulation, compliance of metal foodstuff packaging is managed by a combination of national member state legislation and industry risk assessments.

11.2.1 State of current regulation of metals

Under most regulatory systems, metals are considered under food contaminant regulations rather than FCM regulations. Codex Alimentarius provides international guidance on acceptable limits for metals in foods. In addition, there are some national and EU limits and the Council of Europe has produced

a guidance document on metals and alloys used as FCM (CoE 2001). The metals of relevance to metal foodstuff packaging are iron, tin, aluminium, chromium, and lead.

Iron

Iron is the major constituent of steel which is used either as tinplate or electro chromium coated steel (ECCS). However, the steel surface is always protected by a layer of tin and/or a protective organic coating. Iron is not controlled by specific regulatory limits although the joint FAO/WHO expert committee on food additives (JECFA) has established a provisional maximum tolerable daily intake (PMTDI) at 0.8 milligrams per kilogram bodyweight ($mgkg^{-1}$ bw). Given the strong taint that iron imparts to foodstuffs, this limit is unlikely to be exceeded through the use of steel in foodstuff packaging. Iron migration from metal foodstuff packaging is monitored by industry during qualification testing because of the risk of tainting and because iron dissolution could indicate corrosion of the substrate leading to potential loss of can integrity. Standards exist for food packaging grades of tinplate (EN 10333), and ECCS (EN 10335).

Tin

Tin-coated steel (tinplate) is widely used in metal foodstuff packaging and is manufactured by electrochemical deposition. Levels of tin coating vary between 2.8 and 15.4 gm^{-2} depending on the application. It is usually covered by a protective organic coating although for dry foods and certain specific wet foods, the plain tinplate surface may be used without a coating. In the case of wet foodstuffs in contact with uncoated tinplate, a level of tin dissolution is inevitable and limits (statutory or recommended) are in place in most countries. In the EU, tin is covered by regulation No 242/2004 which limits levels to 200 mg kg^{-1} for canned food other than beverage, 100 mg kg^{-1} for beverages and 50 mg kg^{-1} for foodstuffs specifically marketed for infants. Most non-EU countries use the Codex Alimentarius limits of 250 mg kg^{-1} for solid foods and 150 mg kg^{-1} for liquid foods. However, the Codex limits are currently under review. Tin migration is only an issue where internal protective coatings are not used, although in practice, the EU limits will not be exceeded within the stated shelf life if appropriate foods are packed under good canning practice. It is important for the filler to control residual oxygen and oxidising contaminants, the presence of which control tin dissolution. Tin migration is monitored by industry during qualification testing to ensure that the controls are working correctly. Codex Alimentarius has published guidelines on the prevention and reduction of tin contamination in canned food (Codex 2005).

Aluminium

Aluminium cans, ends and closures are always covered with a protective organic coating which reduces aluminium migration to typically below 1 mg

kg^{-1}. Aluminium as a component of foodstuff packaging is not controlled by specific regulatory limits. However, EU Directive 98/83/EC on the quality of water intended for human consumption gives a standard value of 0.2 mg kg^{-1}, as a compromise between the practical use of aluminium salts in drinking water treatment and discoloration of distributed water. It is a limit that represents good practice and is not a safety limit. Aluminium migration is monitored by industry during qualification testing in order to comply with limits imposed by specific foodstuff fillers, and also because aluminium dissolution could indicate corrosion of the substrate leading to potential loss of package integrity. A standard exists for a food packaging grade of aluminium (EN 602).

Chromium

Chromium is used at very low levels as a passivation coating for tinplate and at higher levels for ECCS. It may also be used to treat aluminium surfaces. The process ensures that the only species present are Cr^0 and Cr^{III} and not Cr^{VI} which is the toxicologically important species. Chromium in food is not generally regulated (there is a World Health Organisation (WHO) limit of 0.025 mg l^{-1} for drinking water). The level of migration from uncoated tinplate cans (the only metal foodstuff packaging where migration is likely to occur) is negligible and not considered to be of concern. Future change in environmental legislation is encouraging work on alternative passivation systems.

Lead

Lead has not been intentionally used in the manufacture of metal FCM for many years. Before welded 'three piece' cans became widespread, the side seams were commonly soldered with a lead based solder, a practice which is now virtually eliminated. However, it is not possible to obtain tin with zero lead contamination as the elements coexist in the ore. As a consequence, the tin content of tinplate will always contain traces of lead. Lead contamination of food is regulated in most countries with different levels for different foodstuffs (e.g. EU regulation No 466/2001) with limits typically in the range of 0.02 to 0.1 mg kg^{-1}. The level of lead in the tin coating of tinplate is controlled by the tinplate specification, which in the past has allowed a maximum 500 mg kg^{-1} lead in the tin. At this level, in practice, lead limits in food should not be exceeded due to migration from metal foodstuff packaging. However, as a matter of due diligence, industry action in Europe and the USA is reducing the maximum level of lead in the tin coating of tinplate for food packaging to 100 mg kg^{-1} as defined in European Standard EN 10333.

11.2.2 State of current regulation of coatings

The regulation of food contact coatings on metal FCMs varies around the world.

USA

The USA has a comprehensive and widely recognised regulatory system that specifically covers polymeric and resinous coatings under FDA CFR21 175.300 which lists authorised starting substances and lays down test conditions and migration limits. Globally, the great majority of coatings are formulated to be compliant with 175.300 and this is an important element of demonstrating the safety of coated metal foodstuff packaging even in the EU where 175.300 is not specifically recognised.

EU

In the EU, harmonised regulations specific to coatings on metal have not yet been developed. However, the Framework Regulation 1935/2004 applies to all packaging types as do substance specific measures such as the 'Epoxy' Regulation 1895/2005 and the Vinyl Chloride Monomer (VCM) Directive 78/142/EEC. Compliance with these measures is essential, and whilst it is clear what needs to be achieved for compliance with the substance specific measures, the Framework Regulation, and in particular the key Article 3 gives no guidance on how compliance may be demonstrated. In the absence of harmonised legislation, EU national member state regulations, where they exist, may be used to demonstrate compliance with the Framework Regulation. The Dutch Verpakkingen- en Gebruiksartikelenbesluit (Hoofdstuk X) is the most comprehensive and has a positive list of permitted starting substances that is also used in other EU member states as a means of demonstrating compliance.

Other EU member states with legislation covering at least some aspects of coated metal FCM include France, Belgium and Greece. In addition to national member state legislation, reference to the CoE Resolution on Surface Coatings AP (2004) 1, together with published opinions of the Scientific Committee on Food/European Food Safety Authority (SCF/EFSA) and EU legislation that does not include coatings within its scope (such as Directive 2002/72/EC on plastics food contact materials and articles) may be used in demonstrating compliance. In the case of thermoplastic polymer coated metal, the thermoplastic layer may, in most cases, be able to be fully compliant with the provisions of 2002/72/EC. However the more generally used thermoset coatings are more complex and can not generally be formulated using only substances authorised in 2002/72/EC. As can be seen, there is no clear path to demonstration of compliance for coated metal foodstuff packaging in the EU at present, and it is hoped that harmonised EU legislation in this area will be developed soon.

CoE Resolution on surface coatings AP (2004) 1

Although it has no legal status, this recently revised Resolution consists of a framework with technical appendices. It also includes comprehensive inventory lists of monomers and additives, all of which have some national member state or USA authorisation. The lists are divided into those which

are already fully evaluated and included in the SCF/EFSA lists 0–4 and those which have not yet been fully evaluated by SCF/EFSA. This latter category is time limited with a deadline of five years from adoption of the Resolution by which time they must have been fully evaluated. There are still some outstanding issues with this Resolution that need to be addressed but it will be a useful reference in demonstrating compliance in the period before the EU is able to fully include surface coatings in its legislative framework.

11.2.3 State of current regulation of can end sealants

Can end sealants are based on natural or more usually synthetic rubber/latex with additives to give them the particular properties of adhesion, elasticity, temperature resistance and resistance to components of foods and beverages whilst ensuring an enduring hermetic seal. Under USA legislation they are specifically covered under FDA CFR21 175.300(xxxi) listing authorised starting substances. As with coatings, these materials are not yet covered under specific EU harmonised legislation so member state legislation may be used to show compliance. In particular the Dutch legislation has a section specifically covering can end sealants (Verpakkingen- en Gebruiksartikelenbesluit – Hoofdstuk IVf). The German recommendations of the BfR may also be useful for showing compliance. A CoE Resolution on Rubber and Elastomers AP (2004) 4 has been published but is not yet complete. In its finished form, it should be useful as a further reference for demonstrating safety and compliance of can end sealants.

11.2.4 State of current regulation of closure gaskets

These materials are fully regulated in the USA under FDA CFR21 177.1210 (Closures with sealing gaskets for food containers) which lists authorised starting substances and lays down test conditions and migration limits but they are not yet covered by harmonised EU legislation. As discussed earlier, these closures fall into two main types – vacuum closures for foodstuffs and non-vacuum closures for beverages. It has become clear that the nature of the gasket materials used for vacuum closures (PVC plastisols) can lead to significant levels of plasticiser migration when use in contact with fatty foods under sterilisation/pasteurisation conditions. The gaskets in vacuum closures are not free standing components but are flowed in place and fused *in situ* forming a soft sealing coating around the sealing surface. It is not clear to what extent such materials are within the scope of EU Directive 2002/72/EC which does not apply to multi material multi layer packaging but the European Commission are drafting a ‘restrictions’ Regulation that should clarify the position. With this measure it should be clear what these closures should comply with but the details were not finalised at the time of writing.

11.2.5 Management of food safety in the EU in the absence of harmonised legislation

It will be clear from the above sections that the current lack of harmonised EU legislation means that there is no single straightforward way to show compliance for most components of metal foodstuff packaging. The main measure which must be complied with is the Framework Regulation 1935/2004, Article 3 of which states that materials and articles should not transfer their constituents to food at levels which could: (i) endanger human health; (ii) bring about an unacceptable change in the composition of the food; or (iii) bring about a deterioration in the organoleptic characteristics thereof. The end-point of this requirement is clear but no guidance is given as to how to arrive at that end-point. This results in manufacturers and users of metal foodstuff packaging having to undertake their own risk assessments and compile justifications for compliance based on other existing legislation, recommendations and guidance. This leads to a range of approaches being adopted and a lack of clarity for all sectors in the chain including the regulatory and control authorities. It is for this reason that the metal foodstuff packaging industry chain is working proactively to help develop and promote harmonised legislation in this area.

11.3 Special considerations of using metals as FCMs

As with all food packaging, the control of migration, regulatory compliance and safety of the finished product is a combination of the intrinsic properties of the packaging and its appropriate use. In some cases, the use of the wrong specification for a particular food product or process may render a potentially compliant package non-compliant. This potential issue is not restricted to the control of migration. As already discussed, the safety of the foodstuff as consumed must also take into account its microbiological safety which can be a significantly more important problem if not controlled. The nature of metal foodstuff packaging lends itself particularly well to long-term ambient-stable products where the stability throughout the shelf life is ensured through the structural integrity of the package after a thermal process of the sealed pack. Inappropriate selection and use of packaging materials for a particular application may prejudice the integrity and thus the intrinsic safety of the finished product. It is therefore most important that where the potential compliance and safety of a package relies on control of the end use regarding the nature of the foodstuff, the packing process and any sterilisation process, these limitations are correctly communicated to the food packer. The need to reinforce communication both up and down the food packaging chain is an area of increasing interest both within industry and also with the regulators. There are some particular cases where the end use of metal foodstuff packaging needs to be taken into account in selecting appropriate materials.

11.3.1 Special precautions related to the use of uncoated metal foodstuff packaging

As already discussed, most metal foodstuff packaging uses an internal organic protective coating to prevent interaction between the foodstuff and the metal substrate leading to product deterioration and potential perforation of the package. This is the case for all metal closures and beverage packaging, but there are some specific food products which, if correctly packed in tinplate containers, do not need this internal protective coating. These foodstuffs include dry foods, food oils and particular wet foods where the electrochemistry of the foodstuff and tinplate surface minimises the risk of perforation of the package or tainting of the foodstuff.

Dry foods and food oils

For dry food packs and food oils, the main precaution that has to be taken is that the products are free of water. The tinplate surface provides significant protection but localised free water can induce corrosion under certain circumstances leading to contamination of the foodstuff, particularly if there are corrosive components present in the foodstuff. The packaging supplier should ensure that the food packer is aware of these limitations, but in practice problems with such packs are very infrequent.

Wet foods

There is a group of wet foodstuffs for which the tinplate surface does not need any further protection as long as the product is correctly packed in the appropriate specification of packaging and an appropriate shelf life is determined. For these foodstuffs such as tomatoes, tomato-based products, white fruits, some soups and certain vegetables (potatoes, carrots, mushrooms), the electrochemistry ensures that the tin on the tinplate surface is preferentially dissolved and that the iron in the steel substrate is protected even where it may be exposed by scratches, etc. The rate at which the tin is dissolved is controlled by the availability of oxidising species in the foodstuffs and by the packaging material selection (chromium passivation and tin coating weight). The major sources of oxidants are residual oxygen in the pack which is controlled by good canning practice, and contaminants in the foodstuff such as nitrates or chlorates which are controlled by proper selection of the food components and control of the product make-up water.

Nitrate levels in the raw foods and in water supplies are an increasing problem that may require de-nitrification plants or conversion for some foodstuffs to internally coated metal packaging. The slow dissolution of tin across the package surface ensures that pitting corrosion does not occur which could lead to perforation and loss of pack integrity. The reducing environment provided by the tinplate surface has additional benefits for particular packs such as white fruits and tomato-based products as it helps to maintain the flavour and colour which would otherwise deteriorate through oxidation, particularly during the thermal sterilisation process. It is, however,

essential that the total level of tin dissolution is maintained below the statutory limits which will ensure that the tin presents no risk to health and does not adversely affect the food product quality. It is also essential that foodstuff selection, packaging selection, good canning practice and proper evaluation of shelf life is correctly managed to ensure the safety and quality of the finished product. As this form of packaging has been in routine use for many decades, the industry has a wealth of experience in the proper control of these products and there are both industry and Codex Alimentarius guidelines (Codex 2005) to assist the food packer. In summary, the uncoated or plain internal tinplate can is an excellent packaging solution for suitable food products but the packaging selection, food selection, filling and shelf life need proper control. Where this control cannot be assured then internal protective coatings must be used.

11.3.2 Precautions relating to the use of metal vacuum closures

Metal vacuum closures are generally used for food products where they are designed to retain a vacuum in the jar headspace during distribution and storage. These products range from intrinsically ambient stable products such as preserves and some pickles where the closure protects the products from environmental contamination and moisture loss through to thermally sterilised products where the closure is an essential element in maintaining a hermetic seal preventing microbiological contamination. The seal integrity of the closure is critical to the safety and quality of the finished food in these applications, and this integrity must be maintained during processing, distribution and retailing where the closure may be subject to handling abuse and damage. It is a particularly demanding application for the sealing gasket which is why, globally, the great majority of metal vacuum closures use PVC plastisol sealing gaskets. However, whilst giving unrivalled seal performance, the presence of significant levels of plasticiser will always lead to challenges in controlling migration into fatty foods.

Three of the key factors affecting plasticiser migration from closures are the availability and distribution of fat/oil in the foodstuff, the method of thermal processing used to sterilise/pasteurise the food and the area of exposed sealing gasket compared with the volume of the jar. The first two factors are specific to particular food products and manufacturing processes, the final factor is partly controlled through the design of the closure but is also controlled by the closure application process and the selection of a particular jar size. Therefore it is not possible for a closure manufacturer to give an absolute compliance statement as it depends on the final application. However, the closure manufacturer can indicate the potential level of migration into recognised simulants using recognised process simulations and defined jar sizes or expressed as migration/closure. It is essential, however, that a proper dialogue takes place between the closure manufacturer and user to ensure that only appropriate combinations of closure, jar, foodstuff and process are used.

11.4 Assessing the safety of metal FCMs

The safety of metal FCMs is of paramount importance. As well as considering the potential for food packaging to transfer contaminants to foodstuffs, it should be remembered that packaging also has an important role in maintaining the safety and quality of foodstuffs by protecting it from external contamination (chemical or microbiological). Whilst the protective properties of packaging are outside the scope of this chapter, this point is raised because there is a need to consider the benefits of food packaging as well as the potential risks.

Assuring the safety of FCM is a regulatory requirement in most countries, either under a general requirement such as the EU Framework Regulation (1935/2004) or additionally under specific detailed legislation such as the USA FDA CFR21 175.300 for polymeric and resinous coatings for use in contact with food. Where detailed legislation exists compliance plays an important part in assessing safety, although non-intentionally added substances and adventitious contamination still have to be considered. Where detailed legislation is not in place, assuring the safety of metal foodstuff packaging entails a self assessment of the finished packaging taking into account the end use application and conditions of use. This self assessment would be by:

- reference where appropriate to legislation and guidelines in place elsewhere in the world for this type of packaging
- legislation and guidance in place for other types of packaging
- the opinions of expert bodies such as EFSA, JECFA
- ensuring the correct use of appropriate starting materials and the appropriate end use of the packaging.

11.4.1 The importance of knowing the end use of metal FCMs

It is not possible realistically to assess the safety of metal food packaging without knowing the conditions under which it will be used. During the development of a food packaging article, the manufacturer will have a concept of the likely potential uses but the range of foodstuffs, food processing conditions and possible consumer re-heating the food in the packaging will all affect the potential for migration from the packaging into the food. Although the packaging manufacturer may set limitations on the uses appropriate for the packaging, good communication between packaging manufacturer and user is essential.

11.4.2 The use of appropriate raw materials

Many of the food contact surfaces in metal foodstuff packaging such as coatings, sealants and gasket materials are bought in formulated specifically for the particular application. Detailed compositional information is rarely available for reasons of confidentiality, so the packaging manufacturer must ensure that the material supplier is aware of the intended application and

conditions of use of their materials and of the finished package so that they can confirm the suitability of their materials. The materials supplier is then responsible for ensuring that their materials are capable of complying with all legislative requirements and that their materials can safely be used in this application. They must also provide the packaging manufacturer with sufficient information to allow them to confirm the actual compliance and safety of the finished article and be able to provide sufficient information onward to their customer. This process of safety and compliance checking at the various different stages may be undertaken by an independent third party who can then certify the compliance and safety of the end package. The use of a third party can be helpful in protecting proprietary information and may also reduce duplication of work where multiple customers are involved.

11.4.3 Compliance with existing legislation, recommendations and guidance

As already discussed, the state of regulation of metal foodstuff packaging differs significantly between countries. In the USA and those authorities that accept compliance with the US regulations, compliance is a combination of using only those substances listed in appropriate chapters of the FDA CFR 21, and complying with the end use test requirements (generally an overall migration limit) appropriate to the application. The most applicable sections for metal foodstuff packaging are 175.300 for coatings and end sealants and 177.1210 for gaskets. The regulations define migration limits, appropriate migration simulants and test conditions in tables of food types and conditions of use. Because of the wide geographical coverage of the US regulatory system, most materials suppliers and test laboratories are well used to demonstrating compliance with these requirements.

EU compliance testing of metal foodstuff packaging is less straightforward as there are no harmonised rules, but in practical terms, it includes the use of US and EU member state legislation together with the CoE Resolution AP(2004) 1 to show compliance with the Framework Regulation (1935/2004). Overall migration and where appropriate specific migration testing may be undertaken using test simulants and conditions derived from the EU Plastics testing Directives (82/711/EEC and 85/572/EEC) or US FDA regulations. However, if the 'plastics' test methods are used, account must be taken of the practical problems they pose for metal foodstuff packaging which are discussed later. In addition, compliance with EU substance specific measures such as the 'Epoxy' Regulation 1895/2005 and the VCM Directive (78/142/EEC) must be demonstrated – most usually this will be achieved via measurement of total extractable analyte rather than migration testing for reasons of convenience and applicability to all end-uses. Where substances used in metal foodstuff packaging have restrictions in the EU 'plastics' directive 2002/72/EC, it is prudent to ensure that these restrictions are considered in the compliance testing and safety assurance of metal foodstuff packaging even though it is

not within the scope of that Directive. The different food consumption and packaging use patterns for metal foodstuff packaging which control consumer exposure may need to be taken into account. Given the complexities of compliance testing in the absence of harmonised comprehensive EU legislation, sub-contracting compliance assurance to independent expert third party laboratories/institutes can be very useful.

11.4.4 Problems in applying test methods developed for non-metal FCMs

One of the difficulties in attempting to apply simulants and test methods developed for plastic FCMs to metal foodstuff packaging is that the reactivity of metals particularly to acidic simulants is quite different from plastics. Other problems include practical difficulties in applying the EU olive oil migration test methodology and difficulties in properly reproducing, in the laboratory, the internal environment of the package and extent of exposure of some components such as sealants and gaskets to the foodstuff. The 3% acetic acid simulant, particularly under typical food sterilisation conditions, would frequently lead to corrosion of the metal substrate which does not occur with real foods even of the same or higher acidic strength because of the passivation and buffering action of some food ingredients. Minimisation of residual oxygen in commercially filled packs also limits corrosion. Corrosion products in the simulant would be wrongly included in the migration measurement. This is not the place to discuss in detail the EU olive oil test, but it can be difficult to perform with sufficient precision even with plastic FCMs. With metal foodstuff packaging the high intrinsic weight of the metal and the difficulty in recovering residual oil makes the test generally unworkable.

These problems were recognised many years ago and a CEN working group (TC194/SC1/WG5) was set up to develop potential alternative methods. The outcome of this group was a proposed set of test methods specifically for surface coatings and varnishes on metal substrates. The report of the working group also recommended that for thermal processing conditions above 130 °C, actual processing temperatures should be used rather than the temperature bands indicated in the existing test methods. This is justified because in practice the control of temperatures in sterilisation is very precise to ensure adequate sterilisation without overcooking the foodstuff. The difficulty in reproducing a realistic package internal environment and control of the area of exposure of sealants and gaskets under non-commercial filling and sealing conditions remain. It is important therefore that any testing is performed in a way which properly reflects actual usage conditions. Work is under way within industry to develop recommendations covering appropriate testing methods for metal closure gaskets.

11.4.5 Management of migration of non-intentionally added starting substances

Regulations governing the use of FCM focus on the selection and potential migration and toxicology of the substances used to make the FCM. However it is recognised that impurities and reaction products may also migrate into foodstuffs together with adventitious contaminants from the packaging manufacturing process such as set off from external surfaces. These potential migrants or 'non-intentionally added substances' should always be considered in the safety assessment of all FCMs and there is an increasing focus in this area from regulators. There are considerable practical difficulties in ensuring complete management of these substances, both analytical problems and problems due to the potential variability in their presence. However, it is increasingly important to include consideration of non-intentionally added substances within any safety assessment of FCM. This is true for metal foodstuff packaging as well as all other FCMs, but the use of predominantly thermoset internal coatings and the use of seals and gaskets add to the complexity of the assessment. The assessment should include prediction and identification of potential impurities and reaction products and use of modern analytical approaches to the detection and identification of such substances present in the finished package together with, if necessary, migration into the foodstuff.

Effective assessments will be possible only through close co-operation along the materials supply chain. This approach is, however, of only limited use unless it is taken in parallel with a more realistic assessment of the real potential for exposure of consumers to these substances. The traditional approach is to use a series of worst-case assumptions which, whilst workable for most intentionally added substances, becomes unrealistically onerous for these traces of non-intentionally added substances. The need for realistic exposure assessment and a description of some of the tools now emerging to facilitate this is covered elsewhere in this book.

11.5 Future trends

Metal foodstuff packaging continues to develop to make use of new materials, new technologies and new market opportunities. The safety assessment of new materials, technologies and applications will always be a fundamental part of any new development, indeed one of the drivers of new product development is to simplify and improve the safety assessment process without prejudicing the existing food safety attributes of the packaging.

11.5.1 Migration 'improvement' through improved materials and packaging design

Migration 'improvement' (that is, a decrease in chemical migration from

metal packaging formats into foodstuffs) can be achieved in a number of ways. This may be either in response to regulatory and market issues or as an element of the continuous improvement process. Improvements in raw materials and in manufacturing processes can reduce migration whilst retaining existing technologies. An example would be the general reduction over recent years in bisphenol A diglycidyl ether (BADGE) levels in epoxy-based coatings with resulting reductions in migration. Migration reduction without significant material changes can also be achieved in the case of components where the contact between the component and the foodstuff can be reduced. This route to reduction has been used for the metal push-twist (PT) closure typically used for baby foods where a combination of modified gasket placement and changes in the food preparation and processing technologies has reduced epoxidised soyabean oil (ESBO) plasticiser migration. Alternatively, by changing technologies, migrants of concern can be eliminated as has been achieved in the instance of semicarbazide (SEM) migration from closure gaskets where a totally different foaming technology has been adopted.

Whilst industry will continue to work to 'improve' the migration performance of metal foodstuff packaging, care must be taken not to jeopardise the existing safety (microbiological as well as chemical) of the package. Any change to existing systems brings with it a risk of package failure due to the lower level of knowledge and experience of the new system. Materials modification is generally the lower risk route with technology change bringing greater risk. These risks need to be managed in parallel with the migration risks.

11.5.2 Safety assessments of new developments in metal foodstuff packaging

Timescales of finalising and pack testing new developments are long (typically 5–10 years in total). It will never be possible to completely predict future legislation or toxicological knowledge but it is prudent, early in a development, to examine potential migrants including the non-intentionally added substances by modelling/predictive testing and using modern analytical techniques as well as assessing their potential impact using internationally recognised scientific principles, including exposure assessments and structure activity relationships. Close co-operation along the supply chain is essential to achieve this. Such effort will help to ensure that there will be no issues regarding current or anticipated future legislation or new opinions regarding the safety of migrants.

11.6 Sources of further information and advice

Regulation and safety assessment of FCM is a rapidly evolving area, particularly within the EU. This is even more the situation with metal foodstuff packaging as the need for harmonised comprehensive legislation intensifies. It seems

probable that such harmonised legislation will be developed imminently with industry's support. The most effective way to maintain awareness both of the current legislative position and also likely future developments regarding metal foodstuff packaging is through the European trade association SEFEL or national trade associations which are affiliated to SEFEL. Additional support should be available through material suppliers and their trade associations (predominantly CEPE covering coatings manufacturers). Other key sources of information include EU DG SANCO, and FDA which both have very useful web sites and also national authorities. For more general background, regular training courses and conferences are arranged by organisations such as PIRA. Finally there are several independent expert institutes that can advise, undertake testing work and even manage complete compliance and safety assessment programmes. Web addresses of useful sources of information follow:

- DG SANCO: http://europa.eu.int/comm/food/food/chemicalsafety/foodcontact/index_en.htm
- Eurolex (for EU legislation): http://europa.eu.int/eur-lex/en/index.html
- CoE: http://www.coe.int/T/E/Social_Cohesion/soc-sp/Public_Health/Food_contact/
- EFSA: http://www.efsa.eu.int/science/afc/catindex_en.html
- EC FCM (EC Food Contact Materials Resource Centre): http://www.efsa.eu.int/science/afc/catindex_en.html
- US FDA: http://www.cfsan.fda.gov/
- SEFEL: http://www.sefel.net/
- CEPE: http://www.cepe.org/homepage.htm
- PIRA: http://www.pira.co.uk/

11.7 References

Codex (2005) *Code of practice for the prevention and reduction of inorganic tin contamination in canned foods*, CAC/RCP 60-2005. Codex Alimentarius Commission.

CoE (2001) *Guidelines on metals and alloys used as food contact materials*. Council of Europe, Technical Document.

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12

Rubber and chemical migration into food

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12.1 Introduction

A rubber can be defined as a material which at room temperature can be stretched to at least twice its original length and, on release of the stress, rapidly returns to its original length. These rubbery properties are brought about by a combination of the chemical structure of the polymer backbone (flexible macromolecules having a glass transition temperature below ambient are essential) and vulcanisation which brings about the formation of a lightly cross-linked three-dimensional structure. Thermoplastic rubbers are also within the scope of this chapter. These are a group of polymers that are similar to rubbers in resilience and rapid recovery, but can be repeatedly softened by heating (i.e. are thermoplastic) to enable processing, regaining their elastomeric character on cooling to room temperature. A sub-set of thermoplastic rubbers exists, named thermoplastic vulcanisates (TPVs), in which the rubbery phase within the material is cross-linked.

In contrast to plastics, rubbers are rarely used in the packaging of food products. Exceptions to this rule are the use of rubber in flip top seals on beer bottles and the seal that is present in food cans. However, in the processing of food, there are a number of situations where significant contact with rubber products can occur. This is due to the fact that the unique properties of rubber lead to it being used in a wide range of products (see Table 12.1). It is also the case that the range of contact conditions encountered (i.e. food type, contact temperature, time and area) mean that a wide variety of rubber compounds are employed (see section 12.2).

Variations in contact conditions have an important effect on the potential of chemical species to migrate from the rubber components into the foodstuff.

Table 12.1 Rubber components used in food contact applications

Location	Component
Food transportation	Conveyor belts, rubber skirting and rubber paddle lips
Pipe work components	Seals, gaskets, flexible connectors and butterfly valves
Pumps	Progressive cavity pump stators, diaphragm pumps
Plate heat exchangers	Gaskets
Machinery/storage vessels	General seals and gaskets
Cans/bottles	Can sealants and bottle seals
Food handling/preparation	Gloves and feather pluckers
Food manufacturing	Silicone sweet moulds
Food wrapping	Meat and poultry nets

In general, the use of rubbers for mainly processing applications means that the contact times with food are short (e.g. minutes) and the contact areas, apart from hose and belting, are small. This is in contrast to plastics which, when used as packaging materials, often have long contact times (e.g. weeks) and relatively large contact areas.

It is also the case that due to their inherent properties and processing requirements rubber compounds are usually much more complex than other polymer products such as plastics. It is common for a rubber formulation to contain a range of additives (see section 12.2.2) typically resulting in a list of from ten to fifteen ingredients. In order to achieve the desired final properties, it is also relatively common for the base polymers to be blended, particularly the diene (e.g. natural rubber, styrene butadiene rubber (SBR), polybutadiene) type rubbers. Hence, there will be a larger range of monomers, oligomers and polymer related substances (e.g. polymerisation catalysts and process aids) to take into account. Another very important consideration with rubbers is that chemical reactions take place during the curing process and further chemical modification of the matrix occurs due to the action of antidegradants in protecting the rubber polymer. These processes result in the generation of low molecular weight reaction products and breakdown products. All of these factors complicate the process of predicting what has the potential to migrate from a rubber product into food.

It is the need for knowledge in these areas that has led the UK's Food Standard Agency (FSA) to fund a number of research projects at independent research organisations, such as Rapra, to look into the use of rubber as a food contact material. At the same time there has been a Council of Europe (CoE) Resolution APRes (2004) covering rubber products which was adopted in December 2004. In addition to this resolution, which should be considered by all European Union (EU) national governments, there are a number of other legally binding national regulations covering rubber and these should be addressed when manufacturing rubber that is going to be sold for food use in a particular market. All of these documents have inventory lists and requirements for migration testing, with overall migration limits and, in the case of certain chemical species, specific migration limits.

The objective of this chapter is to provide a comprehensive overview of the use of rubber as a food contact material, from an initial description of the types of rubber and rubber products that are used in the industry, through the formulation of products, and the contact regulations and migration testing regimes, to the research that is on-going to improve its safety and the trends for the future.

12.2 Rubber materials and products used in contact with food

12.2.1 Rubber materials

As part of a major MAFF-funded research project[1] an extensive review of the food industry was carried out by consultants at Rapra Technology Ltd in order to obtain information on the types of rubber used in the food industry. The following sectors of the food industry were amongst those surveyed:

- dairy and dairy products
- brewery and soft drinks
- abattoir and meat processors
- confectionary producers and bakers
- vending machine dispensers
- food canning and the preserves industry
- breakfast cereal manufacturers
- food packaging.

A relatively large range of rubbers were found to be used in a wide variety of products (see section 12.2.3). One of the more important criteria that are used in selecting a particular rubber for a specific end-use application, is its temperature resistance. Other properties such as chemical inertness, and the types of additives that have to be incorporated to achieve the desired processing and physical properties are also important. The most important classes of rubber used in the food industry are described below.

Natural rubber (cis-1,4-polyisoprene)

Natural rubber (NR) compounds are mainly used for gloves, can sealants, teats and soothers, although the use of NR is coming under pressure from synthetic polyisoprene due to the increasing incidence of protein allergies. In food processing equipment natural rubber products will be found in belting and hosing products, sometimes in blends with other rubbers such as styrene-butadiene rubber (SBR). These rubbers are typically used with aqueous foods under flow or short-term static conditions at low temperatures (<40 °C). The maximum temperature limit for the prolonged use of these products is around 80 °C.

Nitrile rubber
Nitrile rubber (NBR) is widely used in compounds designed for seals and gaskets, and in hoses for both aqueous and fatty foods. In particular, dairy hosing and milk liners are normally manufactured in nitrile rubber or nitrile rubber blends (e.g. with SBR). Nitrile rubber is better able to withstand heat ageing than natural rubber and so the maximum continuous use temperature is higher at 120 °C. In practice most applications involve flow or short-term static conditions at temperatures below 40 °C.

Ethylene-propylene rubber
The principal use of ethylene-propylene rubbers (ethylene-propylene-diene monomer (EPDM) or ethylene-propylene monomer (EPM) types) is in the manufacture of heat exchanger gaskets. When cured using peroxides, these materials can be used for extended periods at up to 150 °C. Normal conditions of service are high temperatures (<130 °C) and flow or static exposure to aqueous food.

Fluorocarbon rubber
There are a number of grades of fluorocarbon rubber (copolymers, terpolymers and tetrapolymers) and they are mainly used in applications where the temperatures would degrade ethylene-propylene rubber products. They are able to withstand prolonged use at temperatures up to 200 °C. Typical conditions are high temperature (<150 °C) gaskets under flow or static conditions, in contact with aqueous or fatty foods (including oils).

Silicone rubber
Most of the silicone rubbers used in the food industry are based on polydimethyl vinyl silicone and these materials have very good high- and low-temperature properties. It is their high-temperature resistance that enables them to be used for seals and tubing, for example, in drinks vending machines up to 100 °C. Cold cured silicones are used as release coatings on items such as food transportation belts and for sweet moulds.

Thermoplastic elastomers
These materials are cross-linked at room temperature, due to the influence of 'physical cross-links' formed by part of the matrix being below its glass transition or crystalline melting temperature. They become thermoplastic at processing temperatures (e.g. >150 °C) and can be processed in the same way as plastics. The fact that they are not thermoset materials restricts their working temperature range to less than 70 °C. Thermoplastic elastomers are used in a variety of food contact products, for example, flexible lids (styrenics, e.g. styrene-butadiene-styrene (SBS) or styrene-isoprene-styrene (SIS)), and belting, gaskets and tubing (particularly polyurethane types). Other types of thermoplastic elastomers available include olefinic blends of polypropylene and ethylene-propylene rubber, and polyesters.

Other types of rubber
In addition to the main groups of rubbers described above there are also a number of other types that are used in the food industry. These include:

- butyl rubber – used for articles such as stoppers and seals in contact with aqueous foods
- polychloroprene rubber – used in articles such as conveyor belts for food transportation
- acrylic and hydrin rubbers – speciality materials chosen when the food/contact conditions combination requires their specific properties, e.g., chemical inertness combined with relatively good heat stability.

12.2.2 Rubber additives

Rubber technology is a mature science with a history going back some 150 years or more. Over the years a number of scientific discoveries (e.g. curing with sulphur to increase resilience and recovery, and the use of antioxidants to lengthen service life) have contributed to the material's dominance in applications requiring elasticity/recovery upon deformation combined with durability. Additives are used in rubbers in order to ensure that they possesses the correct properties to be processed, have the physical properties appropriate for the application, and sufficient stability and resistance to ageing in service. There are three basic steps associated with the processing of rubber:

1. mixing – where additives are incorporated into the base rubber to form the rubber compound
2. a shaping stage – involves extruding or calendering and prepares the unvulcanised rubber compound for the curing stage
3. curing – involves heating the rubber compound under pressure for a period of time during which the cure system chemically cross-links the material.

The finished rubber product will have to meet a specification in which a number of properties (e.g. hardness, tensile strength and elongation) are given target values. A number of other properties can be assessed, and these will depend upon the type of rubber and the application that it is going to be used in. An important example is the overall migration limit test, with the food simulant and test conditions (temperature and time) being dictated by the end use conditions.

The main classes of additive used in rubber compounds are as follows:

- *plasticisers/oils* – used to reduce the viscosity of the compound to aid processing and to modify the physical properties of the final rubber product, e.g. reduces hardness and increases elongation. There is a wide range of substances to choose from, e.g., phthalates, adipates, sebacates and hydrocarbon oils.
- *fillers* – can be regarded in many ways as having the opposite effect to

plasticisers, e.g., they increase hardness and reduce elongation. The principal filler for rubber is carbon black as it interacts with the rubber molecules (rubber-filler interactions) resulting in a large improvement in the strength properties. Other fillers such as silica and the silicates also improve properties, but a number (e.g. calcium carbonate) are mainly used to adjust hardness and reduce cost.

- *curatives* – two main classes of curative are used in rubber – elemental sulphur and peroxides. The first of these is the most important and has had a complete technology (cure accelerators and co-agents) built up around it. Other types of curative are also used in food contact rubbers, e.g., amines and metal oxides.
- *cure accelerators and co-agents* – compounds that are used to modify the chemistry of a curing reaction to ensure that a rubber achieves a good state of cure in a reasonable time at a convenient temperature. There are many different generic groups (e.g. guanidines, sulphenamides, thiazoles, thiurams, carbamates and xanthates) often classified by the rate (e.g. slow or fast) that they accelerate cure. It is usually the case that a blend of accelerators (i.e. slow and fast types) is used to optimise the curing reaction by controlling properties such as induction time and cure rate. This practice has implications for food contact use as reactions between these accelerators can produce additional low molecular weight species with the potential to migrate into food. Typical cure co-agents include zinc oxide and stearic acid for sulphur systems, and triallyl cyanurate for peroxides. Coagents differ from accelerators in that their main function is to improve the efficiency of the curing reaction, which improves final properties such as ageing resistance.
- *antidegradants* – two main classes of antidegradant are used in rubber – antioxidants and antiozonants. There are a number of antidegradants available, the two main classes being amines (staining) and phenolics (non-staining), and a mixture of two or more is often used to confer maximum protection. Other types such as thioesters (mainly used to stabilise the base rubber), phosphates and micro-crystalline waxes can also be used. As the antidegradants protect the rubber in service, reaction/breakdown products result and these, in addition to the products formed from the cure system species, have been the subject of a recent Food Standards Agency research project.[2]
- *miscellaneous* – other additives that can be used include pre-vulcanisation inhibitors (to reduce the possibility of cure occurring during the mixing and forming stages), coupling agents (to promote filler-to-rubber interactions), deactivators (e.g. polyethylene glycol) to stop accelerators becoming adsorbed onto the surface of fillers such as silica, and bonding agents to assist with fabric-to-rubber interactions in composite products. An example of a food contact rubber compound (a milk liner formulation) is shown in Table 12.2. Good quality products would be obtained from this compound by curing it for 15 minutes at 165 °C.

Table 12.2 Example of a food contact rubber compound

Ingredients	Relative Amount
Nitrile rubber	100
Zinc oxide (cure co-agent)	5
Stearic acid (cure co-agent)	2
Carbon black – HAF N330 type (filler)	15
Aluminium silicate (filler)	15
Dioctyl phthalate (plasticiser)	5
Sulphur (curative)	1.5
Diphenyl guanidine (cure accelerator)	0.15
Mercaptobenzothiazole disulphide (cure accelerator)	1.5
Dimethyl diphenyl thiuram disulphide (cure accelerator)	0.3
Phenyl alpha-naphthylamine (antidegradant)	1.0
Styrenated diphenylamine (antidegradant)	1.5

12.2.3 Rubber products and food contact conditions

The majority of the information presented in this section was obtained during the comprehensive survey of the food industry that was undertaken during the course of the MAFF-funded research project.[1]

Types of rubber product

The principal components of rubber products that are used in contact with food are shown in Table 12.1.

Contact areas

Food contact areas for the rubber components in whole assemblies, be these total pipelines, paddle lips, or plate heat exchangers, were found to cover a wide range from less than 100 cm^2 to around 56,000 cm^2. The plate heat exchanger was the assembly found generally to be associated with the highest contact area. The contact area of an individual rubber component was considered as well as the total contact area of the assembly that the component is in. The majority of rubber components have individual food contact areas of less than 1000 cm^2, with around two-thirds of these having contact areas of less than 100 cm^2.

Examples of rubber components usually having contact areas of less than 200 cm^2 include general gaskets, plate heat exchanger gaskets and pipe work seals. Pump components, pipe valves and flexible connectors have greater individual contact areas, up to 1000 cm^2. Some of the highest contact areas found in the survey were for hoses up to 50,000 cm^2, and dry food conveyor belts (e.g. for barley in a maltings) up to 1,500,000 cm^2.

Contact times

In general, contact times with individual rubber components were low (i.e. less than 60 seconds) and even in assemblies the total contact times are still

relatively short. For example, the maximum contact time in a plate heat exchanger was no more than three minutes. Few components or assemblies give longer contact times. Examples of exceptions to this are beer engine seals (up to 12 hours), beer keg seals (up to 12 weeks) and meat and poultry netting (up to four weeks). The longest potential contact times of up to five years are associated with packaging seals, particularly can seals.

Contact temperatures
The temperature at which food products contact rubber components rarely exceeds 80 °C. Temperatures in the range 100 to 140 °C do occur in some processes, e.g., the production of toffee in silicone moulds and the sterilisation of cans and jars, but the contact time of the food at these elevated temperatures is normally reasonably short (< one hour). Some of the highest temperatures are encountered in the refining of vegetable oils where temperatures in the range 170–250 °C are used in the deodorising section of the plant. Meat and poultry nets may be subjected to temperatures of up to 250 °C for several hours during cooking.

12.3 Regulation and the use of rubber as a food contact material

12.3.1 European Union legislation

At the moment there is no specific EU legislation for rubber food contact materials or articles (other than nitrosamines in babies' dummies).[3] All such materials or articles need to comply with the general Framework Directive 89/109/EEC so that in normal use they will not transfer their constituents to food in quantities that could endanger health or cause unacceptable changes in the composition of food or deterioration in its organoleptic properties (i.e. taste, texture, aroma, or appearance).

12.3.2 Council of Europe Resolution on rubber products

The Council of Europe's Rubber Resolution on food contact elastomers contains an inventory list of additives and a small section that deals with breakdown products – nitrosamines and amines. The inventory list is described as 'Technical document No. 1 – List of substances to be used in the manufacture of rubber products intended to come into contact with foodstuffs'. This and other relevant Council of Europe documents are available on the Internet website of the Partial Agreement Division in the Social and Public Health Field : www.coe.int/soc-sp.

In addition to the Technical Document No 1, there are four other documents in the series of statements concerning rubber products intended to come into contact with foodstuffs:

- Technical document No. 2: guidelines concerning the manufacture of rubber products intended to come into contact with foodstuffs
- Technical document No. 3: good manufacturing practices of rubber products intended to come into contact with foodstuffs
- Technical document No. 4: test conditions and methods of analysis for rubber products intended to come into contact with foodstuffs
- Technical document No. 5: practical guide for users of Resolution APRes(2004) on rubber products intended to come into contact with foodstuffs.

Resolution APRes (2004) places rubber products into one of three categories:

- Category I comprises the following rubber products for which migration testing is required:
  - feeding teats
  - rubber products to come into contact with baby food, for which the R-total (defined below) is equal to or greater than 0.001.
- Category II comprises rubber products for which the R-total is equal to or greater than 0.001 and for which migration testing is required.
- Category III comprises rubber products for which the R-total is smaller than 0.001 and for which migration testing is not required, except for rubber products containing nitrosamines, nitrosatable substances or aromatic amines and Category III substances with a specific migration limit (SML) in Technical document No. 1.

These three categories take into account the wide variety of applications for which rubber products are used and the fact that migration may vary with the application. The level of migration for rubber products may be estimated by taking into account four factors, R_1, R_2, R_3 and R_4, referring respectively to the relative contact area, contact temperature, contact time and number of times that the article is used. Categories are based on the intended use or on the result of multiplying the four factors ($R_1 \times R_2 \times R_3 \times R_4$ = R-total).

The factors R_1, R_2, R_3 and R_4 can be defined as follows:

- R_1 refers to the relative contact area (A_R) between rubber products and food or beverage, expressed in cm^2 of rubber surface per kg of food or beverage. For a relative area smaller or equal to 100 cm^2/kg foodstuffs, R_1 has a value calculated according to the formula $R_1 = A_R/100$. For a relative surface area larger than 100 cm^2/kg, R_1 always has the value of 1.00.
- R_2 refers to the temperature during the contact period of the rubber product with the food or beverage. At a temperature lower than or equal to 130 °C, R_2 has a value calculated according to the formula $R_2 = 0.05e^{0.023T}$ where 'e' is the base of the natural or Napierian logarithms and T is the contact temperature, expressed in °C. For temperatures higher than 130 °C, R_2 always has the value 1.00.
- R_3 refers to the time, t, expressed in hours, during which a rubber product

is in contact with the food or beverage. For a contact time shorter than or equal to ten hours, R_3 has a value calculated according to the formula $R_3 = t/10$. For a contact time of more than ten hours, R_3 has the value 1.00.

- R_4 refers to the number of times, N, that one and the same rubber product, or part of that rubber product comes into recurrent contact with a quantity of food or beverage. If the number of contact times is greater than 1000, then R_4 is calculated according to the formula $\log_{10} R_4 = 6 - 2 \log_{10} N$. If the number of contact times is smaller than or equal to 1000, then R_4 always has the value 1.00.

The Resolution also states that rubber products of Categories I and II should not transfer their constituents to foodstuffs or food simulants in total quantities above an overall migration limit (OML) of 60 mg/kg food or food simulant.

Silicone rubbers

There is a separate Council of Europe Resolution, APRes (2004), on silicone materials for food contact. The resolution defines the silicone product group being comprised of silicone rubbers, silicone liquids, silicone pastes and silicone resins. Blends of silicone rubber with organic polymers are covered by the resolution where the silicone monomer units are the predominant species by weight. Silicones that are used as food additives or processing aids (e.g. as defoamers in the manufacture of substances such as wine) are not covered by this resolution, but polysiloxanes used as emulsifiers are. The resolution gives an overall migration limit of 10 mg/dm^2 of the surface area of the product or material, or 60 mg/kg of food. There are restrictions on the types of monomers that can be used to produce the silicone polymers and there is an inventory list: 'Technical document No. 1 – List of substances used in the manufacture of silicone used for food contact applications'.

12.3.3 The US Food and Drug Administration (FDA)

The FDA produces a Guidance for Industry document entitled 'Preparation of Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Chemistry Recommendations'. This is in addition to the Code of Federal Regulations Volume 21, Parts 170 to 199 Food and Drugs which contains the FDA food contact regulations. This is published annually and rubber products for use with food are covered in Part 170, specifically Rubber articles intended for repeat use: 177.2600; and Closures with sealing gaskets for food containers: 177.1210. The FDA regulations are relatively straightforward. Providing that the ingredients in the rubber are listed as being approved, and the water (for aqueous food use) or hexane (for fatty food use) extractables under reflux conditions are within the prescribed limits, then the compound is considered suitable for food use (see Table 12.3).

In addition to listed compounding ingredients, the regulations also allow the use of prior sanctioned ingredients and also additives that are generally recognised as safe (GRAS). Prior sanctioned materials are listed in the following sections of the FDA regulations: Antioxidants (181.24); Plasticisers (181.27); Release agents (181.28); Stabilisers (181.29). Additives described as GRAS that are listed in CFR 21 include zinc oxide and zinc stearate (Section 182), calcium carbonate and calcium stearate (Section 184), and kaolin clay and iron oxide (Section 186). The FDA places severe restrictions (i.e. 3.0 μg per square inch) on the migration of acrylonitrile monomer from nitrile rubbers (Section 181.32) and prohibits the use of polymerised 1,2-dihydro-2,2,4-trimethylquinoline (TMQ) an antioxidant commonly used in rubber compounds (Section 189.220).

12.3.4 German (BfR) regulations

Within Germany, the food contact legislation for rubbers is described in BfR Recommendation XXI 'Commodity Articles Based on Natural and Synthetic Rubber'. Four use categories and a special category are defined as follows:

- Category 1 (test: 10 days at 40 °C). Rubber articles which come into contact with food for periods of more than 24 hours to several months, e.g., storage containers, container linings, seals for cans and bottles.
- Category 2 (test: 24 hours at 40 °C). Rubber articles which come into contact with food for not more than 24 hours, e.g., food-conveying belts, tubes and hoses, sealing rings for cooking pots, lock seals for milk can lids.
- Category 3 (test: 10 minutes at 40 °C). Rubber articles which come into contact with food for not more than ten minutes, e.g., milk liners and milking machine tubes, roller coatings and conveyor belts (fatty foods only in both cases), gloves and aprons for food handling.
- Category 4 (no migration testing required). Rubber articles which are used only under conditions where no migration into food is to be expected, i.e., if the articles comes into contact with the food for a very short time or only over a very small area. Examples of rubber products in this category include conveyor belts, hosing for moving and loading/unloading

Table 12.3 FDA migration limits for repeat use articles

Fatty foods – hexane extractables under reflux	
First seven hours	175 mg inch^{-2}
Succeeding two hours	4 mg inch^{-2}
Aqueous foods – distilled water extractables under reflux	
First seven hours	20 mg inch^{-2}
Succeeding two hours	1 mg inch^{-2}

dried food, tap washers, pump parts and other articles associated with the supply of drinking water.
- Special Category (test: 24 hours at 40 °C). Rubber articles directly associated with the consumption of food and which are being, or are expected to be, taken into the mouth, e.g., toys according to Recommendation XLVII, teats, soothers, gum-shields, balloons.

The following food simulants are used in connection with the German regulations: distilled water, 10% ethanol and 3% acetic acid. The permissible migration limits vary according to the Category and simulant. The BfR regulations also include a number of specific composition (e.g. milking liners and tubes) and migration limits (e.g. for *N*-nitrosamines, *N*-nitrosatable substances, amines and formaldehyde).

Silicone rubbers
Recommendation XV of the BfR regulations covers silicone rubbers, in addition to silicone oils and resins. The section on silicone rubbers stipulates acceptable starting materials and the additives that may be used in processing and manufacture – both types and maximum levels. Separate restrictions are stated where silicone rubber is to be used for teats, dummies, nipple caps, teething rings or dental guards. Dummies and bottle teats must also comply with the requirements laid down in the Commodities Regulation (*Bedarfsgegenstandeverordnung*). The amount of volatile organic material is restricted to a maximum of 0.5%, as is the total extractable material. Test methods are referenced for these determinations as well as a test for residual peroxides which should be negative.

12.3.5 Other European Legislation

Requirements in France
French requirements for food contact elastomers (excluding silicones) are given in the Arrêté of November 9th 1994 which is published in the *Journal Officiel de la République Française*, December 2nd 1994, pages 17029–17036. Four use categories (A to D) and a special category (designated T) are described together with a positive list detailing permitted ingredients in each category. There is an overall migration limit set at 10 mg/dm^2 (60 mg/kg), the same as for plastics. Other specific restrictions also apply, such as a specific migration limit (SML) for primary and secondary aromatic amines of <1 mg/kg.

Requirements in the Netherlands
These regulations, which closely resemble the Council of Europe rubber resolution, can be found in *Verpakkingen en gebruiksartikelenbesluit* (*Warenwet*), Chapter III. There are positive lists of approved additives; food contact rubber products are divided into three parts.

Requirements in Italy
Italian requirements are given in the decree of March 21st 1973 contained with the *Supplemento ordinario alla Gazzetta Ufficiale della Repubblica Italiana*, April 20th 1973, pages 12 to 14. There have since been updates, including the decree of June 3rd 1994.

Requirements in the United Kingdom
UK legislation on food contact materials is published as a number of Statutory Instruments which were published in 1978 and came into operation in November 1979. The use of rubbers in contact with food is covered by the legislation included in Statutory Instrument 1987 No. 1523 *Materials and Articles in Contact with Foodstuffs*. This states that any food contact material should not be injurious to the health of the consumer and that any contamination should not have an adverse effect on the organoleptic properties of the food. The absence of any positive lists for compounding ingredients means that UK rubber compounders normally refer to either the FDA or the BfR regulations depending on the market to be addressed.

There are separate rules for the use or rubber in contact with potable water. These are given in the UK water fitting bylaws scheme and include tests for the following:

- taste
- appearance
- growth of aquatic micro-organisms
- migration of substances that may be of concern to public health
- migration of toxic metals.

The test methods for the above are given in British Standard 6920.[4]

12.4 Special considerations for using rubber as a food contact material

The unique properties of rubber that make it such a useful material in food contact situations can also cause it some difficulties in this field. The lightly cross-linked, mobile rubber matrix makes the migration of low molecular weight compounds in and out of the material relatively easy. Thus, food can penetrate into rubber and leach out the species within. It is possible to limit this ingress by choosing rubber-food combinations that ensure that the effect is reduced to a minimum for a particular application. Although this matching process applies to the type of rubber, it is also important to take into consideration the complete rubber compound. Up to 50% of a compound can be comprised of additives (e.g. plasticisers and fillers – see section 12.2.2) and these can also have a profound effect on the suitability and performance of the product in service. It is possible to make some generalisations in this

regard, for example, silicone rubber performs poorly in contact with fatty foods, and ester type plasticisers are also to be avoided in this type of application. But, in common with all the other food contact materials, it is the contact conditions (time, area and temperature) that also play an important role in dictating ultimate suitability. In practice these inter-relationships are well understood and form part of the body of knowledge used to draft food contact documents such as the Council of Europe Rubber resolution.

The relatively reactive nature of rubber materials is due to either sites of unsaturation in the case of the diene rubbers (e.g. NR, NBR and SBR), or large numbers of aliphatic hydrogen atoms. Hence antidegradants are essential in most formulations if the polymer molecules and hence the materials properties are to be protected. As well as adding further to the list of potential migrants, this reactivity places restraints on the use conditions of different classes of rubber. The maximum service temperatures for different food contact rubbers are given in section 12.2.1. In contrast to materials such as thermoplastics, the technology associated with rubber has been developed over a very long period, much of which predates the period in which health and safety concerns have had a profound influence on manufacturing practice and research and development activities. Hence, a number of the chemicals which have found widespread use for many years in rubber have become the subject of increased scrutiny to ensure they are suitable in today's more demanding climate.

12.5 Assessing the safety of rubber as a food contact material

12.5.1 Migration tests

Overall migration tests

The aim of overall migration tests is to determine if a rubber is suitable for a particular food contact application. The methodology of the test varies depending on the regulations being addressed as does the way of expressing the data and the limits that have to be met. Some of the practical details to the different methodologies are given in section 12.3. A brief review of the tests used in the various regulations is given below.

FDA regulations

Test pieces are cut from the rubber test product to provide a known surface area (cut edges are included in the calculation) and immersed in an appropriate amount (e.g. 100 ml) of food simulant (either hexane or distilled water). The samples are refluxed for seven hours in pre-cleaned glassware and then removed and placed into fresh simulant and refluxed for a further two hours. The test pieces are then removed and both the seven and two hour test portions evaporated separately to dryness in conditioned crucibles and the

residues weighed. Blank determinations on equivalent volumes of the food simulant used are also performed. In order to be acceptable for food use the rubber has to pass the requirements given in section 12.3.

BfR regulations
The three food simulants and the contact conditions for the four different food use categories for which migration testing is required are given in section 12.3. Test pieces of 50 mm × 50 mm to give a total area of 50 cm^2 (both surfaces) are immersed in 100 ml of the appropriate simulant for the intended end use, the test is performed and then the simulant is dried down quantitatively. The BfR limits are shown in Table 12.4.

Council of Europe Resolution
This gives an overall migration limit of 60 mg/kg of food or food simulant for rubber products that are in Categories I and II (see section 12.3.2). The choice of food stimulant and the conditions that are used for the overall migration experiment (i.e. time and temperature) should be appropriate bearing in mind the conditions that the rubber product will see in service. Guidance for the designing of these tests is given in Technical document No. 4 of the Resolution.

Specific migration tests
These tests are used to target specific chemical compounds for which there is a toxicological concern. The tests specified vary according to the regulations that are being studied, but some species (e.g. nitrosamines and nitrosatable substances) appear regularly due to the degree of concern associated with them. Other popular specific migrants include:

- aromatic amines
- other amines (e.g. cycloaliphatic amines)
- peroxides and their breakdown products
- formaldehyde
- monomers (e.g. acrylonitrile)
- accelerators (e.g. ZDBC, CBS, MBT).

Table 12.4 BfR migration limits

	Category (mg/dm^2)			
	1	2	3	Special
Distilled water	50	20	10	10 or 50*
10% ethanol	50	20	10	–
3% acetic acid	150(50)	100(20)	50(10)	–

(value) = permissible organics within total
* dependent on product type
NB: no migration limit for Category 4 (see section 12.3.4)

These lists are not complete as it is recognised that rubber contains two important ingredients (antidegradants and curatives) that are reactive and so produce reaction and breakdown products. Recent work carried out at Rapra for the Food Standards Agency[2] has shown that there are more than 1000 of these products originating from the 200 curative and antidegradant compounds in the Council of Europe rubber resolution inventory list.

12.5.2 Fingerprinting potential migrants from rubber compounds

It is often useful to produce a qualitative or semi-quantitative fingerprint of the low molecular weight species in a rubber compound that have the potential to migrate into food. Gas chromatography-mass spectrometry (GC-MS) is often used for this due to its high resolution (important with rubbers due to their complexity) and the identification power of the mass spectrometer. In order to obtain data on as large a range of species as possible, it is often advisable to use both headspace GC-MS (solid rubber samples being heated to around 150 °C) and solution GC-MS on an extract produced using a relatively non-selective solvent (e.g. acetonitrile or acetone). Semi-quantitative data can be obtained by use of a single calibrant compound such as eicosane. Work using typical food contact rubber compounds has shown that, on average between 20 and 30 compounds can be detected using this approach.[5] The commercialisation of two-dimensional GC-MS instruments has provided the analyst with greater resolving power, coupled with improved detection limits and enhanced deconvolution software, and this has increased this number to over 100.[5]

As in-house, rubber specific databases are developed for LC-MS, the inclusion of this technique into the fingerprinting process will complement GC-MS data by contributing information on thermally labile and relatively large (e.g. oligomeric) potential migrants. This has been demonstrated recently in a paper by Sidwell,[6] which describes how LC-MS was used to provide additional information on the species present in an ether extract of a food contact ethylene-propylene-diene monomer (EPDM) rubber.

12.5.3 Determination of species in rubbers and migrants in food simulants and food products

It has already been mentioned (section 12.3) that the National regulations and the Council of Europe resolution stipulate concentration limits for certain species within food contact rubber compounds and that they have specific migration limits (SMLs) for certain migrant compounds. Analytical work is therefore required on a quality assurance basis:

- to ensure that a food approved rubber compound is fit for purpose (for example, by checking the monomer level)
- to ensure that compounds having SMLs do not exceed them in food simulant or food samples prepared using appropriate contact conditions.

For convenience, potential migrants have been placed into functional groups below and the analytical techniques used to detect and quantify them explained.

Monomers
Monomers are either gaseous or relatively volatile liquids and so GC and GC-MS based techniques are used to determine them in both the rubber compound and the food simulant/food product. To simplify the analysis, a static headspace sampler is often used to isolate the monomer from the sample matrix; an extraction procedure often presenting chromatographic problems with the extraction solvent obscuring the analyte.

Plasticisers and process oils
These additives are essentially high boiling point liquids and so the most appropriate technique to use is liquid chromatography (LC-MS). A range of synthetic plasticisers such as phthalates, adipates, mellitates and sebacates can be detected using the atmospheric pressure chemical ionisation (APCI) mode. Process oils are hydrocarbon mineral oils and require either the atmospheric pressure photoionisation (APPI) head (which can ionise non-polar species) or, where the oil contains sufficient aromatic character, the use of in-line UV or fluorescence detectors. A fluorescence detector is particularly sensitive in the detection of polyaromatic hydrocarbon (PAH) compounds in such oils.

Cure system species, accelerators and their reaction products
This class of additive can present problems as they are often thermally labile, reactive and, in some cases, have a degree of ionic character (e.g. zinc dithiocarbamate salts). In these cases LC-MS is a more appropriate technique than GC-MS. It is also easier to use LC-MS with a number of the approved food simulants as they can be injected directly into the instrument, being compatible with the mobile phase. In some cases the reaction products (e.g. aniline from diphenyl guanidine, and benzothiazole from thiazole and sulphonamide accelerators) are stable and so GC and GC-MS can be used. Peroxides are popular curatives for food use rubbers and the stable, breakdown products of these can be easily detected by GC-MS.

Antidegradants and their reaction products
This class of additive is generally less thermally labile and reactive than the preceding one and GC-based methods can be used for a number of them. However, due to the relatively high processing temperatures used with rubbers, a number of low volatility, oligomeric antidegradants are commercially available and as the higher oligomers of these far exceed the molecular weight limits of GC, LC-MS based methods have to be used.

Oligomers
Prior to the commercialisation of LC-MS instruments, supercritical fluid chromatography (SFC) was mainly used for the analysis of oligomers. As the range of LC-MS instruments can be extended up to 4000 daltons this capability makes them ideal to characterise oligomers. For example, it has been shown that silicone oligomers can be detected by LC-MS in food simulants.[7]

Nitrosamines
These potentially carcinogenic species can be determined at low parts per million levels by the use of a combined GC-thermal energy analyser instrument. Samples can be prepared from rubber compounds by either extraction or food migration studies and then, after a concentration step, injected into the gas chromatograph. The separated nitrosamines enter a catalytic pyrolyser where nitrosyl radicals are generated. These react with ozone introduced into the system to form a new radical which is chemiluminescent as it returns to the ground state. The emitted light generated by this loss of energy is detected and quantified. Care has to be taken both in the choice of rubber sample and in the preparation protocol as the heat history of both can affect the levels of nitrosamines found (see section 12.6.1).

12.5.4 Research studies

A number of research projects have been commissioned by the Foods Standards Agency in the UK to study the effects that rubber has on food. A brief description of the scope of four such projects is given below.

Project FS2219	Reviewed the types of rubber used in the food industry. Five rubber compounds were prepared and used to develop a range of analytical procedures and protocols. Migration data obtained using food simulants.
Project FS2248	Obtained additional information on migrants from rubbers and also assessed the influence on migration of the ageing of the rubbers, and the effects of the use of sanitisers and cleaning agents that are used within food processing equipment.
Project A03038	Produced a predictive list of the breakdown products of the curatives and antidegradants in the Council of Europe rubber resolution inventory list. Nineteen rubber compounds produced and migration data obtained on breakdown products using food simulants.
Project A03046	Commercial examples of food contact silicone rubbers obtained and migration data produced using both food simulants and food products.

Full reports on these projects can be obtained from the Food Standards Agency's library (at Aviation House, 125 Kingsway, London WC2B 6NH).

12.5.5 Published migration data

Some of the principal categories that have received attention in the literature are covered below.

Teats and soothers

A survey of the extractables present in rubber teats was published in 1991.[8] The samples were extracted with diethyl ether or acetone and the extracts analysed by GC and GC-MS. Data was obtained on 49 rubber teats commercially available in Holland and a number of compounds not permitted in the Dutch regulations were identified, including dibenzylamine, acetophenone, zinc dibenzyldithiocarbamate, 4,4′-thio-bis(2-tert-butyl 5-methyl)phenol and bis(2-hydroxy-3-tert-butyl 5-ethylphenyl)methane.

A more recent Dutch retail survey[9] looked at the migration of *N*-nitrosamines, *N*-nitrosatable substances and 2-mercaptobenzothiazole (MBT) from 19 samples of teats and soothers. In addition to these species, screening work was also carried out for any other potential migrants. The majority of the teats and soothers were found to be based on silicone rubber, and the extractable substances were found to be siloxanes. The remaining samples were natural rubber and only one was found to be above the permissible limits, and that was for nitrosatable substances at 0.23 mg/kg. MBT was found in only one of the natural rubber products and this was below the migration limit of 0.3 mg/teat.

Meat netting

Natural rubber has been the traditional material for elastomeric meat netting for many years and this has led to a number of studies into the levels of *N*-nitrosamines, nitrosatable and other compounds. Work carried out in the USA[10] using a typical product produced from natural rubber latex contacted with a 50% ethanol simulant for 150 minutes at 152 °C produced the data shown in Table 12.5.

Work in Canada[11] has looked into the levels of certain *N*-nitrosamines in hams that have been in contact with natural rubber netting and control samples that have not. The average results obtained on a sample group of 20 products are shown in Table 12.6. The results obtained illustrate the ubiquitous nature

Table 12.5 Levels of migrants found in 50% ethanol from meat netting

Compound	Level found (ng/g netting)
Zinc dibenzyldithiocarbamate	860,000
Zinc dibutyldithiocarbamate	<26,500
Zinc diethyldithiocarbamate	<26,000
Dimethylamine	8.8
Diethylamine	8.7
Dibutylamine	<5.2

Table 12.6 Levels of nitrosamines found in ham

Sample type	Level (ng/g of ham)					
	NDMA	NDEA	NDBA	NPIP	NPYR	NMORP
Netted ham	7.3	2.6	<1.4	<4.4	2.1	<1.5
Control ham	4.2	2.0	<1.6	<1.1	1.2	<2.0

NDMA = *N*-nitrosodimethylamine; NDEA = *N*-nitrosodiethylamine; NDBA = *N*-nitrosodibutylamine; NPIP = *N*-nitrosopiperidine; NPYR = *N*-nitrosopyroleidine; NMORP = *N*-nitrosomorpholine.

of nitrosamines and the care that has to be taken in the devising of experiments and the interpretation of any data obtained.

A survey of ten meat netting samples obtained from four different manufacturers has been carried out by workers in the Netherlands.[12] All ten samples consisted of both natural rubber and vegetable fibres and, in addition to nitrosamines and *N*-nitrosatable substances, the samples were screened for other potential migrants. Nitrosamines were detected in concentrations up to 2 mg/kg of netting and the two *N*-nitrosatable compounds dimethylamine and dibenzylamine were found up to 0.4 mg/kg of netting. These values were not considered to be of concern to public health because of the ratio of meat netting to food product. The other potential migrants identified included alkanes, alkenes, acids, antioxidants, plasticisers and sterols, several of which were not authorised for food contact in the Netherlands, but were allowed in other countries.

Rubber gloves for handling food

Wakui *et al*. have obtained GC-MS data on the extractables that can be obtained from disposable gloves using solvents such as *n*-heptane and *n*-hexane. A paper published in 2001[13] reported results that were obtained on a range of gloves, including those produced from natural rubber and nitrile rubber. A range of accelerator and plasticiser type species were identified, but it was apparent that a relatively large number of extracted compounds could not be identified by GC-MS, no match being found in the commercially available libraries. A second piece of work was then carried out[14] to improve the overall quality of the data obtained. Six compounds, which were common to a number of the nitrile gloves used in the original work, were isolated from an *n*-hexane glove extract by silica gel chromatography and then these compounds were identified by NMR and high resolution mass spectrometry.

Alkylphenols

Concerns over their potential to function as endocrine disruptors led to a Japanese study on the levels of alkylphenols in 60 rubber products.[15] Such compounds are used as starting materials in the manufacture of a number of rubber additives, particularly oligomeric phenolic antioxidants. The work concentrated on four compounds: p-*tert*.butyl phenol (PTBP), p-*tert*.octylphenol

(PTOP), p-nonylphenol (NP) and bisphenol A (BPA). The results showed the presence of PTOP in three samples in the range 2.2 to 37 μg/g, NP in fifteen samples in the range 2.6 to 513 μg/g, and no PTBP or NP in any samples. Some specific migration experiments for NP were also carried out using water, 20% ethanol and *n*-heptane. The levels were found to vary from 0.004 to 1.519 μg/ml, with the higher results being obtained with the *n*-heptane.

Peroxide breakdown products

Peroxides are often used to cure silicone rubber. Acidic species are among the breakdown products formed. A Japanese study[16] obtained data on such compounds present in extracts obtained from silicone teats and jar seals using thin layer chromatography and UV absorption chromatography. The amount of 2,4-dichlorobenzoic acid in products that had not been post-cured varied from 7.7 mg/kg to 24.2 mg/kg; the lowest values obtained using water as the extractant and the highest using *n*-heptane. Post curing, which is usually carried out for food use silicone products, significantly reduced the levels of this compound. Peroxides can also be used to cure a number of other rubbers. Work on a peroxide cured nitrile rubber detected between 0.82 and 6.41 mg/litre of the breakdown product diisopropyl benzene in an aqueous food simulant (distilled water).[17]

Silicone rubber

A test report has been produced by the Fraunhofer Institute[18] on the migration of siloxanes from three different silicone rubbers – a high-temperature curing material, a room-temperature curing material, and a cured liquid silicone rubber. Five different food simulants (iso-octane, ethanol, ethanol/water, ethyl acetate and olive oil) were used and one of the things investigated was the degree to which the thickness of the sample affects overall migration. This was found to be more important than the polarity of the simulant, in the case of the hydrophobic solvents. As expected, the results obtained with ethanol/water mixtures showed that the amount of migrating oligomeric material reduced markedly with increasing water content, a virtually zero result being obtained above 30%. The migrants were characterised by supercritical fluid chromatography (SFC) using both flame ionisation and MS detection. A homologous series of methyl-terminated linear siloxane oligomers up to twenty $SiMe_2O$ units were identified.

General surveys

In 1981 a study was undertaken in Poland on 680 samples of rubber products used in food processing plants.[19] In 35% of the samples migration of metals/metalloids into 3% acetic acid was reported (14% of the samples contained lead, 2.6% arsenic and 3% barium). The known carcinogen phenyl-*beta*-naphthylamine was found in 15.1% of the compounds, with amino type antioxidants being detected in 23% of the compounds in total. Poor organoleptic properties were found in 22.1% of the samples. Migration of accelerators

occurred in 14.1% of the samples. Overall 97.2% of the rubber compounds did not meet the requirements of the Polish State Institute of Hygiene. A Polish study has also been carried out in which migration data obtained on Polish produced ether-ester Elitel elastomers was compared with that from a natural rubber and a chloroprene/nitrile rubber blend.[20] When aqueous food simulants that had contacted all of the samples were examined, no phenolic antioxidants, or elements such as arsenic, lead and mercury were found.

A study in Japan[21] looked at the migration of dimethylamine (DMA) into water and hydrochloric acid from 25 rubber articles (including stoppers, chopping boards, spatulas and teats). After one hour of refluxing, the water extracts contained 3 to 1280 mg of DMA per kg of rubber. The study also showed that the thiuram accelerators that were present (TMTD and TMTM) were almost totally decomposed to DMA (a nitrosatable substance). However, in the case of dimethyl dithiocarbamate salts (sodium, zinc, copper and lead examples were included), the decomposition to DMA depended on the solvent used and the salt compound.

Barnes *et al.*[22] developed an LC-MS method to identify vulcanisation agents and their breakdown products in food and drink samples. A large sample of 236 retail foodstuffs were analysed for the presence of 2-mercaptobenzothiazole (MBT) and its breakdown product mercapto-benzothiazole (MB). The accelerators 2-mercaptobenzothiazyl (MBTS) and *N*-cyclohexyl-2-benzothiazole sulphenamide (CBS), which are commonly used in food contact rubbers, were also looked for. MBT and MB are also known to be breakdown products of these two compounds. The detection limit for these species was found to depend on the food product type and ranged from 0.005–0.043 mg/kg. No MBT, MB, MBTS or CBS were detected in any of the samples above these levels.

12.6 Improving the safety of rubber as a food contact material

12.6.1 Nitrosamines

Nitrosamines form as a result of the reaction of nitrosating agents with secondary amines in the rubber. One of the main sources of secondary amines is a number of the accelerators that are used in sulphur-based cure systems, the amines being breakdown products produced as a result of the chemical reactions taking place during vulcanisation. Specific examples of these accelerators, their secondary amine products (i.e. the nitrosatable compounds) and the nitrosamines derived from them, are given in Table 12.7.

With atmospheric nitrogen being one of the most important nitrosating agents, nitrosamines are easily formed in rubber compounds during both the mixing of the compound and the subsequent fabrication steps (e.g. extrusion and moulding) and they can also be formed during analytical work. A significant amount of work has been carried out by Rapra[23] on the influence of mixing

Table 12.7 Examples of nitrosamines formed from common accelerators

Accelerator	Secondary amine	Nitrosamine
TMTD and TMTM	Dimethylamine	*N*-nitrosodimethylamine
TETD	Diethylamine	*N*-nitrosodiethylamine
MBS	Morpholine	*N*-nitrosomorpholine
ZBDC	Dibutylamine	*N*-nitrosodibutylamine
DPTD	Piperidine	*N*-nitrosopiperidine

procedures, vulcanisation temperatures, extraction procedures and analysis techniques. The results obtained have shown that a wide variation in nitrosamine levels can be detected in essentially identical compounds.

The main approaches that have been taken to ensure that the concentration of nitrosamines (and nitrosatable compounds) in a given rubber is as low as possible are as follows:

1. Re-compounding the rubber to wholly or partially substitute accelerators that produce secondary amines with those that do not, such as CBS, MBT and MBTS.
2. Substitution of carbon black filler (or a significant part of it) with white reinforcing fillers (e.g. silica), as carbon black has also been found to act as a nitrosating agent.
3. Switching of the cure system from sulphur based to peroxide based.

All of these modifications have to be achieved with the retention of the processing, physical and ageing properties of the rubber in mind.

Because *N*-nitrosamines are suspected of being carcinogenic to humans, all of the major regulatory bodies have laid down limits for their existence in teats and soothers. The first to do so were the Germans in 1982, followed by the FDA and Canadian authorities. EU Directive 93/11 covering the migration of both *N*-nitrosamine and *N*-nitrosatable substances came into force on 1st April 1995. The limits stated in these documents are shown in Table 12.8.

Table 12.8 National and European limits for nitrosamine levels in teats and soothers

Source	Extraction media	Species	Limit
German	Artificial saliva	*N*-nitrosamines	10 ng/g
		N-nitrosatable substances	200 ng/g
FDA	Dichloromethane	*N*-nitrosamines	10 ng/g
		N-nitrosatable substances	200 ng/g
Canadian	Dichloromethane	*N*-nitrosamines	10 ng/g
		N-nitrosatable substances	200 ng/g
Dutch	Artificial saliva	*N*-nitrosamines	1 ng/g
UK	Solvent	*N*-nitrosamines	30 ng/g
EU	Artificial saliva	*N*-nitrosamines	10 ng/g
		N-nitrosatable substances	100 ng/g

12.6.2 Amines

There are also concerns over amines (particularly aromatic amines) and so reducing their concentration is desirable. In common with nitrosamines, they can originate from accelerators. But they also have a number of other important sources, for example, from amine type curatives and as the breakdown products of the amine class of antidegradants.

Comprehensive rubber chemistry studies such as those carried out by Rapra over the past 30 years[24] have ensured that the origins of the low molecular weight compounds found in rubbers are well understood. Thus compounding steps can be taken to avoid those additives that are known to produce amines. Research and development initiatives by additive manufacturing companies have also led to the commercialisation of additives that do not produce amines, e.g., the xanthate accelerator produced by Robinson Brothers that breaks down during curing to give only isopropanol and sulphur-containing products.[25]

12.6.3 Move to less hazardous ingredients

Polyaromatic hydrocarbons (PAHs)

Within the last couple of years PAHs, also called polycyclic hydrocarbons (PCHs), have been assigned the EU risk phrase R45 (may cause cancer). This has resulted in a significant amount of attention being given to aromatic process oils and carbon black fillers which are both sources of these species. The manufacturers of process oils have addressed the issue by altering the production methods so that oils can be produced that contain significantly less polyaromatics (i.e. compounds having three or more benzene rings). These oils have already been used extensively in tyre compounds to reduce PAHs deposited in the environment and are also available for food contact products. The FDA regulations have stipulated for many years that for milk liners the amount of carbon black should not exceed 15 parts per hundred of rubber (pphr) in the rubber compound. Replacement of carbon black with other reinforcing fillers such as silica is the usual way to ensure that the resulting compound has a lower PAH content.

12.6.4 Use of alternative compounds

The complexity of rubber technology has resulted in a very versatile ‘black art’, but the resulting formulations, often containing up to 15 or more ingredients, have led to potential problems in terms of the range of species generated which have the potential to migrate into food. In recent years there has been the beginning of a trend away from the more traditional rubbers, such as nitrile and ethylene-propylene-diene monomer-based compounds, to more advanced rubbers that have superior inherent properties with respect to heat and chemical resistance, and so do not need such a large range of

additives to ensure that their compounds perform satisfactorily in service. Simpler and safer cure systems (e.g. peroxides) are also used. A rubber which is being used in an increasing number of situations is butyl rubber (a co-polymer of isobutylene and isoprene). Perfectly satisfactory compounds can be made from this material using only five or six ingredients.

Another example of a change in the type of rubber compound used for food contact applications, is the increasing popularity of thermoplastic rubbers. These rubbers have the advantage of not requiring any cure system ingredients and, in the case of the high performance versions (e.g. polyesters) they also require less stabilisation than the conventional diene type rubbers that they are replacing. They therefore have the advantage of containing a lower concentration of low molecular weight species in general and none of the species that have received the greatest amount of attention due to their potential toxicity. A search of the trade and published literature reveals that a significant number of new, food use thermoplastic rubbers compounds are coming onto the market (see section 12.7.1).

12.7 Future trends

12.7.1 Increased use of thermoplastic rubbers and high-performance rubbers

A search of a major abstract database such as that provided by Rapra will reveal the extent to which new thermoplastic rubbers are entering the food contact market. The attraction of these materials has already been explained (section 12.6.4) and in the main they have entered the market in one of two ways: as replacements for existing rubbers or for other food contact materials. Examples of the former are the development of a co-polyester based thermoplastic elastomers with high temperature resistance to replace rubbers such as silicone,[26] and polyurethane food contact gloves as an alternative to natural rubber or nitrile rubber gloves.[27] An example of a replacement for another food contact material is the use of styrene block copolymers to manufacture synthetic corks, for use in wine bottles, instead of natural cork.[28] This trend has been assisted in recent years with the continued proliferation of thermoplastic vulcanisates. The resultant cross-linking of the rubbery phase improves a number of the properties of these materials (e.g. temperature resistance and tensile strength) and enables them to compete more effectively with conventional rubbers. This cross-linking is usually carried out during the manufacture of the polymer via a free radical mechanism and so avoids the problem of residual, potentially toxic reaction products.

The use of 'cleaner' high-performance rubbers (e.g. fluorocarbons and halobutyls) is also expected to continue to grow at the expense of the diene type rubbers. The pressure to ensure ever higher margins of food safety is one reason and the demand for owners of food processing plants for increased time between failures is another. Although there are initial cost implications,

these are outweighed when complete life cycle costs are considered. For example, a perfluoroelastomer seal may cost 1000 times an equivalent made from EPDM, but it will last long enough in service to easily repay this in reduced maintenance and saved production costs.

12.7.2 Developments in additives

The move to cleaner and simpler rubbers (see section 12.7.1) has enabled a number of controversial additives to be avoided completely and this process is being assisted by the development of new compounds, particularly accelerators, that either produce less potentially harmful breakdown products (i.e. no nitrosatable substances) or ones that have much higher molecular weights and so have a reduced capacity to react/migrate. An example of the former is an accelerator from Robinson Brothers which is a xanthate compound producing only isopropanol and sulphur containing breakdown products.[25] An example of higher molecular weight additives is the trend to use benzyl or nonyl thiuram accelerators instead of the traditional methyl and ethyl derivatives.

A particular example of replacement technology that is associated with natural rubber involves the substitution of the use of tetramethylthiuram disulphide (TMTD) in field latex as a preservative with newly developed bacterial chemicals.[29] As previously mentioned, TMTD is also commonly used as an accelerator and produces nitrosatable substances. The resulting latex can then be used to produce food contact products such as gloves and meat netting thread.

Antimicrobial agents are a relatively new class of additive that is finding increasing use in food contact rubber compounds. One company, Milliken, has recently introduced a family of these compounds that are based on silver ion exchange resins and can be used in peroxide cured rubbers such as nitrile rubber and EPDM. The advantage is that they control microbial growth on and within the surface of these rubbers when they are used in food processing lines and this reduces the need for cleaning and part replacement.[30]

Rubber sponge products have traditionally been produced using chemical blowing agents that break down at vulcanisation temperatures to produce gases such as carbon dioxide and nitrogen. In the case of silicone rubber, it has also been possible to produce sponge products by the use of physical blowing agents such as low molecular weight organic compounds. There are some toxicity and/or environmental concerns associated with a number of these chemical and physical blowing agents. Indeed few have food use approval, and this has been addressed by Dow Corning who have produced a new closed cell sponge technology that uses water as the physical blowing agent.[31]

The use of carbon black fillers in rubbers is commonplace, but they can contain low molecular weight organic compounds (e.g. aromatics) due to their method of production (burning of oil). Carbon blacks have an important influence on both the physical (e.g. tensile strength and processing viscosity)

and chemical (e.g. curing rate) properties of rubbers and so extensive development work is required in order to introduce commercially acceptable new products. Due to increasing health and safety concerns and environmental pressures, development work is beginning and new classes of carbon black are appearing such as the Pureblack® class from Columbian Chemicals. This is an ultra-high purity carbon nanoparticle material which is said to combine the properties of both traditional carbon black and graphite and, in addition to having the potential to compete with furnace and channel type blacks for use in food contact compounds, to provide a number of processing and final product advantages.[32]

12.7.3 Surface coatings and modifications

The use of barrier coatings to prevent or eliminate the migration of low molecular weight species has been used for a number of years in the paper and board industry. Recent workers have looked at how this type of approach could be used with rubbers. One group in Russia[33] compared the migration from a nitrile rubber surface that had been fluorinated with a control sample that had not. Fluorination of the surface was designed to interfere with the 'relay' mechanism of migration where low molecular weight species from the bulk replace those that have been lost from the surface. The results obtained showed that the fluorination was effective in reducing migration from the nitrile rubber, but the degree of reduction was dependent upon both temperature (the reduction being more pronounced as the test temperature approached ambient), and the thickness of the rubber test piece.

The use of antimicrobial additives has been mentioned in section 12.7.2, but another route has also been investigated,[34] the deposition of silver nanoparticles, under formaldehyde-radio frequency plasma conditions, onto food-grade silicone rubber. The bacteriocidal properties of the silver-coated surfaces were investigated by exposing them to *Listeria monocytogenes*, with no bacteria being detected after exposure times of 12 to 18 hours.

12.7.4 Developments in analytical techniques

The past five years or so have seen the proliferation of LC-MS instruments to the extent that they have now replaced HPLC in the majority of laboratories. These instruments complement GC-MS and with it enable the analyst for the first time to routinely generate data on both thermally labile and stable compounds of up to 1000 daltons in rubber products and food; 1000 daltons is the established upper limit for chemical absorption in the gastrointestinal tract. This new application of LC-MS, together with the research work that is being carried out on rubbers (section 12.5.4), should enable more accurate conformity checks to be performed on compounds, as well as continuing to add to the understanding of the migration behaviour of rubber-related species.

Development work also continues to advance analytical instrumentation so that there are commercially accessible improvements in important parameters such as molecular weight range, detection limits, software-assisted peak deconvolution, analysis speed, accuracy of library searching, and species selectivity. The introduction of mid-priced multi-hyphenated techniques such as GC × GC-TOFMS and LC-MS × MS are examples of this. These instruments, with their greater resolving power and selectivity are also improving routine, direct analysis of food products, where the potentially large range of low molecular weight compounds can cause problems.

12.8 Sources of further information and advice

There are a number of routes that the researcher can take to obtain further information. It is not possible within this format to provide a comprehensive list, but this section provides a summary of the key areas where knowledge can be found, with a number of examples included in each category.

12.8.1 Professional, research, trade and governmental organisations

1. Council of Europe – Partial Agreement Division in the Social and Public Health Field (www.coe.int/soc-sp)
2. UK Food Standards Agency (www.foodstandards.gov.uk)
3. US Food and Drug Agency (www.fda.gov)
4. Rubber Division of the American Chemical Society (www.rubberdivision.org)
5. German Bundesinstitut für Risikobewertung (BfR) – Federal Institute for Risk Assessment (www.bfr.bund.de)
6. BLIC – European Association of the Rubber Industry (www.blic.be)
7. British Rubber Manufacturers Association (www.brma.co.uk)
8. Institute of Materials, Minerals and Mining (IOM^3), 1 Carlton House Terrace, London, SW1Y 5DB (www.iom3.org)
9. Rapra Technology Ltd, Shawbury, Shrewsbury, Shropshire, SY4 4NR (www.rapra.net)
10. Leatherhead Food International, Randalls Road, Leatherhead, Surrey, KT22 7RY (www.leatherheadfood.com)
11. Central Science Laboratory, Sand Hutton, York, YO41 1LZ (www.csl.gov.uk)
12. Pira International, Randalls Road, Leatherhead, Surrey, KT22 7RU (www.pira.co.uk)
13. Fraunhofer Institute (www.pioneers-in-polymers.com)
14. Rubber Consultants, TARRC, Brickendonbury, Hertford, SG13 8NL (www.rubberconsultants.com)

12.8.2 Commercial abstract databases

1. Rapra Abstracts – Rapra Technology Ltd
2. Chemical Abstracts – American Chemical Society

12.8.3 Key reference books and journals

Reference books

1. *Rubber Technologists Handbook*, J.R. White and S.K. De (eds), Rapra Technology Ltd, 2001.
2. *Handbook of Elastomers*, A.K. Bhowmick and H.L. Stephens (eds), Marcel Dekker, 2001.
3. *Rubber Chemistry*, J.A. Brydson, Applied Science Publishers, 1978.
4. *Rubber Curing Systems*, R.N. Datta, Rapra Review Report, Volume 12, Number 1, 2002.
5. *Rubber Analysis*, M.J. Forrest, Rapra Review Report, Volume 12, Number 7, 2001.
6. *Rubbers in Contact with Food*, Rapra Review Report, Volume 10, Number 11, 2000.
7. *Silicone Elastomers*, Rapra Review Report, Number 137, 2001.
8. *Migration from Food Contact Materials*, L.L. Katan (ed.), Blackie Academic and Professional, 1996.

Journals

1. *Rubber Chemistry and Technology*, Rubber Division, ACS, USA.
2. *Food Additives and Contaminants*, Taylor and Francis Ltd, UK.
3. *Journal of Rubber Research*, Rubber Research Institute of Malaysia, Malaysia.
4. *Gummi, Fasen, Kunststoffe*, Dr Heinz Gupta Verlag, Germany.
5. *Kautchuk, Gummi, Kunststoffe*, Dr Alfred Huthig Verlag GmbH & Co., Germany.
6. *European Rubber Journal*, Crain Communications, UK.
7. *Plastics and Rubber Weekly*, EMAP Maclaren Ltd, UK.
8. *Rubber World*, Lippincott and Petro Inc., USA

12.8.4 UK Food Standards Agency/MAFF research projects

Some of the recent rubber specific research projects funded by the Food Standards Agency and, prior to its existence, the Ministry of Agriculture, Fisheries and Food, are listed below. Copies of the reports issued at the completion of these projects are available from the Food Standard Agency's library (at Aviation House, 125 Kingsway, London WC2B 6NH):

FS2219 Migration studies – food contact materials.
FS2248 Further research on chemical migration from food contact rubber and other elastomers.

A03038 An investigation of the breakdown products of curatives and antidegradants used to produce food contact elastomers.
A03043 Assessment and quantification of latex protein (LP) transfer from LP-containing contact materials into food and drink products.
A03046 Chemical migration from silicones used in connection with food contact materials and articles.

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2. FSA contract number A03038.
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13

Food packaging inks and varnishes and chemical migration into food

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13.1 Introduction

What would packaging be without print? Would anybody buy cereals packed in a blank white box? No, the print is needed. We, the consumers, as well as the producers and retailers of packed products, want and need information printed on the surface of the packaging for several reasons:

- to differentiate between products
- to give the necessary information about the packaged product. This is extremely important as regards food packaging, e.g. dietary details and advice on how to store and prepare the food should be stated
- to make the purchaser interested. The print should have an eye-catching effect and give a positive picture of the contents.

The quality requirements of the appearance of packaging for product brands are extremely demanding. They concern the tone and brightness of the colours and the exact location of the print. Product information must be sufficient and able to communicate with the market. As available space is often limited and consequently the printed text is small, the print must be of high standard.

The objective of this chapter is to give an overview of the processes and problems related to prints on food packages, dealing primarily with the components of inks and their possible migration into the foodstuff. Sensory (odour and taint) aspects and testing will also be covered and statutory requirements will be discussed.

13.2 Major concepts

As the vocabulary varies widely in the literature on printing, it seems necessary to clarify some important concepts.

13.2.1 Printing inks

Printing inks, in this context also called packaging inks, including varnishes, means any product manufactured from colourants, binders, solvents and additives. There are solvent-based, waterborne, oleo-resinous or energy-curing (UV or electron beam) systems. They are applied by printing or varnishing processes, such as flexography, offset, gravure printing and roller varnishing. The term packaging ink is used in order to differentiate the products used on packages from prints for other purposes.

13.2.2 Printing processes

Flexography is, amongst the numerous printing processes, commonly used for corrugated board, plastics and plastic films and metals. Offset (lithography) is generally used for printing paper, board and plastics. Dry offset, which is an offset process without fountain solution, is used for many products intended for food contact, such as plastic tubes, cans, cups and lids. Gravure printing is also used for food packages made of paper or plastic films. The same types of ink may be used in different printing processes.

13.2.3 Varnishing

Varnishing or over-varnishing, also referred to as coating, is a finishing process where rollers apply a thin transparent layer of varnish or lacquer on the printed material. Its purpose is to protect the print from smearing and scratching, to improve gloss and to even the surface. Varnish is a kind of ink without colourant. It is sometimes also applied to the food contact surface in order to improve resistance towards moisture and fat. The term varnish is also used for the combination of binder and solvent in offset printing inks.

13.2.4 Substrate

Substrate is the material on which the print is applied. Substrates are, for example, glass, tin plate, aluminium foil, paper and board, plastics or multilayer laminates.

13.2.5 Substances

Printing ink manufacturers purchase raw materials, which are substances or preparations, and mix them into printing inks.

13.2.6 Set-off

Set-off means mechanical transfer (smearing) of ink or an ink substance from a printed surface to a contacting unprinted surface. It can occur in the stack or on the reel subsequent to printing, when ink transfers from the print to the reverse of the adjacent sheet. It depends on several variables, such as the time of contact, internal pressure in the roll or stack of sheets, the level of retained solvent, the type of ink used and the drying procedure applied in the printing process. Visible set-off, where some colourant has been transferred, results in rejection of the material. Invisible set-off implies that one or several uncoloured substances are transferred to the side of the package that will come into contact with the package content, which may be serious as regards food packaging.

13.2.7 Drying

There are two concepts involved in the drying of ink, setting and curing. They take place simultaneously to some extent. Setting is a phase separation such as resin precipitation, whereas curing consists of evaporation, oxidation or polymerisation. Curing may be enhanced by radiation. Drying and curing occur sometimes as synonyms in the literature.

13.3 Inks and ink components

The main function of the printing process is to provide contrast and colour to the substrate. The ink must meet the requirements that depend on the printing process and the substrate, i.e., rheological properties, surface chemical properties and drying properties. Consequently the composition of inks varies widely. In addition, it should be user and environmentally friendly. As for food packages, toxicological and migration properties must be observed.

13.3.1 Colourants

The task of the colourant is to provide colour to the printed substrate. It absorbs light of a certain wavelength, depending on its structure, and the eye perceives the reflected light as a certain colour. Colourants are either pigments or dyes. Pigments are finely divided particles, insoluble in the medium. They are either natural, such as soot (black) or titanium dioxide (white), or synthetic, i.e., organic compounds. Dyes are soluble in the medium. They are organic substances or organo-metallic complexes.

13.3.2 Binders

The purpose of binders or resins is to bind the pigment to the substrate and to improve the general resistance of the print towards moisture or fat. They

also prevent the sedimentation of the pigment in the ink and provide some gloss to the printed surface. Resins are a variety of polymeric substances ranging from low molecular weight oligomers to high molecular weight polymers of complex structure. Drying oils and alkyds can be regarded as liquid resins or plasticisers.

13.3.3 Solvents

Most inks contain significant amounts of solvent for dissolving the resin and adjusting the ink viscosity. The kind of solvent used depends on the substrate and the end use of the print. Water as well as hydrocarbons are used, also ketones, esters and alcohols. For example ethanol and isopropanol are common in flexo printing. The solution of resin in a solvent is also called 'vehicle'.

13.3.4 Additives

A great number of additives are used in printing inks. Their percentage in the ink is usually very low (1–5%). For example, the purpose of antifoams is to prevent foaming during the printing process. Softeners give flexibility to binders; the task of waxes and lubricants is to improve abrasion resistance, etc. A list of different kinds of additives is given in Table 13.1.

13.4 Regulations and recommendations as regards food packaging

As noted above, there are a great variety of substances involved in printing. Consequently the risk of the packed food becoming contaminated by one or several of these components is always present. To avoid hazards, national as well as international regulations have been issued.

13.4.1 EU regulations

In Europe the essential paragraph in Regulation (EC) No 1935/2004, commonly referred to as 'the framework regulation', applies to all materials intended for food contact and must consequently be observed by manufacturers of printing inks as well as by printers. It states that materials and articles intended for food contact

- shall be manufactured in compliance with good manufacturing practice
- shall not transfer their constituents to foodstuffs in quantities which could endanger human health
- shall not bring about an unacceptable change in the composition of the foodstuffs or a deterioration in the organoleptic characteristics thereof.

Table 13.1 Groups of additives in printing inks (alphabetical order)

Acid catalysts	Chelating agents	Photoinitiators
Adhesion promoters	Dispersing agents	Plasticisers
Amine solubilisers	Driers	Slip agents
Antifoam agents	Flow agents	Suspension agents
Antimists	Gellants	Thickeners
Antistatics	Ink stabilisers	UV stabilisers
Biocides	Optical brighteners	Wetting agents

In an annex to the regulation, printing inks are listed among the subjects that may be covered by specific measures. However, these specific measures seem to be far in the future, as no work on printing inks is in progress within the EU. The draft 'Super-regulation' on plastics introduces a new concept, the 'multi-material plastic multi-layer' – material that is composed of two or more different types of material provided the one intended to come into direct contact with food consists of plastic. According to this, the print could be regarded as a layer in such a material, and consequently the 'Super-regulation' would be applicable also to the print and the substances in the print. This same document specifies that printing ink, when used to manufacture articles for food contact, shall be included in the determination of overall migration.

13.4.2 Council of Europe (CoE)

A committee within Council of Europe – the Committee of experts on materials coming into contact with food – has prepared a Resolution on 'Packaging inks applied to the non-food contact surface of materials and articles intended to come into contact with foodstuffs'. The legal status of such a resolution is not equal to the status of an EU regulation, but the resolution might later become the basis of an EU regulation or directive. The work on this resolution has been going on for many years, but making slow progress. The main obstacle has been conflicting views taken by national delegates and the industry. The national delegates are in favour of openness about the substances used in ink, while industry states the need of secrecy for reasons of competition.

The resolution on packaging inks applies to layers of print situated at the non-food contact surface of any material intended for food contact. Inks in direct contact are excluded from the resolution. Neither does the resolution apply when there is evidence that a substrate stops the migration of any component, and set-off or transfer via the gas phase can be excluded. Consequently it does not apply to glass bottles, aluminium tins and corresponding materials. Its main objective is to regulate prints on fibrous or plastic materials.

As regards responsibility, the resolution on packaging inks, in accordance with the above-mentioned framework regulation, states that the ink supplier

is responsible for the composition of the ink. The supplier should communicate to the business operator (the printer) all necessary information for manufacturing the finished package in compliance with the appropriate rules. Traceability implies that business operators (in this case ink manufacturers and printers) should at least be able to identify the operator from and to whom a substance, an ink or a printed material or article has been supplied.

The CoE resolution on packaging inks is accompanied by a couple of technical documents (TDs). TD 1 provides the requirements for selecting packaging ink substances. It comprises a scheme, an inventory list of substances being used by the industry and an exclusion list. Substances that are evaluated by an international body are noted, and specific migration limits are given, if available. The purpose of TD 1 is to ensure that no substances that are harmful to human health, are transferred into the packed foodstuff.

TD 2, which consists of two parts, is a guide for Good Manufacturing Practice. Part 1 is prepared by the ink industry represented by CEPE (The European Council of Paint, Printing Inks and Artists' Colours Industry). In addition to training of personnel, manufacturing instructions and quality control, it underlines co-operation with the suppliers of raw materials. The ingredients should be carefully selected to ensure that the components of the ink comply with the relevant regulation. Part 2, prepared by European Forum of Flexible Packaging Europe and CITPA (International Confederation of Paper & Board Converters), is intended for converters of flexible and fibre based packaging, i.e., paper, board, regenerated cellulose, plastic film or aluminium foil and laminates of these materials. Its objective is to prevent any health hazards or unacceptable change in the sensory characteristics of the food product that may result from excessive transfer of components of the packaging material into the packed food product. It emphasises strict hygienic standards, choice of raw materials and traceability of all materials.

TD 3 gives guidance on conditions to be used for testing packaging inks applied to the non-food contact surface of food packaging materials. Testing is required regardless of the type of food to be packed, i.e., also for dry, non-fatty foodstuffs. Further details of testing are discussed in section 13.6 below.

13.4.3 National regulations

National regulations concerning packaging inks are scarce in Europe. In chapter XXXVI of the German Recommendation BfR (Bundesinstitut für Risikobewertung), there is a general phrase on colourants and optical brighteners in the material, stating that they should not migrate into foodstuff. It is also stated that no testing is required for packages intended for dry, non-fatty food.

13.4.4 REACH

The proposed EU Regulation for the registration, evaluation and authorisation

of chemicals, known as REACH, might have an impact on the substances used in printing inks in the future. Some small-volume chemicals may disappear from the market. However, according to the current proposal, the period of implementation is over ten years for some substances. Polymers will be exempted from registration and consequently most resins in inks need not be registered according to this proposal.

13.4.5 Industrial attitude

Regulations alone do not ensure the safety of a product. The attitude of the industry and their good manufacturing practice (GMP) are even more important. In addition to GMP, CEPE has published an exclusion list for printing inks. Excluded are substances listed in the Dangerous Substance Directive (67/548/EEC), and pigment colourants based on antimony, arsenic, cadmium, chromiumVI, lead, mercury and selenium. Several solvents are also excluded as are certain stilbenes, butylphenols, benzophenones and cyclohexane. The CEPE list is not identical to that issued by Council of Europe. Also the BCF (British Coating Federation) has issued a guide to printing inks for food wrappers and packagings. It contains recommendations on inks for external food packaging, immediate food wrappings and inks for direct food contact.

13.5 Problems related to packaging inks

13.5.1 Unevaluated substances and degradation products

Unfortunately, the inventory list included in the draft TD 1 to the CoE resolution on packaging inks is incomplete. It appears that many of the numerous substances used in inks for food packaging have not been properly evaluated as regards their toxicological properties. Industry should ensure that there is no detectable migration into food of these unevaluated substances. Very little is known about degradation of substances during printing.

13.5.2 Migration

Prints are almost always applied to the outer surface of a food packaging and are not intended to make direct contact with food. However, low molecular substances in ink migrate (permeate) easily through the packaging material into the food. Only a few packaging materials, such as glass and aluminium foils, are barriers to all substances in the ink. Fibrous materials and most kinds of plastics do not act as barriers to migrants. In particular solvents travel easily through packages made of paper, board or plastics. In the case of polyethylene laminated board, the plastic film acts as a barrier to water, but not to fat-soluble substances. Some recent works on migration of ink components into food are mentioned below. Further references can be found

in a comprehensive Norwegian study on colourants prepared by Brede *et al.* in 2003 (see section 13.7.3 below).

Johns *et al.*[1] have published a report on benzophenone in printed cardboard for food stored frozen. This substance was found at 0.4–3.0 mg/dm^2 in four board samples out of seven. The authors suggest that UV-cured inks had been used with benzophenone as an initiator in the printing of these boards. Three of the corresponding foodstuffs contained benzophenone at a level of 0.6–2.9 mg/kg, though there was a polyethylene layer applied to the board. Model ink substances were added to the carton, which then was in direct contact with foodstuffs stored at –20 °C for a year. It was found that transfer of the volatile substances could be considerable even at low temperatures.

Aurela *et al.*[2] studied migration of alkylbenzenes used as solvents in offset inks. Alkylbenzenes migrated from a hamburger collar into a roll at the level of 2 mg/kg of food. In a risk assessment report published by the European Commission,[3] a NOAL (no observed adverse effect level) value of 50 mg/kg body weight per day was used. Thus, the migration from the printed hamburger collar is quite acceptable.

13.5.3 Set-off and curing

Invisible set-off is not easily detected at the printing house and some printers are not even aware of its existence. A study on plasticisers by Aurela and Ohra-aho[4] showed that the set-off phenomenon considerably increased migration into food when the substrate was a high barrier material and migration through the substrate was low. In order to avoid set-off, emphasis should be put on drying of the print. Inks containing a high proportion of solvents, such as gravure and flexographic inks, are typically dried by evaporating the solvent in an air flow, for example when plastic films are printed. Inks for sheet-fed offset, dry by oxidation and/or polymerisation. As regards corrugated board, drying is no problem as the high mass of fibrous material readily absorbs the solvent. The time required for absorption depends also on the capillary structure of the substrate surface.

Set-off can be avoided by the use of anti-set-off compounds. These are spray powders that reduce the frictional contact between the sheets. Materials like silica and starch, which have a particle diameter slightly greater than the printed ink film thickness, can be used. Slow setting problems may be reduced by the use of less solvent or by a higher ratio of resin to oil. Varnishing with a formula that utilises polymerisation induced by radiation is another way to avoid set-off. The varnish covers the printed surface and direct contact between the layer of print and the inner food contact surface of the substrate is avoided.

UV-radiation is used to achieve rapid curing and to avoid set-off effects in offset printing. The binders in UV-inks are highly reactive acrylate monomers and oligomers to which photoinitiators are added. These initiators start the cross-linking reaction in response to UV-radiation. Photoinitiators are low

molecular weight substances, such as benzophenone. Dry prints still contain residues of photoinitiators or their degradation products. The initiators and their degradation products may cause an undesirable odour or migrate into the packed food. The low molecular products can be removed by careful airing. Photoinitiators are intensily studied in order to avoid problems. In a recent study, Bedolla[5] has shown that on flooding the curing environment with nitrogen, the amount of photoinitiator can be significantly reduced without loss in curing efficiency. Electron beam (EB) curing might also become more common. Its advantage is no need for any initiator, but high costs might restrict its use. Cationically cured UV inks are based on cycloaliphatic epoxy resins. They contain photoinitiators that break down into acids. However, they are unsuitable for offset printing for technical reasons. This type of ink is often used when printing labels.

13.5.4 Sensory contamination, odour and taint (off-flavour)*

Several substances in the ink can have a noticeable smell or they can penetrate through the substrate and cause taint problems to the packed food. Food producers should therefore regularly check the deliveries of packages before accepting the material, in particular when a new grade is introduced. Solvents often contain malodorous substances. Vegetable oils used in offset printing have a tendency to oxidise. The unsaturated fatty acids undergo auto-oxidation reactions resulting in hexanal and other volatile compounds. The reaction is catalysed by the presence of heavy metals, such as iron or copper.

Binders, mainly alkyd resins, in inks drying by oxidation may also be a source of hexanal and other aldehydes. In a study by Landy *et al.*[6] on the odour of paper-based packaging materials printed by the offset process 13 odorous substances were identified, ten of them being aldehydes and ketones resulting from oxidation of printing ink resins. Mineral oils are high boiling point, aliphatic hydrocarbons. Some mineral oils contain aromatic compounds in order to increase their dissolution power. The aromatic compounds can easily diffuse through a fibrous or plastic material migrating into the foodstuff. Aromatic substances like toluene and xylene should be avoided when food packages are printed. Hydrogenation of aromatic hydrocarbons leads to ring-like aliphatic substances. These have a high dissolution capacity, but less smell and lower toxicity compared to aromatic solvents.

Low-odour inks for food packaging are based on odour and taint-free substances, for example, aromatic free solvents and maleic resins. So called semi-drying oils are also used. These are slow to oxidise and therefore do not develop malodorous aldehydes as they dry. However, some smell may be noticed after a long period of time as oxidation proceeds. Other solvents, such as tung oil, develop quite some odour during drying but if properly

* The vocabulary varies. Off-flavour is an atypical flavour often associated with deterioration of the product. Taint is often used as a synonym for off-flavour.

aired they are free of odour when oxidation is complete. Water-based inks are intensely studied by ink manufacturers in order to avoid sensory problems and some ink producers market so called low-migration and low-odour offset inks intended for food packaging. These are based on non-oxidative curing.

13.5.5 Print on food contact surfaces

Publications dealing with substances on food contact surfaces are scarce though the use of direct contact prints seems to increase, at least in the UK. Bradley[7] has investigated the substances used in this kind of print on plastics. The results were reassuring. None of the substances detected had the potential to migrate into food above their specific migration limits (SMLs). For substances not having an SML, 10 μg per kg of food was set as a 'level of interest'. By worst case calculation it was found that only one substance, 2-ethylhexyl acrylate exceeded this limit and only by a small margin. The author states that practical tests would probably have resulted in migration below the level of interest. She recommends that inks intended for direct contact with foodstuffs should be controlled as coatings rather than as packaging inks.

13.5.6 Conclusion

Quality and safety risks can be reduced only by selecting harmless raw materials for the ink, and an appropriate printing process that ensures sufficient curing.

13.6 Testing

13.6.1 General remarks

The ink to be tested should be printed on the same substrate and by the same procedure that is intended for the final product. The ink should not be tested as such because its composition may change during the printing process. Test pieces of a printed material should be selected so that all components of the ink are represented at the same percentage as in the original material. When possible, migration testing should be carried out using the same kind of food that is intended to come into contact with the printed material. If this is not practical, certain food simulants should be used. In situations where migration limits exist for the finished product, only the migration level and not the origin of the migrated substance will affect the compliance decision. Consequently, there is no need to differentiate between migration caused by transfer through the substrate and by set-off.

13.6.2 Sensory testing

Sensory analysis is a subjective sensation by the sense organs. Assessors perform sensory analyses. For a packaging material, transfer of taint is the critical sensory property from a legal point of view. Odour is less significant, but equally important as a marketing consideration. A panel of trained assessors evaluates the sensory properties. The number of assessors is based on the sensitivity desired for the test; fewer assessors result in less statistical reliability. A well-trained panel will give consistent results.

For evaluation of the odour of a printed material, paper, board or plastic, test pieces are stored in jars for a certain time. The odour of the air is then evaluated by the panellists. The intensity of the odour is rated on a scale such as 0 (no odour) to 4 (strong odour). For evaluation of taint, test pieces are stored with a test food in a jar. (One version of this test is known as the Robinson test.) The taint of the food is then evaluated and rated by the panelists e.g., as a triangle test or a multicomparison test. In the triangle test the assessors should select the odd test food out of three test food portions. One has been stored together with the material to be tested and two are reference samples, or vice versa. In the multicomparison test, the assessors receive one known control sample that holds the value of 0. The assessors score the intensities of the taint of the analysis sample compared to the control sample. The scale indicating the strength of taint is usually from 0 (no taint) to 4 (strong taint). Figure 13.1 shows experimental set-ups for odour and taint tests.

Though there are no specific international standards for assessing odour and taint caused by the ink, a general standard for assessing modifications to the flavour of foodstuffs due to packaging has been issued by ISO. There is also a specific standard for paper and board and some standards on sensory analysis in general. See section 13.7.4 below.

Conventional sensory tests are time consuming and require a well-motivated panel. Much work has therefore been done to replace panel evaluations by instrumental methods. An instrument called an electronic nose seems soon to be applicable for routine analysis within the food and the packaging industry. It is based on a chemical sensor array. An investigation by van Deventer[8] on volatile chemicals from inks on plastic films has shown that the quartz sensors of an electronic nose system were able to discriminate between packages with different levels of retained solvents. In a project partly funded by the European Union, the Parfum-Project, an instrument based on an array of eight quartz crystal microbalances (QMB) and eight metal oxide (MO) sensors was investigated. Frank *et al.*[9] showed that there was a very satisfying correlation between the prediction of the 'nose' and human sensory assessments as regards retained solvents in printed wrapping foils. This project has been followed by another European project, ESCAPE (Electronic Sensor System for the Characterisation of Packing Emissions) with the intention to develop a rapid instrumentation system that combines sampling with sensor arrays for monitoring of residual solvents and unwanted odours of packaging materials.

(a)

(b)

Fig. 13.1 Experimental set-ups for (a) odour and (b) taint tests of a packaging material.

Instruments based on sensor arrays will become tools for practical application and should enable rapid screening of printed materials directly connected to the production process. Figure 13.2 shows a commercial electronic nose and a human panellist.

(a)

(b)

Fig. 13.2 Two kinds of 'noses' at work. (a) The electronic nose can smell tens of samples during the night, while (b) a human nose fatigues more easily.

13.6.3 Migration testing

Migration tests are designed to measure the quantity of substances that are likely to transfer from a packaging material to the food. In principle, testing for compliance with established specific migration limits should be carried out using the conditions established in actual EU controls on migration testing. It is, however, extremely difficult in many cases to achieve the limits

of detection required by legislation as a limit might be as low as 10 μg of substance in 1 kg of food. Analytical means are still under development. For practical reasons certain specified food simulants are generally used to replace actual foodstuffs.

In the migration test the specimen to be tested is brought into single-sided contact with a food simulant. The conditions (time/temperature) are chosen depending on the final use of the printed material. After exposure the simulant is analysed or extracted, and the extract is analysed for example by gas chromatography and mass spectrometry (GC/MS). The test was originally developed for plastic materials, but it can be applied also to other printed or unprinted materials. In the case of paper and board, the standard liquid simulants are not suitable, as they penetrate into the material. They are therefore replaced by modified polyphenylene oxide (Tenax) according to a European standard EN14338. Figure13.3 shows the experimental set-up for migration test using Tenax.

Papilloud and Baudraz[10] studied the official European simulants A, B and D, which are to be used in migration tests. Simulant A, water, mimics liquid foods; simulant B, 3% acetic acid, mimics acidic liquids; and simulant D, olive oil, mimics fatty food but is usually replaced by iso-octane or 95% ethanol for practical reasons. Transfer into these simulants of some major acrylates and photoinitiators used in UV-printing was investigated. The printed materials were kept in one-sided contact with the simulants in migration cells made of stainless steel. The aqueous solutions were concentrated by solid-phase extraction, the organic solutions by evaporation. The determination of the migrants was made by GC/MS. Reproducibility and accuracy were good both for the acrylates and the photoinitiators at levels above 10 μg/l. However, the limits of detection were not quite satisfactory, as most real samples would have levels of migrants too low to be detected by present means.

In another publication by the same authors[11] a method was developed for quantification of migrants from UV cationic printed materials, in aqueous simulants. Quantitative analyses were performed by HPLC. The limits of detection were 2.7–17 μg/l for the investigated substances, except for the epoxy monomer. The corresponding limits of quantification were 8.9–58 μg/l. These figures show the need to develop analytical means further.

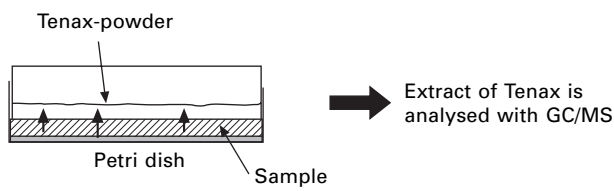

Fig. 13.3 Experimental set-up for a migration test using Tenax as a food simulant according to EN14338.

13.6.4 Testing of materials for use at elevated temperatures

For migration testing of printed materials intended for use at elevated temperatures only Tenax is used as food simulant. Testing should take into account possible degradation products formed at elevated temperatures. Prior to testing, the sample should be preheated in a closed container.

13.6.5 Worst-case calculation and modelling

Migration testing can be replaced by so-called worst-case calculation. The amount of the actual substance applied on the surface of the substrate must be known. It is then assumed that 100% of the substance migrates into the food to be packed. An example of the calculation is presented in the CoE document on test conditions for packaging inks (TD 3). Mathematical modelling or simulation can be used to predict the migration of a substance and to verify compliance with migration limits. Though in migration testing the result represents the sum of a substance transferred through a substrate and the possible set-off, this is not the case when using diffusion models for predicting migration. The transfer resulting from set-off must be estimated separately. Some recognised diffusion models are available: see Chapter 8.

13.6.6 Investigation of set-off

For investigation of the tendency for set-off of a specific substance, a freshly printed surface of a material is brought into contact with an unprinted sheet of the same material under pressure. The unprinted sheet should then be analysed, for example, by extraction and GC/MS. A method to identify spots of invisible set-off of inks and lacquers on the food-contact surface of a food packaging material has been developed by Bradley *et al.*[12] The authors use optical means to excite and observe luminiscence from invisible set-off. In their model experiments with several resins applied on different substrates they have achieved a level of detection of 20 μg per cm^2 of sheet surface. This approach might gain wider use in the future.

13.6.7 Analysis of inks and prints

Inks and prints are analysed in order to ensure safety. This includes testing for harmful substances with potential to migrate into food. Environmental pressure may result in a demand for testing, for example, vegetable oils versus petroleum distillates. There might also be a need to determine the content of aromatic compounds in the ink in order to avoid odour and taint problems. For chemical analysis of prints and determination of ink components a number of methods are available, such as pyrolysis, infra-red spectrometry, gas chromatography and mass spectrometry. Volatile compounds are usually analysed by a headspace technique. The progress in chemical analysis is so rapid that any method may be considered obsolete after a limited number of

years. It is therefore recommended to search the literature in order to find an appropriate method.

13.6.8 Olfactometric analysis

In a recent study by Landy *et al.*[5] on odorous substances in paper-based packaging materials, the main volatile substances that caused odour of an offset printed product were identified by olfactometry. In this technique solvent-free extraction using microfibres was successfully applied. The extract was introduced in a gas chromatograph connected to a sniffing port. The odour was then evaluated by a trained assessor.

13.6.9 International standards for testing prints and inks

There are no specific international standards for packaging inks dealing with the determination of ink components or their migration. Some guidance may be found in the standards dealing with substances in paper and board and in plastics, referred to in section 13.7.5.

13.7 Sources of further information and advice

13.7.1 EU regulations

EU Regulation 1935/2004 – Regulation on materials and articles intended to come into contact with food ('Framework regulation').

Draft Commission Regulation relating to plastic materials and articles intended to come into contact with foodstuffs. 'The SuperRegulation', EMB/993 Rev. 6-3 Brussels 1 Nov 2004.

13.7.2 Council of Europe documents

Council of Europe Resolution ResAP(2005)2 on packaging inks applied to the non-food contact surface of food packaging materials and articles intended to come into contact with foodstuffs, available at www.coe.int.

Technical document no. 1 on requirements for the selection of packaging ink components applied to the non-food contact surface of food packaging materials and articles intended to come into contact with foodstuffs. To be published on the Internet.

Technical document no. 2, Part 1. CEPE: Good Manufacturing Practices for the production of packaging inks formulated for use on the non-food contact surfaces of food packaging and articles intended to come into contact with food. 1999, so far available at www.cepe.org to be published on the Internet.

Technical document no. 2, Part 2. Code for Good Manufacturing Practices for flexible and fibre-based packaging for food. So far available at www.flexpack-Europe.org, to be published as a CoE document.

Technical document no. 3. Guidelines on test conditions for packaging inks applied to the non-food contact surface of food packaging materials and articles intended to come into contact with foodstuffs. To be published on the Internet.

13.7.3 Textbooks and reports

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Oittinen P and Saarelma H, *Printing*, Helsinki, Fapet Oy, 1998.

13.7.4 International standards dealing with sensory testing

EN 1230-1. Paper and board intended for contact with foodstuffs. Sensory analysis. Part 1: Odour; Part 2: Off-flavour (taint).

ISO 13302:2003 Sensory analysis – Methods for assessing modifications to the flavour of foodstuffs due to packaging.

ISO/DIS 4120:2004 (draft) Sensory analysis – Methodology – Triangle test.

ISO/CD 5492 (draft): 2005. Sensory analysis – Vocabulary.

13.7.5 International standards dealing with migration testing

EN 14338. Paper and Board. Migration into modified polyphenylene oxide (MPPO).

EN 1186, parts 1–15. Materials and articles in contact with foodstuffs. Plastics.

EN 13130, parts 1–28. Materials and articles in contact with foodstuffs. Plastic substances subjected to limitations.

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14

Food packaging adhesives and chemical migration into food

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14.1 Introduction

Adhesives are used to fabricate a variety of materials and articles for food packaging. They are used to:

- assemble boxes from sheets of cartonboard
- seal flexible packaging such as plastic wrappers, pouches and lidding
- attach labels or
- laminate sheets or films of different food contact materials together.

The adhesive may be solvent or water-based, hot-melt, coldseal or heatseal and pressure sensitive or chemically reactive. So the solidification process may occur via drying of water or solvent-based adhesives, by cooling of hot-melt and heat-seal adhesives, or by curing of chemically-reactive systems. With two notable exceptions – self-adhesive labels used on items of fruit or vegetables, and heat-sealable layers on packaging films – adhesives are in general not intended to touch the packaged food directly.

The many different types of adhesives and the wide variety of ways in which they can be used influence the potential for migration of chemicals into the packaged food. This then helps to provide a framework for subsequent considerations of specific applications. The two main parameters considered are the surface area of adhesive used and the residual content of low molecular weight substances. Taking surface area first, there clearly is a quantitative difference between small spots or strips of adhesive used at ends and seams to fabricate cartons and pouches or used to attach small sticky labels, compared to an adhesive used to glue whole sheets of materials together to make a laminate. As regards composition, for solvent-based, water-based heatseal

or coldseal adhesives, the high molecular weight 'gummy' substances needed to provide a cohesive bond can be largely pre-formed in the adhesive formulation. The fraction of low molecular weight substances that may migrate can be controlled before the adhesive is used. In contrast, for chemically reactive systems, the high molecular weight material is formed *in situ* and if the reaction is incomplete or if any unwanted side-reaction products are formed, there are limited opportunities to remove them from the glued material.

This chapter provides examples of adhesive types used to make food packaging materials. It details the potential for chemical migration from adhesives and how the safety of these substances can be, and has been, tested experimentally.

14.2 Examples of adhesive types used in food packaging applications

The different types of adhesives, their applications and the nature of any contact made with the packaged food (direct or indirect or incidental) are shown in Table 14.1 for the most common adhesive systems.

14.2.1 Water-based adhesives and solvent-based adhesives

Water-based adhesives are applied as aqueous solutions, dispersions or emulsions and are used mainly in paper and board applications, for example, side-seaming of cartons. Typical examples of adhesives applied in this way

Table 14.1 The different types of adhesives used in food packaging

Application	Adhesive system	Type of contact*
Flexible packaging laminates	Chemically reactive systems water-based hot-melts tie-layers	Indirect
Labelling	Pressure-sensitive solvent-based water-based hot-melts	Indirect, other than direct for, e.g. items of fruit/vegetables
To seal flexible packaging	Coldseal/heatseal coatings solvent-based water-based hot-melts	Indirect but with occasional incidental direct contact with, e.g., side-seams
Box closures	Hot-melts water-based	Indirect but with occasional incidental direct contact with, e.g., end seals

* Does the adhesive touch the food intentionally (direct) or may it touch the food unintentionally (incidental) or is it separated from the food by a layer of another packaging material (indirect)?

are starches, dextrins, animal glues, polyvinyl alcohol, polyvinyl acetate and ethylene vinyl acetate co-polymer emulsions. Solvent-based adhesives are applied as organic solutions. They are used mainly in flexible lamination, with occasional use in some labelling operations. These adhesives rely on the removal of water or solvent to turn them from a liquid state into a solid or viscous ('gummy') layer of glue.

14.2.2 Hot-melt adhesives

Hot-melt adhesives are applied in molten form and a bond forms between the substrates on cooling. These adhesives are used mainly for high-speed operations such as container formation and for some pressure-sensitive labels. The archetypal hot-melt adhesive is sealing wax, but nowadays they are mainly synthetic products such as high molecular weight ethylene-vinyl acetate co-polymers.

14.2.3 Heatseal adhesives

Heatseal adhesives may be used in the sealing of peelable lidding, for example for dairy containers. They differ in function from hot-melt adhesives in that they are heated to melt *in situ*. The adhesive when heated under pressure melts and bonds the two surfaces together. Different types of heatseal systems exist. New polyester diaphragms for yoghurt lids are now commonplace and these require a primer before the heat seal can be applied. Different combinations of substrates may be heat-sealed. These include aluminium-aluminium, aluminium-polystyrene, aluminium-ABS, etc. The melting temperature of the adhesive can be tailored (via its composition) to suit any temperature constraints on the substrates themselves. The main objective of heatseals is to seal in the product, usually to prevent spillage during transportation. However, the bond must be peelable to unpack the food product.

14.2.4 Tie-layers

Tie-layers are used as binding layers in some multilayer materials that are produced without any lamination adhesives. Tie-layers are formed by applying a co-extrudable resin, which is usually a polymer modified with active functional groups to make it adhere to the other substrates.

14.2.5 Pressure-sensitive adhesives

Pressure-sensitive adhesives are used for labelling applications. They are permanently 'tacky' and adhere to the surface of the desired substrate under pressure. A paper or plastic film label is coated with a pressure-sensitive adhesive and applied to a backing layer – usually siliconised paper from which the label can be removed easily. The labels are then printed and sent

to the food packer who uses them to label packaging or directly onto the foodstuff (e.g. to the skin of an item of fruit).

14.2.6 Coldseal adhesives

There are two main types of coldseal adhesive and these are based on natural latex[1] or synthetic polymers.[2] They differ from pressure-sensitive adhesives in that they stick only to themselves. They are applied to form 'dry but gummy' adhesive layers on flexible plastic films or paper and can be subsequently sealed together by pressure alone to form wrappers for food items and especially for confectionery.

14.2.7 Chemically reactive systems

Chemically reactive systems include polyurethane and epoxy adhesives. These adhesives are polymerised *in situ*. Polyurethanes are formed by reaction between isocyanate monomers and polyhydroxy compounds. These adhesives are most commonly used to laminate flexible materials. Epoxy resins may also be used as laminating adhesives. They are most commonly derived from bisphenol A and epichlorohydrin, and are cured with reactive hardeners containing primary and/or secondary amine groups.[3] Investigations into the use of epoxy-based adhesives by Bonnell and Lawson[4] suggested that they are not commonly used in food packaging applications. Epoxy-based adhesives are believed to currently represent about 5% of the market for plastic-based flexible packaging. The main reason why some epoxy adhesives are used is that when between two barrier layers they do not give rise to carbon dioxide bubbles unlike most polyurethane adhesives.

14.3 Regulation of adhesives

No specific legislation exists in the EU for adhesives but all food contact materials must comply with the Framework Regulation (EC) 1935/2004[5] (see Chapter 3). Adhesives are described in Commission Directive 2002/16/EC on the use of certain epoxy derivatives.[6] In the absence of specific harmonised rules then the Practical Guide[7] states that National Legislation should be considered. National legislation exists in Germany (BfR Empfehlungen XXVIII Components of adhesives) and in Slovenia.[8]

Similar basic principles are included in the US Food and Drug Administration regulations (see Chapter 2). In the USA adhesives overall are included in the Code of Federal Regulations (CFR) Title 21 (21 CFR 175.105 Adhesives). These Regulations specify that adhesives may be safely used:

- if they are prepared using substances described, or
- if the adhesive is separated from the food by a functional barrier, or

- for dry foods if the quantity of the adhesive in contact with the foods does not exceed the limits of good manufacturing practice.
- For fatty and aqueous foods the quantity of adhesive that contacts the food should not exceed the trace amount at seams and at the edges.
- Pressure-sensitive adhesives are dealt with in Part 175.125.
- Part 177.1390 permits the use of certain high-temperature laminates providing they are manufactured using only the adhesives specified.

14.4 Chemical migration from food packaging adhesives

In most cases an adhesive is not simply composed of the high molecular weight 'gummy' materials discussed in section 14.2 but it also contains additives which provide specific characteristics. A variety of additive types may be used, including carriers (water or organic solvents), plasticisers, tackifiers, thickeners and fillers, surfactants, biocides and fungicides, catalysts, pH adjusters, emulsifiers, waxes and antioxidants. Adhesives by their 'gummy' nature are difficult to clean up. This is in contrast to bulk polymers where unwanted substances can be removed by vacuum stripping. Hence a variety of different materials in adhesives can, in theory at least, migrate into food:

- solvents used as carriers for solvent-based adhesives
- residues of incomplete polymerisation
- degradation products and reaction by-products of chemically reactive systems that could be retained in the adhesive and
- any additives used to impart the chemical characteristics of the adhesive.

14.4.1 Migration from water-based adhesives and solvent-based adhesives

Work carried out by the Norwegian Authorities identified 29 registered, water-based adhesives that contained one or more resins as major components. These were: polyvinyl alcohol, maize starch, polyvinyl acetate, copolymers of ethylene and vinylacetate, casein, urea formaldehyde resins or modified melamine resins.[9] Additives were also listed in the formulations considered. These included solvents, softeners, conserving agents, dispersing agents and antifoaming agents.

Water-based adhesives are used in the production of paper and cardboard food packaging. Migration of adhesive components from such packaging has been assessed.[10] Migration levels into a food simulant (Tenax) were lower than the specific migration limits for plastics which were used to provide a convenient, informal way of assessing the results. Migration to foodstuffs would be expected to be even lower than into the Tenax simulant used, because food will not be in direct contact with the adhesive surfaces.

For solvent-based adhesives, there is the potential for migration of residual solvent for those systems in which the food is packaged prior to evaporation of all residues.

14.4.2 Hot-melt adhesives

Hot-melt adhesives are usually used for box-sealing applications for coated paperboard products. Migration of mineral hydrocarbons from these adhesives into foods was investigated in a survey.[11] No mineral hydrocarbons were detected but several other substances were present in the adhesives. These were proposed to be natural resins such as polyterpene resins, tall oil rosin esters, and sterol-like natural products.[12] Examples of each of these natural products are described in ref. 13 as being used for hot-melt adhesives.

14.4.3 Heatseal adhesives

When considering the potential for migration from heatseal adhesives, any reaction products formed by the heat applied during the sealing process should be assessed, as well as the ingredients used to make the heat-sealable layer. The identification of potential migrants in several heat-sealable materials has been described.[12] These studies identified several potential migrants. Good mass spectral library matches were obtained for some, but not all of the substances detected could be identified in this way. Migration of butylated hydroxytoluene (BHT) and of some of the unidentified substances was determined using food simulants. Exposure to BHT was much less than the Acceptable Daily Intake for this substance. Some of the unidentified substances were estimated to migrate at relatively high levels, up to 0.7 mg/kg simulant. Without knowing the identity, these substances could not be measured reliably in food because no standards could be used to check analytical recovery or the detector response. So instead, the heat-sealable lidding was exposed to a foodstuff and migration was estimated as the loss from the film during the exposure. Although several substances had been detected in the solvent extracts and exposed food simulants, migration into foods was low or was not notably different relative to the variation in the analyte concentration across the films.

14.4.4 Tie-layers

The function of a tie-layer is to bond dissimilar resins in composite structures, e.g., oxygen and moisture barrier layers in multi-layer food packaging materials. As well as enabling the bonding of dissimilar materials, the use of tie-layers can be better than using adhesive lamination by adding substantial thickness to a multilayer lamination as well as contributing to the strength of the material. Migration tests have been reported[14] for polypropylene barrier

containers incorporating a maleic anhydride-grafted polypropylene tie-layer. The tests used distilled water as a food simulant with exposure conditions of ten days at 40 °C. No migration of maleic anhydride (tested as maleic acid) was detected.[14]

14.4.5 Pressure-sensitive adhesives

The main use of adhesives in labelling applications is in the form of pressure-sensitives, i.e., sticky labels attached either directly or indirectly (behind a potential barrier layer) to a foodstuff. Pressure-sensitive adhesives are a distinct category of adhesives that in 'dry' form are permanently tacky at room temperature. These adhesives will adhere to a variety of substrates when applied with pressure; they do not require activation by water, heat or solvents and they have sufficient cohesive strength to be handled with the fingers or by mechanical means in labelling stations.

The primary mode of bonding for a pressure-sensitive adhesive is not chemical or mechanical but rather a polar attraction to the substrate. This always requires pressure to achieve sufficient 'wet-out' onto the surface thereby providing adequate adhesion. The four main varieties of pressure-sensitive adhesives are derived from rubber-based, acrylic, modified acrylic and silicone formulations. Release liners are used to carry the sticky label and enable it to be printed. The release liners are normally paper, treated with a very thin silicone coating to allow the label to be peeled away easily without tearing. Some transfer of the silicone into the adhesive is inevitable.

If sticky labels are attached directly to foodstuffs such as fruit and vegetables, then some of the adhesive may remain on the foodstuff when the label is removed and the food is eaten. It is not uncommon to be able to detect by eye and by touch the presence of a small sticky label residue on fruit. The presence of adhesive residues on the food surface has been investigated by Fourier transform-Raman spectroscopy[15] although at the low levels present on the foodstuff after removal of the label this technique could not be used to provide quantitative data.

Migration of adhesive components from labels applied to the outside of food packages has been investigated.[12] Several potential migrants were detected in solvent extracts of ten sticky labels investigated, and in simulants exposed to the labels behind a thin polyethylene film. Migration into simulants was also determined from labels behind a layer of polystyrene and polyethylene terephtahalate. The identities of many of the migrants could not be determined exactly although most were considered likely to be natural products. Based on the simulant data, 2-ethylhexyl acrylate migration from one of the sticky labels had the potential to exceed a European Food Safety Authority (EFSA) restriction of 0.05 mg/kg, but tests carried out with two foodstuffs showed that migration was less than that restriction. Migration of benzylbutyl phthalate from another label was also determined in foods. The amounts detected were much lower, when converted to dietary intake, than the recently

assigned Tolerable Daily Intake of 0.5 mg per kg body weight per day for this phthalate.

In a separate study[16] overall migration from several plastic films was compared with and without a sticky label attached to film. The overall migration limit was exceeded for selected material/simulant combinations. The author concluded that 'it could be anticipated, that a certain, possibly very significant, migration of substances from the label to the foodstuff could take place in real packaging also'.

14.4.6 Coldseal adhesives

Chemical migration has also been investigated for coldseal adhesives.[17] Eighteen of 20 packages studied had strips of coldseal adhesive at the packaging seam only. Thus for any chemical migration to occur substances would have to diffuse laterally in the polymer. Otherwise migration could occur only if the food made incidental contact with the adhesive seam. Only low molecular weight substances are likely to diffuse readily through the polymer and the concentrations of such substances in the adhesive were low. Consequently it was concluded that the potential for migration was very low. The other two packages of the 20 studied had the coldseal adhesive applied over the inner (food contact) surface and therefore the potential for transfer by physical detachment existed. Not only low and medium but also high molecular weight substances may transfer by this process.

If coldseal adhesives are prepared from rubber latex there is the special consideration of latex alergenicity. Although the transfer of latex proteins to packaged food is likely to be very low, if measurable at all, at this time it is difficult to come to any firm conclusions on this topic because of the absence of quantitative data on the extent of migration.

14.4.7 Reactive laminating adhesives

The majority of migration studies on food packaging adhesives have been done on materials laminated using reactive adhesive systems. Most of these have focused on polyurethanes.

Primary aromatic amine migration from polyurethanes

Polyurethane adhesives are formed by the reaction of isocyanates (including especially diisocyanates) with polyhydroxy compounds. Isocyanates in plastics are controlled under EU Directive 2002/72/EC which limits the quantity of residual monomer in the finished materials or article. The origin of this restriction is because certain isocyanates are human sensitisers. Although this legislation is for plastics, it is also used by some as a guide for isocyanates used in adhesives, although such presumptive standards have no established standing in law.

Isocyanates can also hydrolyse to form primary amines. Many primary amines derived from aromatic isocyanates are considered to be potential carcinogens and so are subject to an additional restriction in the form of a specific migration limit (SML) on the release of primary aromatic amines (PAAs) from plastics. According to Directive 2002/72/EC[18] food contact materials may not release PAAs (expressed as aniline equivalents) in a detectable quantity, using an analytical method with a detection limit of 0.02 mg/kg (analytical tolerance included). PAAs may be detected in foods as a result of the migration *per se* of PAAs from a laminate, or from the migration and subsequent hydrolysis of aromatic isocyanates (and any isomeric impurites) used as starting substances in the manufacture of polyurethane adhesives. The currently accepted method to determine compliance with this restriction is a colourimetric derivatisation method in which the PAA concentration is determined using aniline as a calibration standard.

Because the reaction between isocyanates and polyols continues for many days after lamination (i.e. the adhesive continues to cure), it is crucial to test laminates for residual isocyanates and for PAA release in a realistic manner. This must not be sooner or later than food packaging would commence. One must also use realistic pre-test storage conditions for the film (especially with respect to temperature and humidity). Indeed, many laminators routinely determine the extent of the cure of the adhesive over time. Only when a pre-defined level of cure has been reached can a laminated film be considered to be ready for packaging food.

Brede *et al.*[9] tested 50 flexible multilayer materials from 13 different manufacturers or suppliers using water as a food simulant, and test conditions close to their intended use. Twenty-two of these materials, from ten manufacturers or suppliers, were found to release detectable PAA using a colourimetric procedure (detection limit was 0.3 μg/l, methylene dianiline [MDA] equivalents). The highest PAA migration was 15 μg/l (MDA equivalents).

The Danish Veterinary and Food Administration determined the migration of PAAs from 33 samples of food packaging materials tested shortly after lamination. They used the food simulants distilled water or 3% acetic acid and a colorimetric method. PAA migration was detectable from only two of the samples. The detection limit of the accredited method was 1 μg/kg aniline/food simulant. In all migration tests performed, any PAA migration was far below the limit of 20 μg/kg.

Although the sensitivity of colorimetric analysis is satisfactory to demonstrate compliance with legislation, it has been established[19] that the responses of individual PAAs differ and therefore an uncertainty exists in the migration result which is dependent on the identities of individual PAAs present. Several of the PAAs give a weak response to this colorimetric test and in these cases the migration will be underestimated. On the other hand certain PAAs give the colour reaction but have been evaluated as being non-carcinogenic and so should not be included in the 'not detectable' restriction.

The suitability of this method to determine compliance with the legislation has been discussed within CEN/TC194/SC1 where it was suggested that the colorimetric method should be used only for screening purposes and that PAA levels above 2 μg/kg (as aniline) should be verified using a specific method. As a result a standardised method of analysis is required to determine the migration of individual PAAs from food contact materials and articles, to ensure compliance with the legislation.

Several methods exist to determine individual PAAs. These include a solid phase extraction (SPE) LC-UV method,[20] an SPE-GC-MS method in which the individual PAAs are first derivatised using solid-phase analytical derivatisation with trifluoroacetic anhydride,[21] and an LC-MS/MS method which involves direct analysis of the exposed aqueous simulants.[22] These methods have been used to determine the concentrations of individual PAAs in food simulants exposed to laminated food contact materials.

In a Danish study[22] an LC-MS/MS method was used to analyse food simulants exposed to multi-layer plastic laminates. 4,4′-Methylene dianiline migrated from four out of ten laminates (1.4–2.5 μg/kg, as aniline) and 2,6-toluenedianiline from one of the ten laminates (0.5 μg/kg). 4,4′-Methylene diphenyl diisocyanate (MDI) and 2,4-toluene diisocyanate (2,4-TDI) are often used to make polyurethane adhesives and therefore the presence of their corresponding amines was not unexpected. The same amines (along with 2,4-TDI) were detected in another study.[21] The levels reported by Brede *et al*.[21] were much lower than those detected by the Danish Authorities.[22] Differences in the reported amounts of PAA migration are likely to be due to differences in the food contact layer, the type and quantity of polyurethane adhesive applied, the curing conditions, and the age of the laminate at the time of testing. The longer the samples are left prior to testing the greater the extent of the cure and hence the lower the migration and hydrolysis of the isocyanates to form PAAs.

Other substances migrating from polyurethanes

To form a polyurethane adhesive the isocyanate moiety is reacted with a range of substances – e.g., monoethylene glycol, 1,1,1-trimethylolpropane, 1,2-propylene glycol, 1,4-butanediol and neopentyl glycol. Higher molecular weight polyhydroxy substances may also be used, up to several thousand Daltons in size. It has been demonstrated that low molecular weight oligomers of polyols may be detected in polyurethane resins and that these can migrate.[2] The migration of unreacted polyol components through polyethylene was observed. Although an excess of isocyanate was present in the adhesive formulation, it was postulated that polyol components had diffused into the polyethylene prior to full reaction with the isocyanate, and this provided a reservoir for subsequent migration.

Some known odour and taint problems derived from polyurethane adhesives include the formation of cyclic 1,3-dioxolane and 1,3-dioxane structures from the reaction of 1,2-diols and 1,3-diols with aldehydes and ketones, and

2-ethyl-5,5–dimethyl-dioxane-1,3, a compound with an extremely strong odour, formed by the reaction of neopentyl glycol with propionaldehyde (present in polypropylene ether polyols).

Early work investigating boil-in-the-bag[23] and microwave susceptor laminates demonstrated that adhesive components can be highly reactive and the reaction products can migrate into foods. For isocyanates, these included isocyanate dimers, pre-polymerisation oligomers, aromatic and aliphatic diamines and carboimides. For the epoxy substance, bisphenol A diglycidyl ether (BADGE), a range of closely related yet unidentified substances were observed at concentrations above that of BADGE itself. This use of BADGE has been withdrawn but this still highlights the possibility of its by-products migrating into the foodstuff in other applications.

Polyurethane adhesives were investigated by Lawson *et al.*[2] but difficulties were experienced due to the rate of technical and commercial development within the polyurethane adhesive industry at the time. Few firm conclusions as to the safety of these adhesives were derived from this work. The overall conclusion from more recent work on the migration of adhesive from laminated multi-layer packaging was that potential migration of laminating adhesive components is likely to be of interest only if an inappropriate type of adhesive has been selected for a particular application.[14] For those products laminated using reactive polyurethanes, adhesives have been developed which contain low levels of monomeric aromatic isocyanates in order to reduce any potential migration of aromatic amines into food in critical applications. Such adhesives were not considered to present any notable aromatic amine migration hazard unless used in high-temperature applications.[14]

14.5 Future trends

General trends in the adhesive industry are a reduction in the use of solvents and minimisation of other low molecular weight components that may migrate. Future development of laminating systems are likely to focus on fast-curing systems, including low-migration isocyanate-containing adhesives and possible UV and electron beam-cured systems.

14.6 Sources of further information and advice

A summary of the proceedings from a Nordic seminar held in June 2001[9] contains valuable information on the use of adhesives in food packaging applications. The UK Food Standards Agency has funded several studies to determine the safety of adhesives used in food packaging applications (reports available from library&info@foodstandards.gsi.gov.uk). Several Internet sites provide examples of adhesives used in food packaging applications:

- www.feica.com (Association of European Adhesives Manufacturers)
- www.basaonline.org (British Adhesives and Sealants Association)
- http://www.britishprint.com/sigs/psma.asp (Pressure Sensitive Manufacturers Association)

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15

Safety assessment of paper and board used in food packaging

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15.1 Introduction

In this chapter the toxicological screening methods that could potentially be applied to paper and board food packaging materials are briefly outlined. The chapter starts with an overview of the present regulatory status regarding the safety testing of fibre-based packaging materials within the European Union (EU). This forms a background for the perceived need for toxicological screening tests and for the general requirements that such tests should fulfil. A number of presently known short-term tests are evaluated in the light of these criteria. The few known instances, where short-term toxicological screening tests have been applied to paper and board are reviewed. Ongoing research in this area is briefly presented, as well as the impact of the research on the emerging European legislation. Finally some relevant research institutes, available websites and other additional information are listed for further contacts.

15.2 Regulatory background

In the EU the legal foundations governing materials and articles coming into contact with food were contained in the Framework Directive 89/109/EEC which stated:

> Materials and articles must be manufactured in compliance with good manufacturing practice so that, under their normal or foreseeable conditions of use, they do not transfer their constituents into foodstuffs in quantities which could either endanger human health or bring about an unacceptable

change in the composition of the foodstuffs or deterioration in the organoleptic characteristics thereof.

These general requirements have been retained also in the new Regulation 1935/2004 EC on materials and articles intended to come into contact with food.

While specific directives exist to address the safety aspects of plastics, ceramics and regenerated cellulose there is, as yet, no specific directive for paper and board intended for food contact. It should be noted, however, that so far there has been no indication of actual harmful consequences associated with food packages consisting of these materials.

15.2.1 The present regulatory status of paper and board based packaging materials

Paper and board are natural materials, which have a remarkably long history of safe use. Consequently there has been no great pressure to apply specific regulatory measures to ensure their harmlessness in various applications, although in some countries (i.e. France, Italy and Germany) the legislation and the guidelines directed to the industry are rather detailed, especially in the case of recycled fibres (Escabasse and Ottenio, 2002). Typically the existing regulations define the chemicals that are allowed in the manufacture of paper and board and set limits for various contaminants (heavy metals, pentachlorophenol, polychlorinated biphenyls, etc.) in the products. A specific concern of the use of recycled fibre is also reflected in the Council of Europe policy statement on paper and board for food contact (see below).

15.2.2 The Council of Europe policy statement concerning paper and board materials for food contact

In the absence of specific EU directives, the Council of Europe (CoE) policy statement on paper and board materials and articles intended for food contact remains, so far, the most authoritative document guiding the regulatory practices in Europe (although, as noted above, more specific national regulations already exist in certain countries). The version of the statement published in December 2002 (Anonymous, 2002) contains the specific resolution on the subject, urging the member states to take into account in their national laws and regulations the principles defined in the document. It is specifically stated that paper and board should not transfer their constituents to foodstuffs in quantities that could endanger human health or cause an unacceptable change or organoleptic deterioration. Further, good manufacturing practice is required, the microbiological quality should be guaranteed, paper and board should not release antimicrobial substances, and specific limits for cadmium, lead and mercury, as well as for pentachlorophenol are defined. Instructions on testing conditions and on good manufacturing practice are given in specific technical documents attached to the policy statement. Aspects on the use of recycled fibres in the food contact material are given special attention in a separate technical document, the content of which is described in more detail below.

The Council of Europe guidelines on the use of recycled paper and board, limits for harmful substances

In the CoE guideline it is stated that some additional requirements are needed to ensure the safety of food contact materials and articles made of recycled fibre, due to the presence of printing inks, adhesives and other substances in the starting material. Aspects that should be considered include the source of recovered paper and board, the processing technologies applied to remove contaminants and the intended use of the product.

The recovered paper and board that is not considered suitable for use as raw materials include waste paper and board from hospitals, paper and board that has been in contact with garbage, stained sacks that have contained chemicals or foodstuffs, certain covering materials, carbonless copy paper, certain types of household waste paper (used kitchen towels, handkerchiefs, etc.) and PCB-containing materials.

Specific requirements for the end products include tests and migration limits for various types of toxic or harmful compounds such as Michler's ketone (4,4′ bis(dimethylamino)benzophenone), 4,4′ bis(diethylamino) benzophenone (DEAB), diisopropylnaphthalenes (DIPNs) phthalates, solvents, partially hydrogenated terphenyls (HTTP), azo colourants, fluorescent whitening agents, primary aromatic amines, polycyclic aromatic hydrocarbons (PAH) and benzophenone. The amounts of these substances should be either below the detection limits or, in some cases (DIPN, HTTP, solvents) as low as can be reasonably achieved. For benzophenone a specific migration limit of 0.1 mg/dm^2 is defined. The requirements generally apply to products intended to be used in contact with aqueous and/or fatty foodstuffs or also with dry, non-fatty foodstuffs (requirements for DIPNs, HTTP, phthalates and solvents).

15.3 The perceived need for toxicological testing

While there is no actual indication of major risks for public health due to fibre-based packaging materials, the increased safety consciousness of both consumers and legislators may lead to situations in which streamlining the regulatory framework on the safety of paper and board products, whether based on virgin or recycled fibre, becomes actual. In the present regulations the emphasis is on the chemical analysis of eventual contaminants and to some degree on the microbiological quality, and no requirements of toxicological safety testing apparently exist, yet. However, the potential usefulness of such tests has been indicated in various documents (Escabasse and Ottenio, 2002; the CoE resolution cited below).

The CoE resolution, when defining the end-product requirements for food contact materials made from recycled fibre, makes the following statement:

> Chemical or toxicological screening tests for possible unknown toxic substances are desirable. However, at present the implementation of chemical

screening tests for unknown substances might not be feasible. Furthermore, the knowledge about the applicability of toxicological screening tests for paper and board is insufficient for the time being although it should be noted that studies are in progress to establish the validity of these tests for paper and board. The use of these chemical or toxicological screening tests on paper and board should be evaluated and should be recommended in the future where necessary, based on new developments and results in this field.

In the following sections some requirements for toxicological screening tests applicable for paper and board are outlined, the presently available tests are briefly reviewed, and some examples of the actual applications of toxicological test to paper and board are given (section 15.5).

15.3.1 The types of toxicological tests and test conditions required

The toxicological tests required for routine screening of food contact materials should, naturally, have endpoints relevant to consumer safety. In addition they should be cheap, not labour intensive, and easy to perform for a large number of samples. They should also be validated and recognised by regulatory bodies. These criteria automatically exclude traditional animal testing either for acute, subacute or chronic toxicity, and also most of the presently known short-term or *in-vitro* tests fall short of fulfilling all of them. However, some experience of either individual short-term tests or their combinations to assay extracts of paper and board is starting to emerge (section 15.5).

An additional aspect that should be considered is the preparation of samples for testing. Extraction methods should take into account the types of food (aqueous, dry, fatty) with which the paper and board would interact in real life situations, as well as such factors as the duration and the temperature conditions of the contact. The selection of the food simulants used for extraction can also be critical. While most of the biological tests are compatible with water extracts, solvents like ethanol or iso-octane are regularly used in immigration tests for the extraction of lipophilic compounds. These are usually not very well tolerated by the various biological systems and cell types used in *in-vitro* tests. This limits the amounts of extractants that can reasonably be tested, and increases the need of solvent controls in the assays. Change of solvents or concentrating the samples by evaporation may lead to problems with solubility, loss of volatile compounds, and unforeseen chemical interactions. Thus, the development of realistic extraction methods, compatible with the tests systems used, should proceed in parallel with the eventual choice of biological tests for toxicological screening.

15.4 Presently available short-term toxicological tests

Several types of *in-vitro* tests are routinely applied to study the harmful effects at either cellular level (cytotoxicity tests) or on the genetic material

(genotoxicity tests). For research purposes the cytotoxicity tests have been valuable screening tools, and in certain cases they can give valuable information on the structure-function relationships and mechanisms of toxicity. However, so far their use in regulatory toxicology has been relatively limited, the emphasis still being on the whole animal studies. Several genotoxicity tests, on the other hand have been thoroughly standardised, validated, and included in various recommended guidelines for toxicity testing (OECD, 2001, pp. 471–486).

15.4.1 Cytotoxicity tests

In general, permanent mammalian cell lines of variable sources are utilised in the most common cytotoxicity tests. Although there are variations in the details of the test protocols, the cell cultures are usually directly exposed to the test agent in the growth medium, and after a certain exposure time, the resulting toxicity is measured. The endpoints can be simply cell death or growth inhibition, which can be detected by various methods, such as measuring the total protein content (TPC), using differential staining (i.e. neutral red uptake, NRU) or following the ability of the exposed culture to grow and form cellular colonies (CFA). These tests can be used to screen both pure chemicals and complex mixtures isolated from food or various environmental samples (Stammati *et al*., 1999; von Wright *et al*., 1992).

In addition to measuring cell death and growth inhibition, which usually do not give much information about the mechanisms of toxicity, cytotoxicity tests with a clear targeted function can sometimes be used. An example is the use of MTT (a tetrazolium salt), which stains blue because of the reaction with the mitochondrial enzyme succinate dehydrogenase. Thus the assay is very sensitive to mitochondrial poisons, although it can be used to measure also general cytotoxicity (Mosmann, 1983).

Tests for sublethal toxic effects

Cell death is a very drastic endpoint usually preceded by various other deleterious effects in the cell. With certain types of short-term tests it is possible to detect some of these effects, and thus gain information of non-lethal toxicity, which, however, could be relevant for the safety aspects. These tests can be based on certain enzymatic activities or other specific targeted functions in the cell. Some examples are presented below.

When hepatic cell lines that have retained their ability to respond to foreign compounds by the induction of specific drug metabolising enzymes (cytochrome P450 variants, such as CYP1A1) are used, this enzymatic activity can be measured and used as an indicator of toxicity (Sanderson *et al*., 1996; Koistinen *et al*., 1998).

RNA-synthesis is a basic function of living cells, and its rate can be influenced by various factors. Measurement of the cellular RNA-synthesis rate after exposure to the test agent by following the incorporation of radio

labelled uridine provides an indication of the toxicity of the sample (Fauris *et al.*, 1985). The method, originally designed for human HeLa S_3 cells, is particularly useful for water samples, since the cell culture medium can be constituted using the test sample as a base. However, the test can also be used by simply diluting the test agent into the growth medium. The test is used as an official test for bottled drinking water in France.

An example of the use of a highly specialised cell type to study targeted toxic effects on the cellular metabolism is the recently developed boar spermatozoon motility inhibition test (Andersson *et al.*, 1998). The motility of a spermatozoon depends on the integrity of mitochondrial functions, and thus the action of toxins affecting the energy metabolism is very rapidly detected as reduction of motility. Other end points that can be measured are plasma membrane integrity, astrodome function, and total cellular ATP and NAD reduction. This test has been particularly useful in the detection of certain types of bacterial toxins from various environmental and food sources.

A bacterial assay, the Photobacterium test, based on the inhibition of light emission of a bioluminescent bacterium *Vibrio fisheri* (ISO, 1998), originally developed to test the toxicity of industrial effluents, gives an indication of the effects of the test agent on the oxidative metabolism of the cell. As a bacterial assay its advantages are rapidity and relatively low costs, but naturally the differences between bacterial and mammalian systems make the interpretation of the results even more difficult than with other short-term tests.

The availability of recombinant-DNA techniques has also made it possible to design cellular lines or microbial strains with highly specific properties for certain types of toxicity tests. In CALUX-test, designed to respond specifically to dioxins, a recombinant mouse cell line, in which the activity of a luciferase enzyme causing bioluminescence is under a control element responding to AhR-receptor. This receptor is specific to dioxin-like compounds, and when combined with a dioxin it activates a cascade in the cell, leading in this case to induction of luciferase, the activity of which can be measured (Amakura *et al.*, 2003). Another example is the use of recombinant yeast cells in which the β-galactosidase gene is under a control element containing an oestrogen receptor. When the hormone or hormone-like compound reacts with the receptor, the enzyme is activated and the activity can be measured spectrophotometrically (Routledge and Sumpter, 1996).

15.4.2 Genotoxicity tests

As already pointed out above, genotoxicity tests represent an exceptionally high level of standardisation and official recognition among the short-term toxicological tests. This reflects the fact that the target of most genotoxic agents, DNA, is similar in all various life forms, and an agent that affects DNA in a bacterium, is likely to do so in humans, too. Due to their well-established status good descriptions of the standard tests can be found in

various text books and laboratory manuals (e.g. Preston and Hoffman, 2001). The *in-vitro* genotoxicity tests can be roughly divided into point mutation tests, cytogenetic tests measuring chromosomal anomalies and tests for DNA damage and repair.

Point mutation tests

The best known point mutation test is the Ames Salmonella-assay or Ames test. The assay was developed already in early 70s and later updated by the introduction of novel tester strains (Maron and Ames, 1983). The test is based on a number of Salmonella strains that are histidine auxotrophs, or mutated so that they cannot synthesise histidine and consequently cannot grow without an external source of this amino acid. If the strains are exposed to a mutagenic agent that reverses the original mutation, a revertant colony emerges on a solid test medium devoid of external histidine. The number of these revertant colonies is the measure of the mutagenic potential of the test agent. A mammalian microsome fraction (usually isolated from induced rat liver) is routinely included in the test to mimic the mammalian drug metabolism and activation of certain mutagens.

Point mutation tests have been developed also for cultured mammalian cells (de Marini *et al*., 1989). These tests are based on the mutational resistance to otherwise cytotoxic agents (i.e. TK or HPRT mutations, conferring resistance to trifluorothymidine and 6-thioguanine, respectively). Compared to the Ames test and other bacterial assays they are, however, more laborious and time consuming.

Mammalian cytogenetic tests

In mammalian cytogenetic tests the changes in the chromosome number and structure (as seen in a typical metaphase plate), resulting from genotoxic action, are microscopically monitored (Galloway *et al*., 1994). The chromosome aberrations include gaps and breakages, deletions and chromatid exchanges. These kinds of analysis can be done both *in vitro* using cultured cells and *in vivo* by exposing experimental animals to the test agent and subsequently collecting suitable cells (peripheral lymphocytes, bone marrow cells) for analysis.

Because of the time and skills needed to analyse metaphase chromosomes, micronucleus tests are increasingly used as a simpler cytogenetic assay. The test is based on the presence of chromosomal fragments or whole chromosomes that have not been incorporated into a daughter nucleus at mitosis. Typically they can be seen as a stained body outside the cell nucleus in an interphase cell. The number of induced micronuclei is a measure of the genotoxic activity of the test agent (Miller *et al*., 1998). Also this test can be performed both *in vitro* using cell cultures and *in vivo* by exposing experimental animals to the test agent and subsequent harvesting and analysis of suitable cells. In *in-vivo* experiments the polychromatic lymphocytes are frequently used, since the micronuclei are naturally very easy to detect against the anucleate background (Hayashi *et al*., 2000).

Tests for DNA damage and repair
The uses of bacterial mutants that are deficient in DNA-repair functions and thus particularly sensitive to DNA-damaging agents are routinely used to screen potential mutagens in assays that usually are based on differential killing. If a repair-deficient microbial strain is more sensitive to the lethal effects of the test agent than its repair-proficient but otherwise isogenic control strain, one of the targets of the test agents is probably DNA (Hamasaki *et al*., 1992).

In mammalian cells the traditional assay for DNA repair has been the test of unscheduled DNA repair, in which the repair of damaged DNA is detected by autoradiography after incorporation of radio labelled nucleotides into the newly synthesised DNA at the site of the damage (Madle *et al*., 1994). A novel mammalian assay that measures the DNA damage directly is the so-called Comet assay or single-cell gel electrophoresis. The test is based on the fragmentation of the nuclear DNA as a result of genotoxic action. When a cell is subjected to electrophoresis after exposure to the test agent, the DNA fragments migrate in the electric field and can be seen as a 'comet tail' after staining with a fluorescent dye. The test can be applied to hepatocytes retaining their ability to metabolically activate mutagens (Uhl *et al*., 2000).

15.5 The application of short-term tests to paper and board

So far there have been relatively few published reports on the application of *in-vitro* toxicological tests to extracts of paper and board. The published results relate to the use of photobacterium test, RNA-synthesis inhibition assay or to a battery of different test systems. The outcomes of these trials are summarised below.

15.5.1 Paper and board extracts in photobacter assay

The photobacter test has been included in the purity and toxicity assays of fibre-based products (Sipiläinen-Malm *et al*., 1997; Jokinen *et al*., 2001). In the latter study samples of pulp and food contact board were systematically evaluated using water extracts obtained from homogenised material. According to the results the light intensity curves were highly repeatable the same samples giving consistently similar responses. However, regarding the toxicity, the results were difficult to interpret, because the samples often produced a pattern of variable photoemission induction and inhibition, depending on the concentration. The main practical result was that each board grade had a typical and highly stable response in the test, and this could be used as a quality control parameter for the stability of the production conditions.

15.5.2 RNA-synthesis inhibition caused by paper and board water extracts

Fauris *et al*. (1998) made a systematic survey on six paper and 15 board samples from different European countries using the RNA-synthesis inhibition test for the toxicity screening. The samples represented both recycled (ten samples) and virgin fibres, among the latter both chemical and mechanical pulps were represented. The recycled fibres represented the four categories according to the CEN 1994 standard (the category A represents raw materials consisting of unprinted or uncoloured paper, the categories B, C and D represent increasing use of printed or coloured raw materials, D being made totally from mixed paper and board of variable origin). In the analysis of water-soluble matter and in the preparation of water extracts CEN standard procedures were used. The substances that were analysed from the actual samples included total and organic chlorine, pentachlorophenol, total sulphur and nitrogen, formaldehyde, glyoxal, heavy metals Cd, Pb and Cr, bacterial endotoxins and aflatoxin. GC analysis of the Tenax-absorbed material from the samples was also performed.

According to the results the cytotoxicity of the samples ranged from very high (RNA synthesis rate 17% of the control) to non toxic (RNA-synthesis rate 94%). The same range of toxicities was found in samples representing both recycled products and virgin fibres. Among the latter, the toxic samples (RNA synthesis rate 60% or less of the control) represented mechanical pulps. The toxicities of the samples did not correlate with any individual analysed chemical component. Instead, there was a correlation between the toxicity and the numbers of peaks in the GC-chromatogram.

15.5.3 Extracts of recycled paper in a toxicological test battery

Binderup *et al*. (2002) have evaluated three different categories of recycled fibre-based food contact papers in a test battery consisting of a standard cytotoxicity test on human skin fibroblasts, Ames test for genotoxicity, recombinant yeast test for estrogenic activity and CALUX-test for the detection of dioxin-like activity. The recycled papers were compared to virgin fibre (paper A). Paper B represented a product consisting of 40% virgin fibre, 40% recycled material from unprinted newspaper cuttings and 20% de-inked paper from newspapers and magazines. Paper C and D were derived from newspapers and magazines, D being de-inked. The samples were extracted both with 99% ethanol and water following the relevant CEN-standards. The extracts were monitored for migrants using GC-IR-MS or GC-HRMS. The papers were also subjected for microbiological analyses (total aerobic bacteria, aerobic and anaerobic spore formers, *Bacillus cereus/thuringensis*, yeasts and moulds).

In the test applied ethanol extracts showed more toxicity than water extracts and also contained higher amount of material in the chemical analysis. Sample A produced least extractants, and was also least cytotoxic. Among the recycled

products the sample C was the most toxic in the cytotoxicity assay. None of the extracts gave a positive effect in the Ames test, and all were too cytotoxic to the recombinant yeast cell line to produce meaningful results. Signs of dioxin-like activity were detected in all ethanol extracts sample C showing the highest positive response, while with samples A and B this activity was non significant. With water extracts a weak positive response was observed with samples B, C and D.

15.5.4 Genotoxicity of ethanol extracts of selected paper and board samples

Ozaki *et al*. (2004) have studied both the chemical composition and genotoxicity of ethanol extracts of altogether 28 different paper products intended for food contact and representing both virgin and recycled materials. Altogether 20 different contaminants, including, among others, Michler's ketone, and related benzophenone derivatives, hydoxyphenylpropane compounds, chlorophenols and other chlorinated aromatics, were chemically analysed from the extracts. The genotoxicity test battery included a bacterial *rec*-assay (a differential killing assay using DNA-repair-proficient and repair-deficient *Bacillus subtilis* strains) and Comet assay (see page 340).

Not surprisingly, recycled papers contained both a wider variety and higher amounts of different chemicals than virgin products. In virgin products benzophenone and bisphenol A were typically detected, although at low amounts. Michler's ketone and related bisphenols were typical for recycled products. Of the 12 extracts of recycled products nine were positive in the rec-assay, while only three of the 16 extracts of virgin materials showed genotoxic activity in this test. Eight extracts positive in *rec*-assay were also subjected to Comet assay, in which six proved to be positive. Significantly, three of the positive extracts were from virgin material. When individual compounds identified in the extracts were tested as pure chemicals for genotoxicity and the observed activities were related with the actual concentrations detected in the extracts, it was concluded that the concentrations were too small to explain the genotoxicty of the samples, the actual gentoxic agent(s) remaining thus, so far, unknown.

15.6 Conclusions

There is a wide variety of different *in-vitro* tests that could be applied to extracts of food contact paper and board. However, there are few published reports of their use for this purpose, and at present it is not possible to form a consistent picture of their general applicability. The outcomes of the three most comprehensive studies published so far (Fauris *et al.*, 1998; Binderup *et al.*, 2002; Ozaki *et al*., 2004) illustrate this point. While all studies agree that the toxicity is correlated with the chemical complexity of the paper and

board and apparently not attributable to any single compound alone, the different samples and different test systems applied make these the three studies difficult to compare. While the studies show that *in-vitro* tests can be applied to paper and board products, they also show that application of different tests and testing conditions could lead to a rather different interpretation of the results.

As has been stated in section 15.3, CoE has recognised the potential value of toxicity tests as a method to ensure the safety of the food contact paper and board. In order to be of use for the consumers, industry and regulators, the proposed tests should be evaluated, standardised and validated. This requires that same paper and board samples would be tested simultaneously using different test systems in order to find out eventual correlations or discrepancies between the results obtained. Also the relevance of positive results should be carefully evaluated in the light of whether they really reflect any toxicological risks to consumers or whether they can be regarded as artefactual. As pointed out in section 15.3.1, proper and realistic sample preparation is also essential for toxicological testing to be meaningful.

In an ideal case the industry and regulators could have available a selection of validated short-term *in-vitro* tests with sufficient historical background for the safety assessment. This would reduce the need of extensive chemical analysis of the products and would circumvent the practical impossibility of applying traditional toxicological tests routinely to paper and board for food contact. The tests should have relatively broad toxicological endpoints so that many types of harmful compounds could be detected, but the test battery could be complemented with highly specialised tests for specific types of chemical or biological risks (special assays for microbial toxins, endocrine distruptors, hormone-like compounds, etc.). An additional demand, from a practical point of view, is that the set up and performance of at least some of the tests should be feasible in an industrial quality control laboratory, and that a large number of samples could be processed in a relatively short time. The use of the photobacterium test to screen the stability of the products and production conditions (see section 15.5.1 above) illustrates the point.

In order to answer those needs specified above, a collaborative effort (BIOSAFEPAPER) was undertaken in the fifth EU framework programme. In this project, coordinated by the University of Kuopio, Finland, nine European research institutes and 16 industrial partners aimed at establishing a test battery with relevant toxicological endpoints and allowing a decision-tree approach to ensure consumer safety. An important aspect of the undertaking was also the development of extraction procedures compatible with the tests and reflecting real-life conditions.

As the project was considered as a pre-normative research effort, special emphasis was devoted to the translation of the toxicological data to risk assessment, to the provision of a scientific basis for safety recommendations on fibre-based food contact materials and to the dissemination of the results to various stakeholders (industry, regulatory bodies, consumers). The project was presented in the 3rd International Symposium on Food Packaging (ILSI,

Europe, Barcelona 11/17/2004 – 11/19/2004), and a description of the results obtained by the mid-term evaluation of the project was given in the special issue of the journal *Food Additives and Contaminants* dedicated to the proceedings of the symposium (Severin *et al*., 2005). More detailed information on the project and its progress can be seen on the project homepage (http://www.uku.fi/biosafepaper/).

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16

Chemical migration from multi-layer packaging into food

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16.1 Introduction

Many types of flexible and rigid packaging used for the storage or transportation of food have a multi-layer structure. Such technology enables several materials to be combined in a laminated (bonded) structure so that the properties of the packaging are optimised for the specific end application. The structure of the packaging may be achieved using co-extrusion or by laminating films together using adhesives. Potential chemical migration and thus food safety relates to the choice of materials and additives used for the different layers and whether the food-contact surface layer acts as a barrier to migratory species from underlying materials. Most migration research has focused on the migration of species from laminating adhesives.

16.1.1 Materials used in multi-layer packaging

Typical substrates found in flexible multilayer packaging and reasons for their inclusion are summarised in Table 16.1. Individual component layers in flexible materials normally range in thickness from ~2.5 μm to ~125 μm, with the total thickness normally being less than 250 μm. Thicker laminates are normally considered to be sheet materials and are rigid in nature.

Polyamides and ethylene vinyl alcohol do not readily adhere to polyolefins, so a laminating adhesive or tie-layer is necessary to hold the co-extruded structure together. Other polymers such as polycarbonate (PC) or polyethylene terephthalate (PET) are also used as outer layers in multi-layer structures.

Table 16.1 Materials found in multilayer packaging

Material	Comments
Paperboard	Provides stiffness and barrier to light transmission.
Aluminium foil	Provides a barrier to oxygen, moisture and light.
Metallised film	Provides a barrier to oxygen and light.
Ethylene acrylic acid (EAA)	Provides good seal quality and adhesion. Often added to films to give puncture resistance.
Low-density polyethylene (LDPE)	Provides some barrier to moisture transmission. Used in sealing layers.
Linear low-density polyethylene (LLDPE)	Provides some barrier to moisture transmission. Used in sealing layers. Main benefits with films are for increased tear and puncture resistance.
Ethylene vinyl acetate (EVA)	Frequently used in sealing layers.
Polyamide (PA)	Provides tear and puncture resistance. Relatively low oxygen transmission.
Polypropylene (PP)	Provides barrier to moisture transmission and tear resistance to films.
Polystyrene (PS)	Provides stiffness.
Polyvinylidene chloride (PVDC)	Provides excellent barrier to oxygen and moisture transmission.
Ethylene vinyl alcohol (EVOH)	Provides excellent barrier to oxygen transmission when dry.

16.1.2 Composition and applications of multi-layer packaging

Most packaging applications can benefit from a multi-layer structure. Typical uses are described below.

Vacuum packaging

Films made with barrier polymers, e.g., polyamide (PA)/polyethylene (PE) laminates, ethylene vinyl acetate (EVA) copolymer/polyvinyl chloride (PVC)-polyvinylidene chloride (PVDC) copolymer laminates, and ionomer/PA/EVA laminate films are used for vacuum packaging, particularly products like red meat.

Modified atmosphere packaging

Most chilled prepared food is generally packaged under nitrogen/carbon dioxide gas with little or no oxygen present (modified atmosphere packaging). The packages for these products usually comprise high barrier laminate films, e.g., PVC-PVDC/low density polyethylene (LDPE) or polyethylene terephthalate (PET)/PVDC/LDPE), sealed onto rigid trays.

General purpose, dry packs

Packaging for crisps and other dry snacks typically utilise laminates with the structure; orientated polypropylene (OPP) ~18 μm)/print ~5 μm/adhesive ~2 μm/aluminium metallised OPP (~18 μm).

Long shelf life foods
Flexible multilayer packaging is used for retort processing of various food products. These 'retort pouches' are capable of preserving their contents for many months up to 1–2 years. A layer of aluminium foil normally provides the primary barrier properties of the packaging. A typical structure would be PET polyester (~18 μm)/print ~5 μm/adhesive 3–4 μm/aluminium foil (~20 μm)/adhesive 4–5 μm/cast PP ~30 μm.

Bag-in-box structures for liquid products
A laminate barrier film commonly used for the 'bag' component of bag-in-box structures is a three-ply laminate consisting of EVA (~50 μm)/metallised PET polyester (~325 μm)/EVA (~50 μm). Softening/melting temperatures of film components need to be considered for hot fill e.g. > 90 °C.

Dual microwave/oven-usable laminated packaging materials
Paperboard is available as a dual microwave/oven-usable material in the form of trays, plates and cartons. The paperboard is coated, typically with a fine particle size clay on one side to impart higher surface gloss and a surface for printing, along with an extrusion coating of a film made of PET or in some cases 4-methly pentane-1 copolymer (TPX). The plastic prevent fats and moisture entering the paperboard. Other plastics are extrusion coated onto paperboard, notably LDPE and PP. However, the maximum temperature resistance of LDPE is ~100 °C and ~ 130 °C for polypropylene, making such materials unsuitable for oven use. Polypropylene coated paperboard is used for microwaveable-only packages although there can be potential problems of softening of PP in 'hot spots'. Other dual microwave/oven-usable materials such as CPET are normally of a monolayer construction.

Milk cartons
A typical construction of a coated board milk carton would be (from outside to inside); LDPE/paperboard/ionomer/aluminium foil/ionomer/LDPE.

Boil in bag packaging
Boil in the bag food packaging is usually a laminate of LLDPE and polyamide 6. Adhesive lamination is normally used to bond these materials together.

Bottles
Bottle structures are often manufactured in PP with a thin core barrier layer of EVOH. The outer layers of PP protect the EVOH, which is sensitive to water, thus preventing a deterioration of its properties.

16.1.3 Converting and laminating processes and migration risk

Rolando (2000) has reviewed the adhesives, coatings and processes used for multilayer flexible packaging. The converting processes used, include printing,

laminating and finishing. When the printed surface is to be on the outside of the multilayer flexible package, a protective layer, or overprint varnish is often applied over the ink to prevent scuffing and to provide a gloss effect. Polymers/resins for print over-coatings include urethane, acrylic, acrylic copolymers, polyamide materials, nitrocellulose and vinyl based polymers. Reverse printed polypropylene is also commonly used. Laminating processes include adhesive or extrusion laminating.

Dry bonding with adhesives
The majority of adhesive laminations in multilayer flexible packaging are manufactured using the dry-bond process. In this technique, a liquid adhesive is applied to one substrate. The adhesive is then dried using hot air. This dried surface can be adhered to a second substrate using heat and pressure at a nip point. The adhesive formulations themselves represent a reactive chemistry (typically urethanes or acrylics) that is chosen to withstand the processing and storage/distribution environment of the filled product. The adhesives polymerise and/or cross-link during production of the laminated product.

Wet bonding with adhesives
This is similar to dry bonding, except that the solvent or water-based adhesive is dried after the material plies are joined. This normally means that one of the substrates must be paper. Wet bond adhesives are often dried via the use of a drying tunnel during the lamination process. Adhesives used in wet bond laminating for flexible packaging are generally based on vinyl acetate (VA), ethylene vinyl acetate (45% VA content), vinyl acetate acrylic (VAA), acrylic, styrene butadiene rubber (SBR) and polychloroprene. Often, wet bond adhesives are formulated with other polymers, adhesion promoters, thickeners, rheology modifiers, surfactants, defoamers and occasionally cross-linkers to enhance performance. The vast majority of wet bond adhesives are water based. Wet bond adhesives are typically used to laminate paper products to metallised films (typically metallised PET) for use in microwave and ovenable packaging.

Using cohesives
Cohesives are essentially contact adhesives. Cohesives are water borne products typically formulated with natural rubber latex polymers modified with other polymers such as acrylics and acetate polymers to yield the necessary peel and block resistant properties. Cohesives are used for a wide variety of applications on various paper products and films particularly for confectionery packaging.

Extrusion and co-extrusion lamination
Other processes for bonding of multi-layer structures include extrusion and co-extrusion lamination. Extrusion lamination involves extruding a thin layer

of plastic, typically low-density polyethylene (LDPE) or anhydride or acid modified polyolefin tie-layers, to bond together two layers of film, paper and/or foil. This can have the advantage over using adhesive lamination of adding substantial thickness to a multilayer lamination as well as contributing to the strength of the material.

PE can be considered as an extrudable adhesive. PE is used in extrusion lamination of paper to aluminium foil. The PE is extruded at very high temperatures. The melt is oxidised by contact with air creating polar functionality on the surface of the melt. This provides chemical bonding to the aluminium oxide on the surface of the foil. The low viscosity of the melt and its polar nature allow for good wetting on the paper and encapsulation of the paper fibres. Copolymers of ethylene and vinyl acetate are also useful extrudable adhesives and capable of bonding polyethylene to polyvinyl chloride. However, for more demanding applications, polyolefins with either acid or anhydride functionality are employed. Acids and anhydrides are particularly reactive and can create strong bonds to a number of different materials in extrusion processes.

Examples of acid modified polyolefins are the copolymers of ethylene with acrylic acid or methacrylic acid. Variations include the partially neutralised acid copolymers with metal ions (ionomers) or terpolymers of ethylene, an acid and an acrylate such as methyl acrylate or isobutyl acrylate. Acid-containing extrudable adhesives are widely used to bond to aluminium foil. Examples of anhydride-modified polyolefins include terpolymers of ethylene, maleic anhydride and acrylates such as ethyl acrylate or butyl acrylate and the anhydride-grafted polyolefins. Some typical applications and structures of a variety of multilayer materials with extruded polymer tie-layer adhesives, as described in Du-Pont trade literature, are detailed in Table 16.2.

16.2 Regulation and the use of multi-layer packaging

European Commission Directive 2002/72/EC, as amended, relating to plastic materials and articles intended to come into contact with foodstuffs covers multi-layer materials comprising two or more layers each consisting exclusively of plastics, which are bound together by means of adhesives or by any other means (EC 2002). The conventional overall migration limit (OML) and specific migration limits (SMLs) given in this Directive apply to these materials. Substances for which SMLs are given include aromatic amines, BADGE (2,2-bis(4-hydroxyphenyl)propane bis(2,3-epoxypropyl) ether) and bisphenol A, all of which may be present in laminating adhesives.

Multi-layer packaging which includes materials other than plastics, e.g., metals and paper, even if the food contact layer or part of the food contact layer consists of plastic, is currently not covered by any specific legislation. These multi-layer materials are regulated either by national legislation or by Article 3 of the Framework Regulation (EC 2004). Article 3 states that

Table 16.2 Typical multilayer structures using extruded polymer adhesives

Product	Packaging type	Structure
Apple sauce	Cup	PP/anhydride modified PP/EVOH/anhydride modified PP/PP
Cereal box liners	Film	HDPE/anhydride modified PE/EVOH/anhydride modified PE/peelable adhesive blend with ionomer or EVA
Condiments	Sachet	PET/LDPE/aluminium foil/ethylene acid copolymer resin
Cook-in poultry and ham	Film	Nylon/ethylene acid copolymer resin
Frozen seafood	Film around product with polystyrene tray	Ionomer/EVA
Cereal bar	Film wrap	Paper/LDPE/aluminium foil
Hot dogs	Wrap	Ionomer/anhydride modified PE/EVOH/anhydride modified PE/nylon
Jelly	Lidding film on PP cup	PET/primer/LDPE/ethylene acid copolymer resin/LDPE
Fruit juice	Box	Paper/LDPE/ethylene acid copolymer resin/ aluminium foil/ethylene acid copolymer resin/LDPE
Fruit juice	Carton	Board/LDPE/anhydride modified PE/nylon/ anhydride modified PE/LDPE
Ketchup	Squeeze tube	PP/anhydride modified PP/EVOH/anhydride modified PP/PP
Liquid packaging e.g., wine	Film	EVA/metallised PET/EVA
Noodle cups	Lidding film on foamed PS cup	Paper/primer/aluminium foil/LDPE/mixed polymer lidding sealant resin
Oil	Sachet	Ethylene acid copolymer resin/nylon
Peanuts	Bag	OPP/anhydride modified PE/HDPE/ionomer
Desserts	Cup	PS/anhydride modified EVA/EVOH/anhydride modified EVA/LDPE
Meat	Film	Nylon/anhydride modified EVA/ionomer

materials and articles in contact with food must not release constituents into foodstuffs in quantities that could endanger human health, bring about an unacceptable change in the composition or deteriorate the organoleptic characteristics of the foodstuffs. Possible changes to EU harmonised legislation that could deal specifically with multi-layered materials containing different materials are discussed in Chapter 3.

16.2.1 Laminating adhesives

Substances used in the manufacture of adhesives for laminated materials are not specifically listed in the Plastics Directive 2002/72/EC. Within the EU,

there is no legislation relating to adhesives other than that contained within Commission Regulation (EC) No 1895/2005 on the restriction of use of certain epoxy derivatives (EC 2005), namely BADGE, BFDGE (bis(hydroxyphenyl)methane bis(2,3-epoxypropyl)ethers) and NOGE novolac glycidyl ethers and their derivatives. Adhesives are of course covered by Article 3 of the Framework regulation 1935/2004 and are included on the list of groups of materials and articles, which may in due course be covered by EC specific measures.

National legislation on adhesives includes German BfR Recommendation XXVIII (Components of adhesives) and US FDA Title 21 Part 175 on adhesives. Part 175.105 deals with adhesives overall and Part 175.125 deals with pressure-sensitive adhesives. In addition, FDA Part 177.1390 permits the use of certain high temperature laminates that may be safely used for food contact at temperatures up to 275 °F, given that only the specified adhesives are used to bond the layers that make up the laminate. Part 177.1395 permits certain laminates that may be safely used at temperatures between 120 °F and 250 °F. However, it does not specify permitted adhesives.

16.3 Special considerations about multi-layer packaging and chemical migration

Apart from the possible migration of additives and low molecular weight oligomers into food from the food-contact plastic surface of multi-layer packaging, the main potential source of migration relates to the nature of the laminating adhesive employed. The use of polyurethane-based adhesives for multi-layer packaging is widespread. The technology employed has developed with time.

16.3.1 Solventless polyurethanes

Most laminators use solventless polyurethanes. The composition and comparative properties of typical products are summarised in Table 16.3.

First generation (introduced 1975)

First-generation solventless polyurethane adhesives are one-component isocyanate terminated prepolymers formed by the reaction of MDI (4,4′ methylene bis (phenyl isocyanate)), or other isocyanates with polyether and/or polyester polyols. One-component 100% solids adhesives rely on moisture from the air or substrates or from induced moisture misting during the converting process, to cure the adhesive via an isocyanate/water reaction and subsequent polyurea-polyurethane polymer formation. Typically the high viscosity of the adhesive is such as to require adhesive delivery equipment and application rollers heated from 65–80 °C for use. They have a high level

Table 16.3 Comparison of 100% solids film laminating technologies (Rolando 2000)

Property	One-part moisture cure adhesive	Two-part isocyanate (higher monomer)/ polyol	Two-part isocyanate prepolymer (low monomer)/polyol
General reference term	First-generation adhesive system	Second-generation adhesive system	Third- and fourth-generation adhesive systems
Chemistry	MDI-based isocyanate prepolymer, polyether and/or polyester polyols, reacts with water to form polyurea-polyurethane backbone	Often MDI-based isocyanate prepolymer (some are aliphatic isocyanate based), polyether and/or polyester polyols (some contain epoxy based materials), reaction forms polyurethane backbone	MDI-, TDI- and some aliphatic isocyanate-based prepolymers, polyether and/or polyester polyols, reaction forms polyurethane backbone
Viscosity at ambient temperature	Range from 5–100 Pa.s	Range from 2–10 Pa.s	Range from 10–100 Pa.s
Application temperature	Typically 65–80 °C	Typically 50–65 °C	Typically 65–80 °C
Adhesion properties	Good film to film Good film to foil Excellent film to paper	Excellent film to film Excellent film to foil Moderate film to paper	Excellent film to film Excellent film to foil Good film to paper
Resistance properties	Good to excellent	Excellent	Excellent
Cure rate	2–7 days	1–3 days	2–7 days
Handling requirements	Heated hoses, heated tanks, water misting for curing assistance	Generally none	Often heated hoses, heated tanks for third-generation products, occasionally water misting for curing assistance
Relative cost	Moderate	Moderate	High
General comments	Oldest technology	Most widely used technology	Rapidly gaining popularity due to reduced diamine extractable components

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of isocyanate monomer, typically 20–40%. One-component 100% solids adhesives are especially useful for laminating films or foils to paper products (moisture for the reaction coming from the paper).

Second-generation solventless polyurethane adhesives
Two-component second-generation adhesive systems are the most widely used of the 100% solids products. These two-part adhesives comprise an isocyanate terminated prepolymer based on the reaction product normally of MDI and polyols (polyether or polyester) in the presence of excess isocyanate, and a polyol (polyether or polyester based).

Part-reacting the isocyanate and mixing in additional polyol *in situ* has the effect of reducing the viscosity and ease of handling of the adhesive in comparison with first-generation single component systems. Both components are normally liquid at room temperature and therefore these types of products can be processed at lower temperatures. They still contain 20–40% monomer but are of much lower viscosity and thus adhere well to a variety of substrates and have rapid cure rates.

Third- and fourth-generation solventless adhesives
Concerns over diamine or other extractable components from first- and second-generation adhesives have led to the development of two-component adhesive systems (isocyanate-terminated prepolymer/polyol) with reduced free monomer, known as third-generation products in that they have very low free monomer content (<1% and occasionally <0.1%). Third-generation products are higher in viscosity compared to second-generation products and require higher temperatures for processing. Fourth-generation products are simply lower viscosity, third-generation products. Third- and fourth-generation products are slower curing and more expensive than second-generation products and often require a warm room at 30–50 °C for curing.

Components of solventless polyurethane adhesives
Aliphatic isocyanates used in polyurethane adhesives include:

- Bis-(4-isocyanatocyclohexyl) methane (H12MDI)
- Hexamethylene diisocyanate (HDI)
- HDI isocyanate prepolymers (addition products of HDI and a di- or higher functional polyol)
- Isophorone diisocyanate (IPDI)
- IPDI prepolymers (addition products of an IPDI and a di- or higher functional polyol).

Aromatic isocyanates include:

- 4,4′ Methylene bis (phenyl isocyanate), MDI. Both ‘pure MDI’ – the 4,4′ MDI isomer – as well as mixtures with 2,4′ MDI and 2,2′ MDI isomers are used. The level of the isomer affects melting point and storage stability. For example, the melting point of pure 4,4′ MDI is 47 °C; this drops to ~18 °C in the presence of 50% 2,4′ isomer (Sood *et al*. 1997)

- MDI polyester isocyanate prepolymers (addition products of MDI and a di- or higher functional polyester polyol)
- MDI polyether isocyanate prepolymers (addition products of an MDI and a di- or higher functional polyether polyol)
- toluene diisocyanate (TDI) (both 2,4- and 2,6-toluene diisocyanates are used alone or in different mix ratios)
- TDI polyester prepolymers (addition products of TDI and di- or higher functional polyester polyols)
- TDI polyether prepolymers (addition products of TDI and di- or higher functional polyether polyols)
- 1,3-bis-isocyanato-1-methylene ethylene benzene (TMXDI).

Migration of amines from the use of isocyanates

If the elapsed time between lamination and food contact is too short, unreacted monomeric isocyanate can be available to react with water to form low molecular weight amines. The presence of aromatic amines can be an issue with the use of MDI or toluene diisocyanate (TDI) containing isocyanate systems. Often aromatic isocyanates are selected to obtain good adhesion under moist and low temperature conditions. Aromatic isocyanates are also cheaper than aliphatic systems. The crystallinity of the film can reduce permeation rates of monomeric isocyanates into adjacent film layers. Other factors that can influence the rate/degree of cure (isocyanate reaction) include the following:

1. Humidity at both the laminating and curing stages.
2. Temperature – the isocyanate reaction is very slow at temperatures below 10 °C and probably stops below 5 °C. Curing at 30 °C is faster than at 20 °C.
3. The presence of a polyamide in the laminate as it can compete for water with the adhesive.
4. Curing times with high barrier laminates containing aluminium foil may also be prolonged.
5. High adhesive coating weights.
6. Poor control over mixing ratios.

Migration of unreacted polyurethane polyol components can also occur.

Polyester polyols

The polyester type polyols used in polyurethane laminating adhesives are produced by the direct esterification of polyfunctional carboxylic acids and glycols. Polyester polyols provide the soft segment in polyurethane products giving the adhesive flexibility. Ester groups of the polyol also contribute to adhesion. Polyester polyols provide limited wetting and adhesion of olefinic surfaces with amide slip additives (in contrast to polyether polyols). Typical examples include adipic acid, caprolactone, maleic acid and isophthalic based polyester polyols.

Polyether polyols
Polyether polyols are usually produced by the polymerisation of ethylene or propylene oxide in the presence of a polyfunctional alcohol or amine as an initiator. Copolymers are also produced from mixtures of ethylene oxide and propylene oxide with di and tri –OH functionality. Polytetramethylene ether glycols (PTMEG) from tetrahydrofurans are also found.

Chain extenders/cross-linkers

Alcohol based
1,4-Butane diol is an important chain extender for polyurethanes. 1,4 Cyclohexane dimethanol is also used.

Amine based
Primary and secondary di- and polyamines are used as chain extenders and cross-linkers. Aromatic amines are more reactive than aliphatic ones.

Epoxy based
Bisphenol A epoxy based and related materials are used in two-part urethane epoxy adhesives.

Adhesion to aluminium
Silanes are sometimes used to improve adhesion to metals. Phosphoric epoxy chelating agents are used to protect against attack by acids.

Catalysts
Tin compounds such as dibutyl tin dilaurate at ~30–40 ppm are found in polyester polyols. Phosphoric acid can be found in polyols for control of pH and side reactions.

Antioxidants
Hindered phenol antioxidants are commonly used in polyols.

16.3.2 Systems applied from solution in organic solvents (solvent borne) and dried prior to lamination

Solvent-borne laminating adhesives are particularly utilised for demanding applications such as boil in bag or retortable packaging. There are two main types of chemistry used for solvent borne systems for dry bond flexible packaging laminating applications: one-component isocyanate based moisture-curing adhesives and two-component polyol and isocyanate-based adhesives. The use of solvents enables higher molecular weight polyols and isocyanate prepolymers to be employed, (in comparison with solventless systems), thus improving the adhesive properties of the laminate structure. However, to take account of solvent release issues, substitution by liquid (100% solids) occurs in many cases.

One-component solvent-based adhesive systems employ a wide range of polyols (polyester and/or polyether based with a functionality of two or greater to induce polymer formation where desired). They are reacted with an isocyanate (typically MDI) to form an isocyanate-terminated prepolymer typically having an isocyanate (NCO) value from 5–15%. The resulting isocyanate-terminated prepolymer is diluted in a non-hydroxyl containing solvent such as ethyl acetate and supplied to a converting operation in this form. The adhesive when applied must react with water in a similar way to solvent-free systems to form an amine-terminated intermediate that can further react with the isocyanate-terminated polymer. Typical cure rates range from 2–7 days. In general, one-component moisture-curing solvent-borne adhesives are used in lower-performing end-use applications, which include snack foods, dry goods, film overlay and decorative bag applications.

Two-component systems comprise a polyol (typically polyester but sometimes polyether based) reacting with an isocyanate-based material (typically based on MDI, TDI, HMDI or IPDI). The polyol component, if a polyether, is typically based on polypropylene glycol and/or polyethylene glycol, and if polyester-based, is typically based on diol adipates (and higher functionality polyols) often copolymerised with a range of dibasic acids. The isocyanate component is a prepolymer formed by the reaction of the chosen diisocyanate and polyol(s) to form an isocyanate-terminated species. Molecular weights of both the polyol and isocyanate prepolymers can vary depending on desired viscosities, but generally range from 500 to 5000 g/mole.

The polyols can have a functionality of two or greater. Higher functionality results in increased viscosities (or reduced molecular weights) and increased cross-link density. Likewise, the isocyanate can have a functionality of two or greater. Epoxy systems have been incorporated into the polyol component to offer dual curing mechanisms and increased product-resistance properties.

The two-component polyol and isocyanate solvent-borne laminating adhesive systems are used for medium- and higher-performing applications which include meat and cheese packaging, boilable packaging, retortable packaging, lidding and other applications requiring a higher degree of moisture and chemical resistance properties.

16.3.3 Systems applied from aqueous solution (water borne) and dried prior to lamination

The main type of water-borne, dry bond laminating adhesives used for laminating food contact materials are the epoxy urethane adhesives. As there are no reactive isocyanate groups in epoxy urethane adhesives, there is no risk of the generation of aromatic amines during use. However, BADGE (bisphenol-A diglycidyl ether) and bisphenol A can be potential migrants from epoxy urethanes.

A typical formulation of a two-component epoxy urethane adhesive would include 100 parts of a water dispersed polyurethane resin with carboxylic

groups on the polymer chain and amine terminal groups. An amine such as aminoethylethanolamine and five parts of a bisphenol A glycidyl ether epoxy resin (average molecular weight <700) may be included. These two components are mixed together and applied to the film before drying and film lamination.

16.3.4 Extruded polymer adhesives

The migration risk from extruded polymer adhesives is considered to be low (Table 16.4) (Barber *et al*. 2003).

16.3.5 Energy curable (UV and electron beam)

Energy curable adhesives for use in flexible packaging based on ultraviolet or electron beam irradiation are in their infancy. The potential use of these types of adhesive is promising due to the fast cure rate (essentially full cure on irradiation and hence low risk of migratory components) and the potentially

Table 16.4 Migration risk assessment of extruded polymer adhesives

Typical polymers	Potential migrants	Migration risk	Hazard assessment
Polyethylene	Hydrocarbons	Low	Low
Air oxidised polyethylene	Aliphatic aldehydes and ketones (detected by odour)	Low–medium	Medium
Ethylene vinyl acetate copolymers	Vinyl acetate monomer (rarely detected in quantity)	Low	Low SML = 12 mg/kg
Copolymer of ethylene with acrylic acid or methacrylic acid	Acrylic acid Methacrylic acid	Low	Low Neither is restricted by SML
Partially neutralised acid copolymers with metal ions (ionomers)	As above plus non-toxic ions, e.g., zinc, calcium	Low	Low
Terpolymers of ethylene, an acid and an acrylate such as methyl acrylate or isobutyl acrylate	Non-reacted free acid and acrylate esters	Low	All generally not restricted by SML
Anhydride modified polyolefin*	Maleic acid (SML 30 mg/kg)	Low	Low
Terpolymers of ethylene maleic anhydride and ethyl acrylate or butyl acrylate	Maleic acid and acrylate esters	Low	Low

*For polypropylene barrier containers incorporating a maleic anhydride grafted polypropylene tie-layer, normally, no migration (as maleic acid) is seen with distilled water over ten days at 40 °C.

increased line speeds. However, the high equipment and installation costs are currently restricting growth of these types of laminating adhesives.

16.4 Published data on migration from laminating adhesives

16.4.1 Aromatic amines

Lawson (1994) examined levels of aromatic amine migration from a number of laminate samples. Specially prepared laminate pouches containing distilled water were boiled for one hour and tested for primary aromatic amine (PAA) migration using a diazotisation procedure. Olive oil migration data at the same temperature was also obtained. Results are shown in Table 16.5 (detection limit 0.3 μg dm^{-2}). These results, if expressed using the conventional surface area to volume ratio of 6 dm^2 per kg of food, would range between 3 and 11.4 μg/litre (assuming a density of 1).

Danish aromatic amine survey

In August 2001, following reports in the Danish press about the possible contamination of packaged foods with PAA, the Danish Veterinary and Food Administration instituted a pilot study (Trier and Petersen 2001a) and also a more detailed examination of the potential contamination of food with PAA from laminated packaging (Trier and Petersen 2001b). In the pilot study, no detectable migration of PAA was found from any of the samples analysed. In the more detailed examination, both a quick test (as used in the pilot study) and also standard migration testing using appropriate test simulants were undertaken. The PAA migration from 33 samples was analysed in the more detailed study. In only two samples, the PAA migration was found to be higher than the detection limit of the accredited method of 1.1 μg aniline/kg

Table 16.5 Aromatic amine migration from polyurethane adhesives (Lawson 1994)

Laminate	Migration μg dm^{-2} as MDA
Distilled water	
50 μm LLDPE/50 μm HDPE*	0.70 ± 0.14
15 μm LLDPE/15 μm HDPE*	0.91 ± 0.21
15 μm HDPE/15 μm LLDPE*	1.03 ± 0.47
50 μm Nylon/50 μm LLDPE*	1.10 ± 0.20
50 μm Nylon/15 μm LLDPE*	0.49 ± 0.13
Retail	0.69 ± 0.24
Olive oil	
50 μm Nylon/15 μm LLDPE*	1.90 ± 0.20
50 μm Nylon/50 μm LLDPE*	1.53 ± 0.43

* Side in contact with simulant

food simulant (calculated using the convention of 6 dm^2 of food contact material per one kg of packaged foodstuff). A further eight samples showed migration above an 'internal' detection limit of 0.2 μg aniline/kg in acetic acid tests and 0.5 μg aniline/kg in distilled water. The detection of PAA migration was thought to probably reflect that the samples had been taken for analysis shortly after the lamination process when compared to the pilot study. However, in all migration tests performed, the resulting PAA migration was far below the current EU migration limit of 20 μg aniline/kg food simulant (EC 2002).

Co-authors of these studies have recently published a method for the specific determination of 20 primary aromatic amines in aqueous food simulants by liquid chromatography–electrospray ionisation-tandem mass spectrometry (Mortensen *et al*. 2005).

16.4.2 Migration of polyol components

Lawson *et al*. (2000) examined the migration of constituents from solvent-free adhesives used to bond 12 μm PET film to 45 μm LDPE. The technique of MALDI-MS, a soft ionisation technique capable of looking at sample mixtures over a mass range of 150–500,000 Da without prior separation, was employed. The adhesives studied were based on a solution of mixed isomers of MDI in polymeric MDI with either polyether or polyester-based polyols. Pouch testing of cured laminates with distilled water was undertaken (two hours at 70 °C) with the LDPE surface in contact with the water.

Migration of unreacted polyol components through the polyethylene for the polyether-based laminate was observed. Although an excess of isocyanate was present, diffusion of polyol components into the polyethylene prior to reaction with isocyanate was postulated to explain the migration. Cyclic oligomers from the polyol starting materials were identified as the main migrants from the polyester-based adhesive.

16.4.3 Research for the UK Food Standards Agency

Rapra Technology Ltd has undertaken a detailed investigation into the migration of species from different types of adhesives used with laminated multi-layer materials (Barber *et al*., 2003). Migration of aromatic amines, BADGE, bisphenol A and polyols were examined. A description of the samples used and a brief summary of some of the results obtained from this analytical work are given below.

Solventless MDI based adhesive systems

Sample 1 – oxygen barrier packaging used for lidding films for meat and cheese
20 μm orientated polypropylene
Laminating adhesive (coating weight =1.60 g/m^2)
40 μm LLDPE/Tie/EVOH/Tie/LLDPE coextrusion (food-contact surface).

Sample 2 – lidding film packaging for meat or cheese

12 μm PET(PVDC coated on inner surface)
Laminating adhesive (coating weight = 1.65 g/m^2)
38 μm LLDPE (food-contact surface).

Sample 3 – used for packaging rice and cereals in vertical form fill and seal packs

12 μm PET
Laminating adhesive ~2 g/m^2
70 μm LLDPE (food-contact surface).

The laminating adhesive for Samples 1–3 was a 100:25 mix of an isocyanate terminated polyurethane prepolymer based upon polypropylene glycol and MDI (amount of free monomer approximately 25%) and a tri-functional polypropylene glycol with a molecular weight of approximately 450.

Sample 4 – packaging for washed lettuce

15 μm OPP
Laminating adhesive (two-component solvent-free laminating adhesive: 100 parts of MDI based prepolymer, 35–50% free monomer)
20 μm CPP (food contact surface).

Sample 5 – packaging for smoked fish

12 μm PET
PVDC coating
Ink
Laminating adhesive (solvent-based MDI-based polyether polyurethane 2.5 g/m^2 containing 1–5% 4,4′ MDI)
70 μm polyethylene (food contact surface).

Sample 6 – packaging for sweets
19 μm polypropylene
Ink
Laminating adhesive – water based epoxy amine, 2.5 g/m^2
(100 parts polyurethane resin including some (<2%) aminoethylethanolamine, 5 parts epoxy resin, average MW <700)
Metallisation
20 μm polypropylene
Laminating adhesive 2.5 g/m^2 (solvent-based two-part MDI polyester polyurethane), resin solution 1 containing 1–5% 4,4′ MDI, solution 2 including 3-aminopropyltriethoxysilane
38 μm polyethylene (food contact surface).

Solventless epoxy amine laminates

Sample 7 – packaging for crispbread

Clay coated paper
Laminating adhesive – epoxy amine (polyurethane backbone)
20 μm polypropylene (food contact surface).

Sample 8 – packaging for wrapped sweets

25 μm polypropylene
Ink
Laminating adhesive (water based epoxy amine) 2.5 g/m^2
100 parts polyurethane resin including some (<2%) aminoethylethanolamine
5 parts epoxy resin, average MW <700
50 μm polyethylene (food contact surface).

IPDI based solventless adhesives

Sample 9 PET/adhesive/PA/adhesive/PP (microwaveable pouch)

12 μm PET
Ink
Laminating adhesive (IPDI based aliphatic) 4 g/m^2
Silicon oxide coating
15 μm polyamide
Laminating adhesive (IPDI based aliphatic) 4 g/m^2
70 μm polypropylene (food contact surface).

Migration of MDA from Samples 1–6
Migration was studied using the food simulant 3% acetic acid for two hours at 70 °C. Acetic acid is generally considered to be the worst-case simulant for primary aromatic amines. A standard photometric procedure involving diazotisation in hydrochloric acid solution, coupling with N-(1-naphthyl)-ethylenediamine dihydrochloride, concentration using solid phase extraction columns and colorimetric determination at 550 nm was first used to measure migration. Test pouches were prepared of dimensions 200 mm × 100 mm filled with 100 ml of test simulant prior to sealing with minimal air space. Known deficiencies of this colorimetric method include possible interference from other extracted components and variation in the maximum wavelength of absorption of different amine complexes in comparison with the 550 nm stated in the method (wavelength for the aniline standards). The 2,4′ and 2,2′ MDA isomers also give a lower percentage response than the more reactive 4,4′ isomer. Later in the studies the technique of liquid chromatography-mass spectroscopy (LC-MS) was employed. Levels of extracted MDA depended on the length of time following lamination and the sample storage condition and environment as demonstrated for Samples 3 and 4 in Tables 16.6 and 16.7.

Table 16.6 PAA results obtained on Sample 3 (colorimetric method)

Test material	Maximum colour absorbance	PAA migration µg/100 ml/4 dm^2 as aniline hydrochloride (as 4,4′ MDA)	PAA migration µg aniline/kg (6 dm^2/kg)	PAA migration µg 4,4′ MDA/kg (6 dm^2/kg)
4 days after lamination, 10 layers into roll	0.112	3.1 (2.4)	3.3	3.6
4 days, 10 layers into roll (duplicate)	0.119	3.3 (2.5)	3.6	3.8
7 days, 10 layers into roll	0.065	1.8 (1.2)	1.9	1.8
10 days, 1 layer into roll	0.079	2.2 (1.6)	2.4	2.4
14 days, outer layer	0.071	2.0 (1.4)	2.2	2.0
14 days, 2 layers into roll	0.058	1.6 (1.1)	1.7	1.6
14 days, 10 layers into roll	0.068	1.9 (1.3)	2.0	2.0
23 days, 10 layers into roll	0.073	2.0 (1.5)	2.2	2.2

Table 16.7 PAA results obtained on Sample 4 (colorimetric method)

Test material	Maximum colour absorbance	PAA migration µg/100 ml/4 dm^2 as aniline hydrochloride (as 4,4′ MDA)	PAA migration µg aniline/kg (6 dm^2/kg)	PAA migration µg 4,4′ MDA/kg (6 dm^2/kg)
3 days after lamination, 10 layers into roll	0.125	3.4 (2.6)	3.7	3.9
8 days after lamination, 10 layers into roll	0.054	1.5 (1.0)	1.6	1.5

Note that Sample 3 had a 70 µm LLDPE layer between the acetic acid and the laminating adhesive. Sample 4 had a 20 µm layer of cast polypropylene between the simulant and adhesive. Both Samples 3 and 4 were provided to Rapra on a roll, which was stored at ambient temperature in the laboratory prior to removal of material for testing.

The primary aromatic amine (PAA) migration was determined using both aniline hydrochloride and 4,4′ MDA standards. Results are expressed as µg/100 ml/4 dm^2 as aniline hydrochloride, as µg/100 ml/4 dm^2 as MDA (using

the MDA calibration), as µg aniline/kg (using the 6 dm^2/kg convention) and as µg MDA/kg (using the 6 dm^2/kg convention and the MDA colorimetric data). Data can be viewed against the EU migration limit for PAA of 20 µg/kg expressed as aniline (EC 2002).

Examination of MDA migration using LC-MS
The following conditions were employed for the examination of spiked solutions and sample extracts.

Instrument:		Agilent 1100 LC/MSD model SL
Column:		Aqua 3 µm C18 125A, 150 × 2.0 mm, (Phenomenex) 30 °C
Flow rate:		0.5 ml/minute
Mobile phase	A:	Acetonitrile
	B:	5 mM ammonium acetate in distilled water
Timetable:		Time %B (minutes) 0 92 5 89 20 10
MSD		Electrospray $+^{ve}$* SIM ion 199 Fragmentor voltage: 80 V Gas temperature: 350 °C Drying gas: 10 l/min Nebuliser pressure: 40 psig Capillary voltage 4000 V

A cation exchange clean-up of the method was employed in the examination of samples. Amines were eluted from the clean-up column using 70 vol% 0.1M sodium citrate buffer (pH 2.5) + 30 vol% methanol. This solution was then injected into the LC-MS. A slow drop-off in MS response was observed using this procedure. In later studies, delaying the introduction of the LC mobile phase into the mass spectrometer for three minutes (i.e. not introducing any ionic non-retained components) overcame this problem.

Levels of specific migration of the different MDA isomers from Sample 3 are detailed in Table 16.8. For Samples 1 and 2 and Samples 5 and 6, when tested several months after lamination, levels of MDA migration, calculated on the basis of 6 dm^2 of film being in contact with 1 kg of food, were <1 µg/kg.

*Better ionisation of amines was found using electrospray (+ve ion) compared to APCI ionisation.

Table 16.8 MDA migration from Sample 3 (two hours at 70 °C)

Sample	4,4′ MDA µg/litre	2,4′ MDA µg/litre	2,2′ MDA µg/litre	Total MDA isomers µg/100 ml/4 dm^2
4 days, 10 layers deep	10.1	12.0	0.3	2.24
8 days, 3 layers deep	6.6	7.3	0.07	1.40
10 days, 1 layers deep	0.9	1.2	0.06	0.21
14 days, 2 layers deep	7.3	9.3	<0.06	1.67
14 days, 10 layers deep	6.8	8.0	<0.06	1.49

Examination of extractables from Samples 1 and 2 into food simulants using GC-MS

In addition to examining aromatic amine migration from Samples 1 and 2 using the colorimetric procedure, two-hour pouch extracts at 70 °C were also examined by GC-MS. Water and 3% acetic acid test solutions from pouch tests undertaken three days after lamination were examined by GC-MS. The pH of 50 ml of test solutions was adjusted to alkaline by adding 0.1 molar sodium hydroxide solution. Resulting solutions were shaken with 5 ml of dichloromethane in a separating funnel and the layers allowed to separate. The dichloromethane layer was then transferred to a GC-MS vial and examined by GC-MS under the following conditions.

Instrument:	Agilent 6890 GC with autosampler and 5973 mass-selective detector
Column:	SGE BPX50 (50% phenyl polydimethylsiloxane)
Column length:	30.0 metres
Nominal diameter:	250 µm
Film thickness:	0.25 µm
Temperature programme:	40 °C for two minutes and then 20 °C per minute to 300 °C (15 minutes run time)
Ionisation:	70 eV electron impact.

No MDA was detected in the water or 3% acetic acid extract solutions from either Sample 1 or Sample 2 in the three-day samples using reverse searching (looking for ions at m/z 198, 106 and 182). However, two species could be identified in the extracts.

Bisphenol A (chemically similar to MDA but having –OH groups rather than amine groups) was identified in the water and 3% acetic extracts from Sample 2. Bisphenol A was not detected in the extracts from Sample 1. Infra-red transmission spectra recorded through Samples 1 and 2 showed that the MDI isocyanate was slower to react in Sample 2 and so the bisphenol A could possibly relate to the laminating adhesive. As a result, LC-MS tests were undertaken later in the research, on extracts from Sample 3 (laminated with the same adhesive) specifically looking for bisphenol A – none was detected. Tri-ethyl phosphate, thought to be used as a cure catalyst, was identified in the extracts from both Sample 1 and Sample 2.

Examination of migration of BADGE and its derivatives from Samples 7 and 8

LC-MS was used for the determination of BADGE and its derivatives. The chemical structure of BADGE is shown in Fig. 16.1.

The following LC-MS conditions were employed:

Instrument:	Agilent 1100 LC/MSD model SL	
Injection volume:	5 µl	
Flow rate:	0.5 ml/min	
Pump sequence	A: 50/50 methanol/water (v/v) (some initial runs 75/25 methanol water) B: 50/50 ethyl acetate/acetonitrile (v/v) 90% to 0% A, via linear gradient over 25 minutes held for five minutes, reverting to 90% A at 30 minutes. Total run time 30 minutes	
Column:	Phenomenex Aqua 3 µm C18, 125 A, 150 × 2.00 mm	
Column temp:	50 °C	
APCI $-^{ve}$:	SIM m/z 211 (fragmentor voltage of 290 volts)	
Spray chamber:	Gas temperature	350 °C
	Vaporiser	400 °C
	Drying gas	4.0 l/min
	Nebuliser pressure	35 psig

Using a high fragmentor voltage of 290 V, BADGE and its derivatives were detected using specific ion monitoring at m/z 211 (Fig. 16.2). Some differences in sensitivity were observed as shown in Fig. 16.3.

Samples 7 and 8 laminated with epoxy amine adhesives were examined for BADGE migration. In order to overcome matrix ionisation effects,

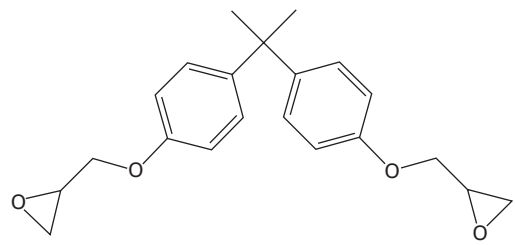

Fig. 16.1 Chemical structure of BADGE.

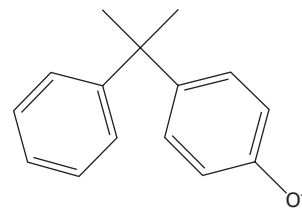

Fig. 16.2 BADGE ion examined (exact mass 211.12).

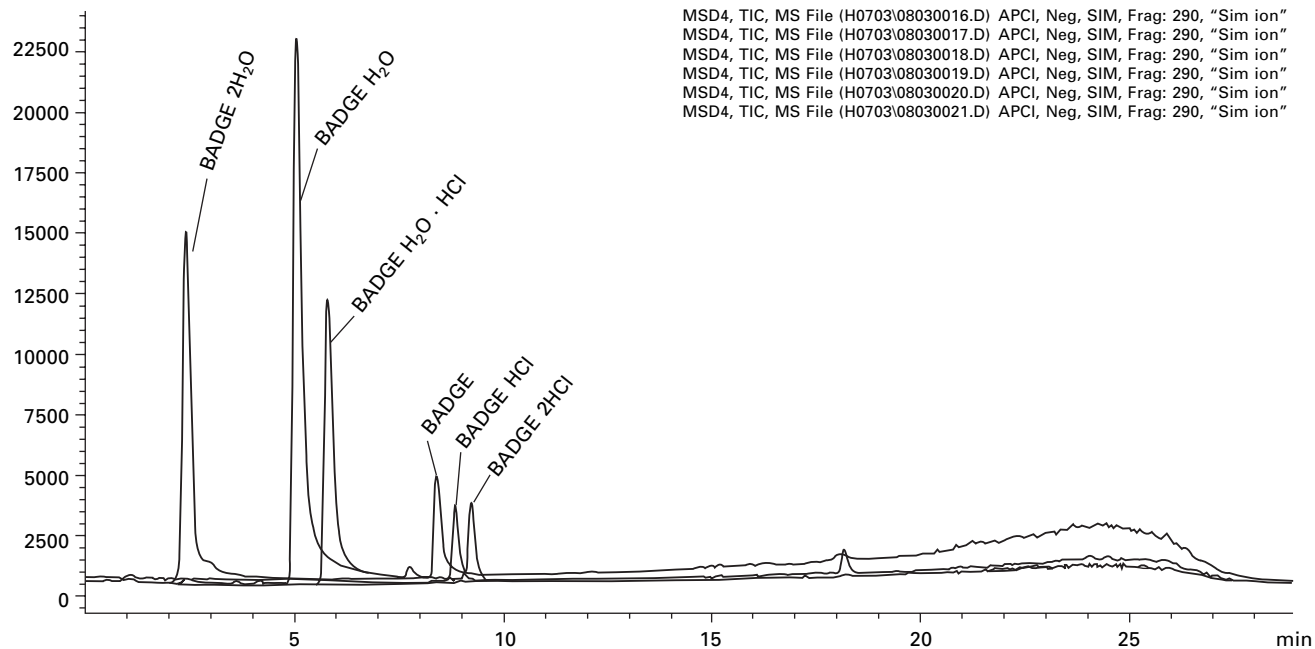

Fig. 16.3 BADGE derivatives at 0.5 mg/kg in acetonitrile showing the difference in response for the various derivatives (SIM 211 ion).

quantifications were made against standards prepared by spiking each food simulant type. BADGE and its derivatives were extracted from olive oil test simulant with acetonitrile. Aqueous simulants were diluted 1:1 with acetonitrile prior to examination.

Some BADGE migration into olive oil was found. Hydrolysed BADGE was found in the aqueous simulants. Levels of migration are detailed in Table 16.9. BADGE HCl and BADGE 2HCl were not detected.

Examination of polyol migration from test samples
Samples 5, 6, 8 and 9 in the form of pouches were subjected to ten-day testing at 40 °C with the food simulants distilled water, 3% acetic acid, 10% ethanol and olive oil. The three aqueous simulant extracts (1 ml of each) were diluted 1:1 with acetonitrile prior to analysis. Olive oil extracts (5 g) were shaken and extracted with 3 ml of acetonitrile prior to examination, using the same conditions. No evidence was found from the total ion traces to suggest migration of any unreacted polyols under the ten days at 40 °C test condition.

16.5 Improving the safety of multi-layer packaging with regard to chemical migration

For those products laminated using reactive polyurethane based adhesives, suppliers have been aware for many years of the potential migration of amines formed by the reaction of unreacted isocyanate monomer with water and recommend that laminated products are given time to fully cure before they are used in contact with food. Adhesives have been developed that contain low levels of monomeric aromatic isocyanates, in order to reduce any potential migration of aromatic amines into food in critical applications. Such adhesives are not considered to present any notable amine migration hazard unless used in high-temperature applications.

FDA regulations only allow the use of aliphatic isocyanates in laminating adhesives for high-temperature applications. (Cured aromatic systems can decompose to regenerate isocyanate and thus form aromatic amines at retortable or boiling water temperatures.) Discussions with a number of UK packaging producers revealed that they are aware of the need to use adhesive systems

Table 16.9 BADGE migration expressed as µg/kg (assuming 6 dm^2 per 1 kg of food)

	Olive oil BADGE	Distilled water BADGE $2H_2O$	10% ethanol BADGE $2H_2O$	3% acetic acid BADGE $2H_2O$
Sample 7 10 days at 40 °C	15	1.95	1.2	2.25
Sample 8 2 hours at 70 °C	19.5	Not examined under this test condition		
Sample 8 10 days at 40 °C	15	1.05	0.6	3.0

in compliance with FDA for high-temperature applications. The studies undertaken in the Rapra research supported the conclusion that this is done in practice.

Laminating adhesive is always behind a barrier film layer. The thickness of this layer, the levels of crystallinity as well as polymer type all influence the migration rates of adhesive components through this layer. The rate of permeation of food or food simulant into the packaging is also controlled by the nature of the food contact layer. Because of the presence of this barrier layer between the adhesive and the food, it is only low molecular weight mobile chemical species that have the potential to contaminate food.

The overall conclusion from the Rapra studies was that 'Potential migration of laminating adhesive components is only likely to be of concern if an inappropriate type of adhesive has been selected for a particular application. This assumes that correct adhesive mixing and curing procedures are used'.

16.6 Sources of further information and advice

Euroflex, the European forum for the flexible packaging industry, is a useful source of further information (http://www.flexpack-europe.org).

The Wiley *Encyclopaedia of Packaging Technology*, 2nd edition, 1997, editors A. Brody and K. Marsh (ISBN 0-471-06397-5) is a comprehensive textbook on packaging.

The Rapra review report on flexible packaging (Rolando, 2000), provides a large amount of information on lamination and the adhesives used in multi-layer packaging.

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17

Chemical migration from active and intelligent packaging materials into food

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17.1 Introduction

Food safety is the major issue in consumer perception of foodstuffs. Quality, price, appearance are important but at the end they can come in second place with consumers. Often a consumer is not able to judge the safety of the food at the stage of purchase and he mainly relies on the information provided on the product and the apparent reliability of the supplier. To avoid accidents of food deterioration, chemical or microbiological, the food producer will do the best possible. There are many protocols for producing safe foods, e.g., by maintaining high standards of hygiene and proper preservation. Food manufacturers also have a strong interest to market foods with an attractive appearance, good taste and smell. Of course all these properties start with the quality of the food itself. Packaging is a tool to protect the food from the environment and enables distribution of the food. Today packaging materials are available in a wide variety and are often developed for specific foods.

In spite of all these precautions a number of foods remain perishable to deterioration by microbial growth or chemical reactions. The sensory appearance of the food may be improved by adding or removing food constituents from the packaged food. 'Active packaging' materials are available for various applications that may solve some of the problems found in food production and distribution and they may extend the shelf life or improve the appearance of foodstuffs.

Producers, retailers and consumers are often interested in reliable information on the quality of the food. Information on composition is often printed on the outside of the package as well as a 'use by' or 'best before' date. However, this does not provide information about whether the food has been contaminated

microbiologically or whether a modified atmosphere package has failed, or whether the storage temperature was appropriate during its shelf life. New developments usually referred to as 'intelligent packaging' or 'smart packaging', are capable of providing information on the quality of the packaged food. This information may be assessable by some or all the stakeholders in the supply and consumption chain. In this chapter 'active and intelligent packaging' refers to any form, shape or size of active and intelligent, materials and articles. Where 'packaging' is used this is not restricted to packaging materials used only to wrap the food.

The benefits of active and intelligent packaging are evident, but there may also be some risks, such as unacceptable migration, misleading the consumer or providing incorrect information. Because of the potential risks and because individual countries in the European Community have not drafted any regulation on the conditions for using active and intelligent packaging, the EU commission has published general requirements and has drafted a specific regulation. The aim is to have safe materials with harmonised requirements all over the European Community. Legislation has been influenced by a European Commission funded project (FAIR-project CT-98-4170) known by the acronym of 'ACTIPAK'.[1] The Actipak project included an inventory of existing active and intelligent packaging, classification of active and intelligent systems in respect of:

- legislation on food contact materials
- an evaluation of microbiological safety
- shelf-life-extending capacity, efficacy of active and intelligent systems
- toxicological, economic and environmental evaluation of active and intelligent systems and recommendations for legislative amendments.

The results of the investigation contributed to the revision of framework Directive 89/109/EEC[2] on food contact materials. In the new Framework Regulation (EC) No. 1935/2004[3] the use of active and intelligent packaging systems is now included.

A project group under the Nordic Council of Ministers published in 2000,[4] a comprehensive report on legislative aspects of active and intelligent food packaging, also contributed to proposals for new legislation.

17.2 Use of active and intelligent packaging

The application of active packaging is certainly not new. The most likely, oldest application of active packaging is the use of wood barrels for the storage and maturation of wine, whisky and other alcoholic stimulants. If the wooden barrels were used initially to store spirits, it was discovered a long time ago that due to the release and absorption of substances, the sensory properties of the stimulants were improved.

Initially steel cans were tin coated to protect the steel from acidic foods. But it has been known for a long time that the tin coating has a positive influence on the colour of canned pineapple and therefore these products are still packed in tin-coated cans although alternatives for protecting the steel can are now available. Now there is a great focus on packaging materials that are deliberately developed to influence the quality, shelf life or appearance of the packaged food. Any packaging material will have that function but conventional packaging materials act only as a barrier to influences from the outside and they do not modify the conditions of the packaged food. Generally they are referred to as 'passive packaging'. Active packaging has an additional function by removing or adding substances from or to the packaged food. In active packaging two different types of active compounds can be assigned: one absorbs, the other releases. Some materials do both.

Due to the great variety of packaging with special functions the difference between 'active' and 'passive' packaging is not always unequivocal. A barrier film, preventing gas transmission between packed food and its environment, is clearly passive packaging. A polymer film with built-in chemicals to react with the oxygen inside the food package is clearly defined as active packaging. But a film made of polymer blends, with selective permeability to different gases that allows the food to breath and thus influences the atmosphere inside the package (so-called equilibrium modified atmosphere packaging, EMAP) may cause doubts. When comparing such an EMAP film to one in which chemicals are added to absorb and transmit gases (ethylene absorber) from the inside to the outside, then it can be concluded that in the last example chemicals are added deliberately to achieve a certain function. This is by definition active packaging. In the EMAP film no specific chemicals are added and thus it should be classified as passive packaging.

Intelligent packaging does not affect food. It provides information on the conditions of the packaged food. This information can be related to storage conditions, gas composition (generation of CO_2, leakage detector). It can also detect metabolites or chemical reaction products. Accordingly. intelligent packaging is placed either inside or outside the primary food packaging.

17.2.1 Active absorbers and scavengers

Active absorbers/scavengers are designed to remove constituents from the food or from its environment. Chemicals include oxygen, excessive water, ethylene, carbon dioxide, taints, and other specific food compounds.[5] Typical examples are:

- Oxygen absorbers. Based on iron or iron oxide, enzymatic oxidation, ascorbic acid oxidation, light activated quinone containing film or photo initiated polymers and applied to remove oxygen to avoid bacterial growth and oxidation. Oxygen absorbers are available in many forms (sachet, film crown cork). They are related to the intended needs. High volumes of oxygen will require a high capacity oxygen absorber.

- Oxygen scavenger + carbon dioxide generator. Based on the dye-sensitised oxidation of furoic acid which consumes oxygen and generates a similar volume of carbon dioxide.[6] Also enzymatic systems based on the enzymatic oxidation of glucose to gluconic acid will absorb oxygen and release at the same time carbon dioxide.
- Moisture absorbers. Based on cellulose fibres or a cross-linked polymer hydro gel to remove the drip from fresh meat resulting in a better appearance of the food. In some packaging, mixtures of herbs are added to the absorbing pad to avoid microbiological growth in the drip juice and as a result a longer shelf life. For dry foods, e.g., biscuits, moisture regulators based on silica gel or molecular sieve may be employed.
- Moisture regulators. Based on sugar solution contained in a water permeable plastic bag. The regulator is used to absorb excessive water released from fresh meat or fish and to obtain better backing properties.
- Ethylene scavenger. Based on potassium permanganate on an inorganic substrate. Due to its toxicity this application is only used in produce packages. The ethylene is oxidised to acetate and ethanol and thus reduces the ethylene content in the package. The ethylene triggers the ripening of fresh fruits. Other systems include plastic films with finely dispersed minerals, e.g., silica gel, zeolite or active carbon. A new development is the reaction of tetrazine with ethylene. The tetrazine is coloured while the reaction product is colourless. In this way the packaging also indicates saturation of the ethylene scavenger.[6]
- Aldehyde scavenger. Based on the reaction of amines, incorporated in the packaging, with aldehydes (Schiff bases). The aldehydes are the by-products of oxidation of fats and oils. This application is also close to misleading the consumer and should be applied with great caution.
- Amine scavenging film. Based on ionomeric polymer. Depending on the degree of free acid groups in the polymer, a film made of ionomer has a capacity to absorb and remove amines from fresh fish.[7] Use of these types of films may be close to misleading the consumer. The capacity of amine binding should not go beyond the shelf life of fresh fish. The film may be acceptable when only the amines released during the first period of storage are absorbed.
- Sulphite scavenger. Based on absorption of sulphite by zeolite-containing polymers.[7] Generation of sulphites is not caused by bacteria but by degradation of amino acids present in poultry.
- Bitter taste remover. Based on an immobilised enzyme, naringinase, in a cellulose acetate film to remove the bitter taste (naringin and limonin[8]) from grapefruit juice.
- Carbon dioxide absorber. Carbon dioxide is scavenged by calcium hydroxide provided the water content is sufficiently high. This is an irreversible system. Reversible systems are based on absorption on zeolite of active carbon.[9]

17.2.2 Active releasers

Releasing packaging actively adds components to packaged food, e.g., carbon dioxide, antioxidant or preservatives to avoid deterioration of the food. Also releasers may be used, like flavour or colour releasers, to improve the quality of the food.

Antimicrobial systems

Preservatives released to the food should already be permitted as food additives and the overall safe intake of these by consumers should not be exceeded when the preservatives are added to both food and packaging. Many proposed systems comply with this requirement but some do not. The release of an antimicrobial component can be achieved by transfer of the substance through the gas phase, when the preservative has sufficient volatility. A typical example is ethanol-releasing packaging, used for preservation of, e.g., buns. Also the release of SO_2 or CO_2 does not require direct contact with the food.

Many other substances are being proposed and tested. The disadvantage of non-volatile substances is that they require intimate contact with the food. For this reason the preservatives are blended in a primary packaging. This means that the preservative should be compatible with the polymer and can survive the thermal treating of the polymer when making a film material. In addition attention should be given to reaction products. If this requirement is fulfilled then the release from the film should be great enough to be effective. Organic acids, nisin, lysozyme chitosan, herb extracts and allyl isothiocyanate have all been proposed and tested. None of the systems is generally applicable but combined with specific foods they may be efficacious. Research is ongoing to improve antimicrobial packaging, using slow-release principles or release on command.

Heat releaser

Microwave susceptors are used for crisping and browning food in a microwave oven. The susceptor is a multi-layer material usually made of a paper layer, a thin aluminium layer and finally a polyethylene terephthalate layer which is in contact with the food. The susceptor absorbs the energy of the microwaves and this heat is transferred to the food resulting in a crispy surface at the part in contact with the food.

Other releasers

Packaging that can release antioxidants, flavours, and colours has great interest. Some packaging is or has been used for some time, e.g., a smoke flavour releaser used for flavouring certain types of sausages. The releasers are of great interest but are usually applicable to a limited number of foods. A real breakthrough has not yet occurred although potential is high.

17.2.3 Intelligent packaging

Intelligent packaging provides information on packaged food. This information

may relate to storage conditions and to the quality of the food. It may be readable by the consumer but in some cases the information is accessible only to manufacturers or retailers. Without being exhaustive, some typical examples follow.

Time/temperature indicators
Many time-temperature indicators (TTIs) are available today. Most of the indicators are based on the diffusion rate of one layer into a second layer of the TTI, leading to colour change. Some indicators register only the time or the temperature. A system using enzymatic reaction is commercially available. In general all these indicators are readable by the consumer. An example of an indicator intended only for the retailer is a printed bar code label. The bar code will change in time and that package will be recognised as unsuitable for sale. All these indicators are positioned on the outside of the packaged food.

Oxygen indicators
These indicators can detect the presence of oxygen and are mainly used to detect any leakage in, for example, modified atmosphere packaging.

Carbon dioxide indicator
Carbon dioxide indicators are available in the form of a label stuck to the inside of primary packaging. When the indicator changes colour the generation of carbon dioxide is detected. This generally means that the food is microbiologically active?

Microbial growth indicator
Indicators to detect metabolites are of great interest, but reliable systems are not yet commercially available.

Ripening indicator
Packaged fruits may be provided with an indicator that shows the ripening of fruit.

17.3 Regulation of active and intelligent packaging

17.3.1 Regulation (EC) No 1935/2004

In 2004 a new framework Regulation (EC) No 1935/2004[3] applicable to all materials intended to come into contact with foods was accepted. In this regulation, general requirements applicable to all food contact materials (FCM) are established. Specific provisions are included to allow the use of active and intelligent materials and articles, and a specific measure on active and intelligent materials was announced. In order to define the scope of

active and intelligent packaging, the following definitions of active and intelligent materials are given:

> 'Active food contact materials and articles' (hereinafter referred to as 'active materials and articles') means materials and articles that are intended to extend the shelf-life or to maintain or improve the condition of packaged food. They are designed to deliberately incorporate components that would release or absorb substances into or from the packaged food or the environment surrounding the food. 'Intelligent food contact materials and articles' (hereinafter referred to as 'intelligent materials and articles') means materials and articles which monitor the condition of packaged food or the environment surrounding the food.

The definition of active packaging refers to 'deliberately' incorporated components with the intention to release or absorb substances. This distinguishes active materials from passive packaging materials which in a few cases may have an effect on the food, but which are added for other reasons, e.g., a monomer. The definition also excludes all packaging materials from natural sources. For instance, wooden barrels are therefore not subject to the provisions on active materials. The substances released from these are not deliberately added to food. But if a wood extract were to be incorporated into an active packaging system then this would fall under the general and specific measures on active materials and articles. The definition on intelligent materials is restrictive as it refers to packaged foods only. This means that an ordinary thermometer or recording equipment used in food production are not considered 'intelligent' articles.

Article 3 of the framework regulation requires that food contact materials shall not transfer their constituents to foods in quantities which could 'endanger human health, or bring about an unacceptable change in the composition of the food, or bring about a deterioration in the organoleptic characteristics'. In particular, releasing materials cannot meet these requirements as they are designed to change the composition or the organoleptic properties of the food. Absorbing materials may also change the composition or organoleptic properties of the food. Therefore a special Article 4 has been inserted which allows changes in the composition or organoleptic characteristics of the food, provided the changes comply with the provisions of Directive 89/107/EEC[10] on food additives and its related implementing measures. In the absence of Community measures national provisions shall be applicable. Inserting this provision took away the hurdle, in the old framework Directive 89/109/EEC[2], for the introduction of active packaging with a releasing function. Additional requirements on active and intelligent materials are related to misleading the consumer and to labelling. Active packaging used to change the composition of food or its organoleptic properties in order to mask spoilage of that food is not acceptable, whilst information provided by intelligent packaging shall be reliable and not mislead the consumer. The regulation introduces the European Food Safety Authority (EFSA) and its role, including

procedures and time frames. These are in accordance with 'general food law'.[11] The EFSA has to be consulted on issues affecting public health. This means also that the authorisation of active and intelligent materials will be subject to an EFSA evaluation.

If required in a specific measure, then relevant food contact materials (FCM) shall be accompanied with a declaration of compliance, while appropriate documents shall be provided to relevant authorities to demonstrate such compliance. As most of the requirements in the framework regulation are applicable to all FCM, active and intelligent materials are subject to these rules as they can be considered FCM. In some cases there may be no direct contact with the food, e.g., intelligent packaging positioned on the outside of the primary package, but they are subject to the framework regulation for the reliability of the information provided to the consumer.

17.3.2 Draft regulation on active and intelligent materials and articles

A specific regulation[12] on active and intelligent packaging is under preparation and approaching its final stage. In spite of the fact that this is still a draft regulation, it is most likely that the final regulation will not differ significantly from the document now available. Therefore the document can be taken as a starting point for requirements on active and intelligent packaging.

The draft regulation in particular deals with the authorisation procedure for active and intelligent 'components'. Active and intelligent components are defined as 'individual substances or a combination of substances which cause the active function or provide the intelligent information'. It should be taken into account that most active and intelligent packaging has a complex structure. In general, active and intelligent packaging can be divided into two types. One consists of the active or intelligent components, while the second part concerns the so-called carriers or passive parts that contain the component. Carriers may be interpreted to include a material on which a releasing component is adsorbed and the packaging of the components. In the example of an ethanol releaser, the ethanol is absorbed on a silica gel which in turn is packaged in a paper or plastic sachet. The ethanol is defined as the active component that is subject to authorisation. The silica gel and the sachet form the passive part and should comply with safety requirements as defined in the framework regulation and implemented EU or national measures.

Migration from food contact materials (FCM) is subject to EU or national regulations. Overall migration and specific migration limits are established in the various regulations.[20,40] These limits are set to ensure inertness and safety of the FCM. Active releasing packaging is not designed to be inert. It will in many cases exceed the overall migration limit and in some cases the specific migration limits set for FCM. Therefore a substance released deliberately from an active packaging material should not be included in

overall migration. Special protocols may be needed for the determination of overall migration. CEN methods EN 1186, Parts 1–15[13] may not be suitable. Specific migration limits may be exceeded provided the final food complies with the rules and restrictions applicable to processed foods.

Finally the draft regulation requires that active and intelligent packagings 'are suitable and effective for the intended purpose' and that the active and intelligent components are authorised. Authorisation will be granted after a positive opinion of the EFSA and will be valid only to the applicant for an authorisation. The authorisation will be valid for a period of ten years and may be renewed for another period of ten years. The authorisation will be published in a Decision to the applicant. In addition the active and intelligent components will be inserted in a list of authorised components.

A requirement, in line with Regulation (EC) No 1935/2004,[3] concerning a declaration of compliance and the availability of appropriate documentation, has been confirmed in the draft regulation. It means that for any active and intelligent material a statement shall be provided that certifies that the material is safe to be used in contact with food under specified conditions of contact. To support such a statement the certifier shall have documentation that can prove the validity of the certificated. These documents shall be available to relevant authorities for inspection. In many cases this will include analytical data on, e.g., migration, total release, and effectivity of the active and intelligent of active components.

17.3.3 Requirements for authorisation – EFSA guidelines

The EFSA has been appointed to advise the European Commission on the safety of substances to come into contact with foods. Opinions of EFSA are based on a risk assessment. In general the conclusions given in an opinion will be adopted by the Commission, although occasionally the Commission may decide to deviate from the EFSA opinion as a risk management issue. In Fig. 17.1 a flow scheme related to the authorisation procedure is depicted.

The Scientific Committee of Food (SCF), the predecessor of the European Food Safety Authority (EFSA), established guidelines for food contact materials[14] and in particular for plastics. EFSA's working group on food contact materials provided detailed explanatory guidance[15] in the Note for guidance. The guidelines are not generally applicable to active and intelligent packaging, and EFSA will publish additional guidelines and explanatory guidance that may support applicants when drafting an application and developing a testing protocol. This guidance should be available at the moment the regulation on active and intelligent packaging is ready for implementation. Only a rough and predictive overview of the guidelines is feasible at this stage. EFSA will require all data needed to make a proper safety assessment, and in spite of any guidelines they will always be authorised to ask for additional information. It is likely that an application should contain:

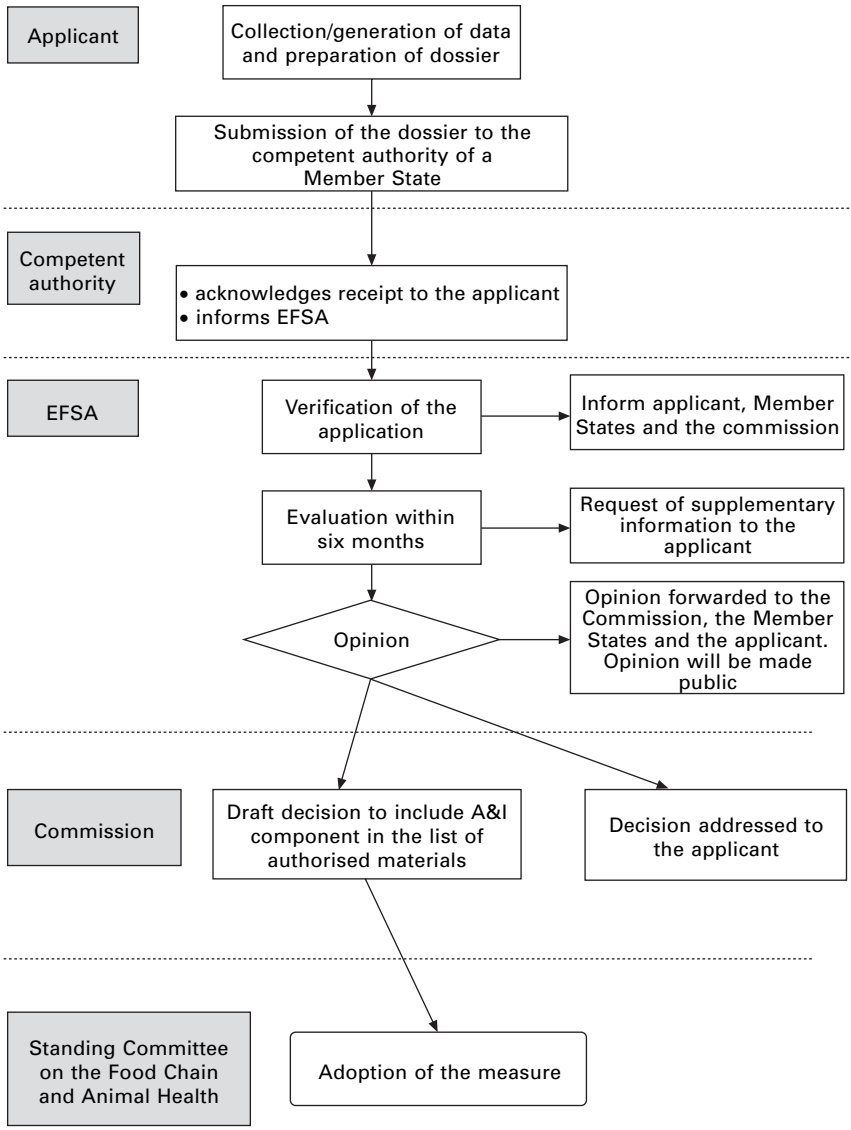

Fig. 17.1 Procedure for application, evaluation and authorisation of active and intelligent components.

- general information on the identity of the applicant
- summary document which summarises all the information provided
- technical dossier containing a description of the active or intelligent material, its function and the active or intelligent components. Additional information may be required but this could depend on the type of active or intelligent packaging.

For releasing materials it is likely that there will be a focus on the releasing component and its authorisation as a food additive, including any quantitative restriction or a restriction on the types of food. The information on efficacy may be important, e.g., in the case of a released preservative the final efficacy in the food should be demonstrated. A general rule may be considered that if the released component shows insufficient or no technical effect on the food, then the food additive does not comply with the requirements on food additives[10,16,17] or any other relevant regulation on the composition of food and its additives, e.g., the requirements on food flavours.[18,19] As a consequence such a material may not obtain a favourable opinion. Some information may be requested on the carrier of the releasing substance, but as this will not be part of an authorisation the safety of the carrier is the responsibility of the producer and the final user. In many cases the carrier may be subject to other provision on food contact materials. In principle the carrier should be inert and should not migrate to the food at an unacceptable concentration.

For absorbing materials the focus will be on the toxicological properties and quantities of components that (unintentionally) migrate into the food. If the absorber consists of plastic then only the plastics Directive 2002/72/EC[20] will be applied. Many active materials are composed of various types of materials, e.g., plastic, paper, metal and adhesive. No harmonised EU regulation exists on these materials and therefore they are subject to the framework regulation[3] and relevant national provisions of EU Member States. As mentioned for releasing materials, the efficiency or capacity of the absorber will almost certainly be considered in the final evaluation. As an example, the use of an oxygen absorber which has insufficient capacity to decrease and maintain the oxygen content to a low concentration may at best mislead the consumer or create in the worst case an even more dangerous situation due to the overgrowth of specific microbes. Also the possible growth of anaerobic bacteria present on some foodstuffs may be a reason not to apply an oxygen scavenger. It could be questioned whether this can be covered in an authorisation. It may be better to maintain the responsibility for final food safety with the food packers, who are familiar with their food products and possible problems.

Intelligent materials will probably need a demonstration of the reliability of the information provided, to comply with the respective requirement in the draft regulation. In respect of unintended migration a distinction may be feasible for materials that are positioned inside or outside the primary packaging. In the latter case the actual migration of any intelligent component may be negligible and it would be logical to adapt the need for toxicological information to the 'no migration' or 'functional barrier' principle. This would mean that un-authorised substances can be used behind a barrier layer, provided the substances are not mutagenic, carcinogenic or toxic to reproduction according to Directive 67/548/EEC.[21] If the intelligent material is or may come into contact with the food then the intelligent ingredients will need an evaluation based on migration level and toxicological properties as outlined in the Note for guidance.[14,15]

17.3.4 General safety

Many EU directives and regulations related to food and food safety have been published. All relevant regulations have been extensively discussed before.[22] Without being exhaustive, the following subjects could be subject to relevant European or Member States' regulations and might be taken into account in an evaluation procedure performed by EFSA:

- food contact materials
- food additives
- flavourings
- hygiene
- biocides
- labelling
- general product safety
- misleading claims
- weight and volume.

As a general rule all the regulations related to food have the requirement that the final food should be safe for consumption. This may relate to chemical composition or to microbiological deterioration. Chemical composition may refer to food additives,[10] flavouring substances[18,19] or sweeteners.[23] If these substances are added via active packaging then the final food must comply with the relevant requirements for food production. The regulation on hygiene[24] requires that all measures shall be taken to assure the wholesomeness of the food. Active packaging may be a useful tool to comply with this requirement as it is usually applied to extend the shelf life of the food or at least to maintain the quality of food during its shelf life. The regulation on biocides[25] is actually not applicable as biocides are not allowed in processed food. Only substances that are authorised as preservatives in food may be applied. Food contact materials with antimicrobial surfaces (e.g. after incorporation of silver ions in food contact materials) are frequently, but incorrectly, referred to as active packaging. The anti-microbial surface has no effect on the food itself and therefore it is excluded from the definition of active packaging.

Products shall be safe as established in Directive 2001/95/EC.[26] 'Safe products' means that under normal or reasonably foreseeable conditions of use the product does not present any risk or only the minimal risks compatible with the product's use. In judging safety aspects, the characteristics of the product, presentation, labelling instructions and the category of consumers, especially children, should be considered. Also the shape and size of active or intelligent packaging in the form of, for example, a sachet that is packed together with the food may give reasons for concern. A sachet filled with active compounds may be misunderstood by consumers and pose a threat. In some cases a visually attractive object may be packed together with the food. In such instances extreme care should be taken to avoid confusing consumers. Equally, controls must stop possible dangers to human health, for example,

from consumers trying to eat sachets filled with active compounds. Appropriate labelling will be essential.

Some active packaging is designed to absorb components from the packaged food, e.g., a moisture absorber. When using this type of absorber the final weight of the food available for consumption may change. Directives 75/106/EEC[27] and 76/211/EEC[28] include labelling of weight and tolerances. When part of the food is absorbed by an absorber then the final weight may no longer comply with the intended and declared food weight.

Besides the framework Regulation 1935/2004[3] and the specific Directive 2002/72/EC[20] on food contact materials, other directives on food contact materials have been adopted and may be relevant in assuring the safety of active or intelligent packaging. This concerns directives on regenerated plastics,[29,30,31] ceramics[32] and a regulation on certain epoxy compounds.[33] In the absence of harmonised EU regulations, existing national regulations may be applicable and may be useful to demonstrate safety of active or intelligent packaging.

17.3.5 Labelling

Labelling of foodstuffs is meant to give consumers information on the composition of the food and so protect their interests. Labelling appears to be a complex issue as there are many EU directives and regulations that include requirements on labelling. Food labelling may concern the food, food additives or food contact materials as well as active and intelligent packaging. Framework regulation 1935/2004[3] requires labelling of food contact materials that are not yet in contact with food. This labelling could be done by 'for food contact', or indicating use (e.g. 'soup spoon'), or by using the symbol in Fig. 17.2. Exceptions to this rule are articles that from their shape are clearly designed for food contact. In addition, food contact materials should be labelled with instructions for safe use. Identification should be added to allow food contact materials to be traced. Labelling of food contact materials should not mislead the ultimate consumer. For active packaging, information on the permitted use and the identity and quantity of the released substance has to be provided in order to allow a food packer to comply with any restriction. Materials that may be mistaken as a part of the food, such as loose sachets, must be labelled using the symbol for a non-edible item (Fig. 17.3).

Fig. 17.2 Symbol for food contact materials.

Fig. 17.3 Symbol proposed for labelling active materials.

Directive 2000/13/EC[34] deals with labelling, presentation and advertising of foodstuffs and is applicable to all foodstuffs intended for sale to consumers or caterers. Also Directive 89/107/EEC[10] sets requirements on labelling of food additives. In principle, all substances used in the manufacture or preparation of foodstuffs and still present in the finished product should be declared on the label in order to inform the consumer about the substances present. It is of no interest how or when the substances are added to the food and therefore substances released from an active packaging system should be declared.

A minimum durability date should be provided and for highly perishable foodstuffs a 'use by' date should be given. This latter requirement is a hindrance to the use of a time temperature indicator (TTI). A 'use by' date should also cover foreseeable incorrect storage conditions, e.g., during transport. Therefore 'use by' dates are set on a very safe (short) period. By use of appropriate TTIs the total safe consumption period could be used for the benefit of both the consumer and the manufacturer or retailer. It is assumed that further effort by TTI manufacturers may result in a legal recognition of TTI as a replacement for 'use by' dates.

Modified atmosphere gases are regulated as food additives (Directive 95/2/EEC[35]). Gases that may be added are listed. When modified gas packaging is applied this should be labelled. However there are no provisions for the removal of gases from the packed food. This means that a CO_2 releasing system falls within the definition of food additive. But an oxygen scavenger does not comply with the definition as the oxygen is removed. The final gas composition in a modified atmosphere may be comparable to that in packaged food using an oxygen absorber, but it is not yet clear whether there is any regulation that would prevent the use of oxygen absorbers. On the other hand there is no prohibition on the removal of oxygen from packaged food and no labelling requirement for the modified atmosphere. Only Regulation 1935/2004 requires that the use or presence of an active device, extending the shelf life of the food, should be labelled.

17.4 Migration from active and intelligent packaging into foodstuffs

17.4.1 Basic rules

Active packaging and intelligent packaging are considered to be food contact materials. This means that the migration of packaging substances should be examined according to the existing EU directives or national provisions. At the EU level the framework Regulation 1935/2004[3] sets the general requirements of which Article 3, stating that the packaging material should not endanger human health, is the most important. Following up the framework regulation, specific directives on plastics (2002/72/EC[20]), regenerated cellulose (93/10/EEC[29]) and ceramics (84/500/EEC[32]) have been published and implemented in national legislation in the EU. The plastics directive contains a positive list of monomers and an incomplete list of additives for use in plastics. To support testing of plastic materials for compliance with the plastic directive two additional directives are available. Directive 82/711/EEC[36] as last amended by Directive 97/48/EC[37] sets requirements (time temperature conditions, selection of simulants) for testing of plastic materials and articles with food simulants. Directive 85/572/EEC[38] indicates the simulants that shall be used for specified foods or groups of foods. See Chapter 5 for further details on these controls. Regulation of chemical migration from plastics into food and drink has developed over many years. EU regulatory control of active and intelligent packaging will therefore have to fit in with this well-established system of controls.

To support the analyst in applying such controls, CEN (the European Standardisation Commission) has in TC 194 adopted and validated analytical methods for the determination of the overall migration[13] and the migration of some specific substances.[39] These methods are intended to be applied for testing plastic materials and articles. At national level, e.g., in The Netherlands,[40] the methods and simulants may also be used to demonstrate compliance with national regulation of non-plastic or multilayer materials composed of plastics and non-plastics (e.g. plastic on paper, coating on metal).

The principle of the methods is rather simple but analytical problems are frequent. A food contact material is brought into contact with the selected simulant(s) under selected conditions of time and temperature. Homogeneous materials are contacted by submersion while multi-layers or thin films are often in single-sided contact with the food simulant. After the contact period the simulant is separated from the food contact material and the overall migration is determined gravimetrically while specific migration is determined using a suitable analytical method like gas or liquid chromatography with spectroscopic detection. The determination of the overall migration in olive oil is more complex and sensitive to analytical and systematic errors. An indirect method is required to determine overall migration.[13]

17.4.2 Active and intelligent packaging

Some active and intelligent materials function as primary packaging by wrapping or holding the food, but most active and intelligent packaging has varying shapes, sizes and compositions. In many cases conventional migration tests use single-sided contact and cannot be applied for technical reasons related to, e.g., the size of the packaging. Within the Actipak project migration experiments were performed by total immersion of active and intelligent packaging into the various simulants. It appeared that in many cases overall migration was exceeded.[41] Table 17.1 summarises the results of that investigation.

Based on these results it was concluded that determination of overall migration from active and intelligent packaging using conventional methods is not applicable in many cases. There is a need for dedicated tests that simulate better the conditions of contact for some types of active and intelligent packaging.[42] The development of dedicated methods is required in order to allow a proper judgement of the suitability of active and intelligent packaging. However, this requires a closer look at the origin of the problems in determining migration. Although this is a complex problem, almost requiring a different approach for each type of packaging, a number of starting points can be distinguished:

- active or intelligent packaging being at the same time primary food packaging
- active packaging as a releasing material
- active material as an absorber
- intelligent material being inside the primary packaging
- intelligent material being outside the primary packaging.

Another variable is the type of food in contact with the active or intelligent packaging. Here there may be liquid contact (e.g. for an oxygen-scavenging crown cork for beer), dry contact (e.g. a preservative releaser for buns) or semi-solid contact (e.g. an oxygen scavenger for processed ham).

17.4.3 Different approaches for each type of packaging

Some active and intelligent packaging functions in primary packaging include, e.g., an oxygen scavenger with the active ingredients incorporated in the polymer backbone, or a casing containing a smoke flavour to be released to the packaged food. Certainly in new developments the primary packaging will more often be combined with the active or intelligent function. The composition of the packaging should comply with EU regulations, relevant national regulations and with the active or intelligent component mentioned in the authorisation. Compliance of overall and specific migration with EU limits can be examined according to Directives 82/711/EEC[37] and 85/572/EEC[38] applying the conventional test methods outlined in the CEN methods EN 1186[13] and EN 13130.[39] Both single-sided contact or total immersion

Table 17.1 Overall migration from selected active packaging materials

Code	Unit	Water 10 d–40 °C	3% acetic acid 10 d–40 °C	15% ethanol 10 d–40 °C	Olive oil 10 d–40 °C	Iso-octane 2 d–20 °C	95% ethanol 10 d–40 °C
OS1	mg/object	617 ± 32	1707 ± 310	796 ± 39	–	2 ± 1	211 ± 25
OS2	mg/object	88/38/95	467/447/310	90/79/71	–	1 ± 1	41/30/57
OS3	mg/dm^2	1 ± 0	2 ± 0	2 ± 1	28 ± 0	–	–
OS4	mg/dm^2	4 ± 1	4 ± 1	8 ± 3	<1	–	–
OS5	mg/dm^2	<1	<1	<1	2 ± 1	–	–
ES1	mg/dm^2	<1	<1	<1	6 ± 1	–	–
ES2	mg/object	2 ± 1	4 ± 1	2 ± 1	–	18 ± 1	17 ± 3
MR1	mg/object	<1	967 ± 133	<1	–	<1	2 ± 1
MR2	mg/object	<1	11 ± 3	<1	–	<1	<1
MR3	mg/object	9 ± 1	46 ± 8	7 ± 1	–	18 ± 3	21 ± 3
MR4	mg/object	5333 ± 189	5945 ± 91	6063 ± 307	–	3 ± 1	168 ± 15
AMP1	mg/object	<1	4.2 ± 1.4	1.7 ± 0.1	–	<1	<1
AMP2	mg/dm^2	<1	<1	<1	41.8 ± 4.2	27.7 ± 0.1	–
AMP3	mg/dm^2	2.6 ± 0.6	3.5 ± 0.7	<1	<1	–	–
AMP4	mg/dm^2	4.9 ± 1.1	4.8 ± 1.0	5.6 ± 0.6	1.9 ± 0.4	–	–
AMP5	mg/dm^2	11.0 ± 1.0	20.0 ± 4.0	37.0 ± 9.6	73.0 ± 2.0	<1	909 + 34
O1	mg/dm^2	56 ± 3	61 ± 3	62 ± 1	19 ± 4	–	–
O2	mg/dm^2	<1	<1	<1	2 ± 1	–	–

OS = oxygen scavenger; ES = ethylene scavenger; MR = moisture regulator; AMP = antimicrobial system; O = releaser.

may be applied. For verifying compliance with the restrictions the conventional assumption that 6 dm^2 of packaging is in contact with 1 kg of food will generally be applicable, as it is for conventional packaging materials.

Available migration test methods may not be suitable for the determination of migration from releasing materials. For overall migration the release of the active component may be much greater than the overall migration limit. According to the draft regulation on active and intelligent packaging the release of the active component should be excluded from overall migration. From an analytical point of view there are two options. One could be to determine overall migration from the packaging material without the releasing substance as this is frequently done for the conventional passive packaging. Alternatively, overall migration of the active packaging can be determined and from this could be deducted migration of the active component. In this way migration of the passive part of the packaging can be determined. Of course, this will introduce a rather large analytical error depending on the amount and nature of the released component. This method may be applicable only for a few types of active releasing packaging.

When active packaging acts as a releasing material it is often included in the primary packaging as a small sachet, box or label and cannot be compared to conventional (passive) packaging materials. For conventional packaging materials the usual ratio of 1 kg of food in contact with 6 dm^2 is applied. For sachets and the like, the surface to volume ratio is usually much smaller. Active releasing packaging is mostly composed of very different materials. An ethanol releaser consists of ethanol absorbed onto a powdered silica gel carrier in a plastic-coated paper sachet. This type of active packaging is not intended for contact with liquid foodstuffs, but for contact with dry and semi-solid foods. For this type of packaging it should be realised that Article 3 of the framework regulation (EC) No. 1935/2004 applies as well as relevant provisions on food additives.

It is difficult, if possible at all, to determine migration of the carrier using model tests with simulants. On the other hand there must not be unacceptable migration from the carrier to the food. The most simple and efficient way to certify compliance with the framework regulation on food contact materials is to use approved materials in the manufacture of active packaging. This means composition and migration (overall and specific) should comply with relevant EU regulations or national provision. This, however, is not feasible for enforcement purposes. Enforcement authorities could determine specific migration of the carrier constituents in the actual food. In simulating tests the use of the 'dry simulant' MPPO may be useful for the determination of specific migration of substances. For semi-solid contact the so-called sandwich method, which is still under development and validation (TNO, Zeist, Netherlands), may be applied, provided conditions of contact are selected with great care.

Active absorbers and intelligent packaging by definition have no intentional migration. Nevertheless, migration may occur as this is noticed from passive

packaging. This type of active and intelligent packaging shall comply, as a minimum, with the framework regulation on food contact materials. Also the migration of active or intelligent components has to comply with this framework regulation. For testing for compliance, in the first instance, the composition of the active and intelligent component should be covered by an authorisation. Secondly, the composition of the packaging of the active or intelligent component should comply with the relevant EU or national regulations on food contact materials.

Chemicals used as a carrier of the active or intelligent component may not be subject to a specific regulation, e.g., presence of sodium chloride in an iron based oxygen scavenger (discussed below). Following the principle of inertness of food contact materials the carrier should not migrate to the food. Rules for inertness and migration behaviour of food contact materials are well defined but how to demonstrate this is not yet established and will be complex because of the almost endless variations of types of food, shape and size of active packaging and conditions of contact. Many types of active and intelligent packaging inserted in the primary packaging together with the food cannot be tested by conventional means and dedicated test protocols are needed. Up until now only a few protocols have been found suitable for dedicated testing of some active and intelligent packaging in contact with semi-solid foods.

Testing iron oxide-based oxygen absorbers for overall and specific migration (used for shelf life extension of semi-solid foods, like cooked ham) should be carried out with 3% acetic acid when the pH of the ham is less than 4.5. Total immersion of the oxygen scavenger is not realistic. Performing a submersion test results in a simulant coloured brown with iron oxide. As this brown colouring does not occur on the food, the contact mode by total submersion is obviously different from contact in real life. In Directive 97/48/EC[37] provisions are made to deviate from the prescribed test conditions (time and temperature) when physical or other changes are observed that do not occur in contact with the food. This opens the way to using dedicated methods. Experiments with satisfying results have been obtained by using a so-called sandwich method as depicted in Fig. 17.4.

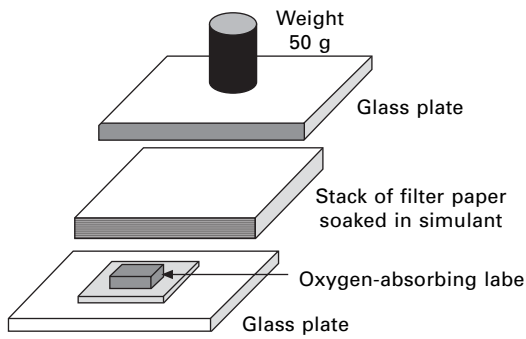

Fig. 17.4 Exploded view of dedicated testing of active packaging labels or sackets.

In this experiment a sample of active packaging (label or sachet) was placed on a glass plate and covered with a stack of filter paper that first had been extracted extensively with the test simulant. Free-flowing simulant should be removed by allowing the simulant to drip for about 30 seconds. Then the filter paper is covered with another glass plate and, in case the weight of the food should be simulated, a weight can be put on top of the upper glass plate. To avoid evaporation of the simulant the whole package can be wrapped with a plastic film or aluminium foil. The packaged is stored under selected conditions of time and temperature. After the storage period the filter paper is analysed for overall or specific migration. For the overall migration the filter paper is extracted in a soxhlet apparatus using the test simulant or a more suitable solvent. The extraction residue is determined gravimetrically. Correction of the blank value for the filter paper is necessary. For the determination of the specific migration of substances the soxhlet extract can be analysed. Volatile substances can be analysed using filter paper without extraction. For non-volatile substances that give problematic recovery (in this case, iron ions) the filter paper may be combusted and the migration of iron can be determined using atomic absorption spectrometry. This procedure is applicable to various types of active absorbing and intelligent packaging that have a more or less flat shape like a sachet, label or pad.

A moisture-absorbing pad may be tested with this protocol. In principle such a pad will absorb the meat drip into its fibres or in a cross-linked polymer. Due to the absorption capacity the migration of the absorber's constituents is not likely. However, in case the absorber starts to become saturated, migration is more likely. To simulate this, an absorber should first be saturated with water to approximately 80% of its capacity before migration testing.

Active and intelligent packaging in contact with liquid foods can be tested by submersion in simulant as this is equivalent to real-use conditions. Packaging used in dry foods should not be tested with liquid food simulants. If testing is considered necessary then the use of MPPO may be suitable. MPPO is dry, has a large surface area and a strong absorptive capacity. Any migration into dry foods occurring in real life can also be detected by using MPPO, which may be analysed after extraction or directly by thermodesorption.

When intelligent material is outside the primary packaging, some intelligent packaging (e.g. time/temperature indicators, TTI) is placed *in situ* on the outside of the packaging. Taking into account the construction of most TTIs and the barrier of the primary food packaging, it is assumed that a functional barrier prevents the migration of any of the intelligent components. Migration testing should then not be necessary. Of course, the composition of the authorised component and the carrier shall be in compliance with regulatory requirements.

Many forms of active and intelligent packaging, not used as primary packaging, are designed to have little or no contact with food. For instance, an oxygen absorber, based on iron oxide, applied in the shape of a sachet has

a contact area of only a couple of square centimetres. The conventional surface to volume ratio of 6 dm^2/kg food will never be achieved. Similar arguments are valid for many types of intelligent packaging. Plastics Directive 2002/72/EC[20] allows the use of the real ratio of surface to volume. Therefore migration should be expressed in mg/subject and divided by the quantity (kg) of food in contact with the subject. This should be done before using overall or specific migration limits listed in relevant regulations. It should be borne in mind that there may be a contribution to overall or specific migration originating from the primary packaging.

17.5 Future trends and sources of further information

Today, mainly oxygen and moisture absorbers and time/temperature indicators are used on food packaging. A survey of consumers' attitudes to active packaging revealed that consumers appreciate the use of active packaging materials that improve or maintain the quality of the food.[43] Consumers expressed a wish for invisible active packaging. The presence of a sachet or box with 'chemicals' was considered a disadvantage as the sachet easily could be confused with food ingredients such as a salt or dressing.

New developments more and more try to incorporate active components in the primary packaging material (e.g. oxygen absorber film OS 2000). This is a technical challenge as the active component should be compatible with the packaging material, often being a polymer, and it should be resistant to thermal processing. In respect of consumer demand for mildly preserved food, the development of anti-microbial packaging has considerable interest. Packaging with a 'release on command' function is under development.[44] Intelligent systems are focusing on the detection of spoilage precursors of the food. However, this is a very complex issue and reliable indicators are not yet known. Further development and validation of dedicated migration methods for active and intelligent packaging will be necessary. In the first instance this may be a task for manufacturers. In the authorisation procedure for new active and intelligent packaging, the development of such methods may become evident.

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18

Chemical migration from secondary packaging into foods

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18.1 Introduction

As can be seen from the preceding chapters, considerable attention has been paid to migration from packaging materials to foods where the packaging is in direct contact with foodstuffs, i.e., transfer from primary packaging materials and articles. Far less attention has been paid to materials and articles that are used in the packaging, transportation, distribution and storage of foods but which are not intended to come into direct contact with the food. These materials are referred to as secondary packaging materials.

18.2 Materials in use

The most obvious secondary packaging material is the corrugated board box. This is used in all sectors of the food transportation and distribution process. The normal practice during the manufacture of a food product is for the food to be packaged in some form of direct contact packaging during the production process (typically towards the end of production) and then for several of these packages to be placed into corrugated board boxes for transport to distribution depots or direct to the retail store. An example of this would be for dried pasta. This product is commonly packaged in a plastic wrapper or, less commonly, in a cartonboard box as primary packaging. A number of bags or cartonboard boxes of pasta will then be packed together in a corrugated board box for onward distribution from the production facility. It is normal practice for many corrugated board boxes to be stacked together on a pallet, and the whole stack to be over-wrapped with some form of plastic stretch-

wrap. These are then transported to a distribution depot and/or cash and carry before final transport to retail stores. The product is likely to remain in the corrugated board box through all these stages until it is finally unpacked and placed on the shelf for retail sale.

Other widely used secondary packaging materials include cartonboard boxes. Examples include cartonboard boxes used for packaging breakfast cereals, where the foodstuff is packaged in a plastic bag or paper wrapper as the primary packaging and then the primary pack placed inside a cartonboard box. The box serves to protect the product from contamination, light and physical damage. It also offers the possibility of a large, flat surface area for printing so that information about the product and related products from the manufacturer can be conveyed to the customer. Other examples of cartonboard boxes used as secondary packaging include pizzas, where the pizza is over-wrapped with plastic film as primary packaging and then placed in a printed cartonboard box; cakes and pastries; teabags; cake mixes; ice cream bars; stuffing mixes, etc. As with the pasta example described above, foodstuffs with a cartonboard box secondary packaging component will themselves be further packed into corrugated board boxes for distribution from the production facility. Plastic films may also act as secondary packaging materials. Examples include crisps and confectionary products in multipacks, where the larger, outer pack containing individually wrapped single packs can be considered as secondary packaging. Again, these types of products will be distributed in corrugated board boxes.

It is becoming more and more common for foodstuffs to be imported from or exported to other countries. Some foodstuffs may be bulk shipped. Examples include wheat and sugar. These foodstuffs are likely to be stored directly in a ship's hold. This is a direct food contact situation. There are, however, a number of foods that are shipped in secondary packaging. Examples include frozen and chilled meat, frozen fish, tomato paste, fruit intended for juicing and honey. Frozen and chilled meat and frozen fish and prawns may be shipped in corrugated board boxes which have a plastic liner that loosely envelops the food. The food may or may not be packed in some form of primary packaging such as cryovac plastic or woven bags. Waxed corrugated board boxes may be used to ship frozen meat and fish with a plastic liner over-wrapping the foodstuff.

Intermediate bulk containers (IBC) are used widely for the bulk shipping of foodstuffs. IBCs are large volume containers and can be made from plastic, stainless steel or corrugated board. Corrugated board IBCs employ a plastic liner as the primary packaging layer. Tomato paste is shipped in corrugated board IBCs with a plastic liner as primary packaging. Steel drums are not used widely for shipping foodstuffs to the UK, although they are used to transport honey, with the product contained in a plastic liner as primary packaging inside the drum.

18.3 Length of time in secondary packaging

In most large-scale food production facilities, corrugated board boxes containing the food product are stacked together on pallets, often then over-wrapped with some form of plastic wrap to minimise shifting during transportation and handling. The whole pallet is then transported. The food being transported is not in direct contact with the corrugated board box but may remain in the box for some time, depending on the nature of the food and the distribution network. For example, for large supermarket chains, the pallet and associated stack of boxes may be transported to a distribution depot where it may sit for several weeks or months, depending on stock turnover rate, before boxes are removed from the stack for onward distribution to the retail store. The food may then be stored in the corrugated board box for a further period in the store until the foodstuff is transferred to the supermarket shelves. In some stores, foodstuffs are stored in corrugated board boxes in the retail area of the store. Some foodstuffs may also be transported a long distance in corrugated board boxes. For example, as noted in Section 18.2, foods may be exported by ship, rail or air in corrugated board box secondary packaging.

Where there is a rapid turnover of stock, the length of time a foodstuff spends in secondary packaging may be limited. However, there may be situations where storage in secondary packaging is considerable. For example, confectionary products produced for Christian festivals such as Christmas and Easter will be manufactured some months ahead and then stored in packaging until required for retail display. Products such as pasta, breakfast cereals, gravy browning, etc., have a relatively long shelf life and hence may be stored in secondary packaging for some considerable time, including storage in the home.

18.4 Legislation and testing

Part 2 of Article 1 of European Commission (EC) Regulation No. 1935/2004 states

> This Regulation shall apply to materials and articles, including intelligent food contact materials and articles which in their finished state: (a) are intended to be brought into contact with food; or (b) are already in contact with food and were intended for that purpose; or (c) can reasonably be expected to be brought into contact with food or to transfer their constituents to food under normal or foreseeable conditions of use.

Clauses (a) and (b) clearly do not apply to secondary packaging materials. It is clause (c) which is more applicable 'materials and articles …which…can reasonably be expected to…transfer their constituents to foods.' Thus, although the title of the Regulation indicates that it applies to 'materials and articles intended to come into contact with food', Article 1 can be taken to include secondary packaging materials.

This then begs the question 'Should secondary packaging materials be subject to the same testing requirements as primary packaging materials?' This is a difficult question to answer because information on transfer from secondary packaging materials to food is limited, although it is well recognised in industry that packaging materials can give rise to odour and taint problems. Article 3 of EC Regulation No. 1935/2004 states that

> Materials and articles, including active and intelligent materials and articles, shall be manufactured in compliance with good manufacturing practice so that, under normal or foreseeable conditions of use, they do not transfer their constituents to food in quantities which could: (a) endanger human health; or (b) bring about an unacceptable change in the composition of the food; or (c) bring about a deterioration in the organoleptic characteristics thereof.

Thus the provisions of Articles 1 and 3 of the EC Regulation give a clear indication that all those involved in the food packaging chain need to consider whether the secondary packaging materials they use comply with the Regulation.

Converters, printers and board manufacturers typically carry out some form of organoleptic testing for their products. This is certainly carried out for primary packaging materials and is also widely applied to secondary packaging materials, particularly where the material is used to package taint-sensitive products such as confectionery.

In terms of migration testing, it is doubtful whether this is carried out to any great extent for secondary packaging materials, unless they are materials that are also used for primary packaging. It is also doubtful whether the sort of migration testing as applied to plastics materials and articles would be appropriate for assessing the safety in use of secondary packaging materials. Given that they will not contact food directly, testing using food simulants in direct contact with the material or extraction testing using solvents such as isooctane or ethanol is not appropriate in that it does not mimic real-use conditions. However, if a secondary packaging material was tested in this way and 'passed', then it would almost certainly be acceptable in real use. This comment on the appropriateness or otherwise of migration tests as developed for plastics materials and articles should not be taken to mean that migration testing for secondary packaging materials is not appropriate. Suitably designed migration tests which mimic the true packaging situation would certainly be appropriate.

18.5 Chemical migration from secondary packaging materials

Transfer of substances from secondary packaging to foods can be considered to take place by two main routes. The first is via direct contact where the

secondary packaging material directly contacts primary packaging material. Depending on the nature of the substance and the primary packaging material, there may be partition of the substance from the secondary packaging into the primary packaging and then diffusion through the primary packaging material to the packaged food. This obviously requires good contact between the two materials but one can envisage transfer as for multi-layer materials (Chapter 16).

The second route for transfer of substances is via the gas phase. For transfer of this type to occur, substances must have a sufficiently high vapour pressure to be able to enter the airspace surrounding the packaging. Once in the vapour phase, where plastic primary packaging materials are used, substances may partition into the plastic and, depending on the diffusion coefficients and the nature of the primary packaging material, they may transfer to the packaged food. In the case of paper or board primary packaging materials, substances volatilised from the secondary packaging material may diffuse through the cellulose fibre network and hence transfer to foods. Transfer may be prevented or delayed, depending on the nature of the primary packaging material. The primary packaging material may or may not provide a functional barrier to migration for substances volatilised from the secondary packaging material. Chapter 9 should be consulted for further details on functional barriers.

18.5.1 Potential for gas phase transfer

The most extensive evidence for gas phase transfer comes from odour and taint studies. Odour and taint has long been recognised as a potential problem, with packaging manufacturers carrying out odour and taint testing on finished products. Odour is typically assessed by placing a sample of paper or board in a sealed container and then allowing a trained panel of assessors to sniff the headspace. A comparison is made between the odour from the test material and that of a control material deemed acceptable in terms of odour. This is, therefore, an assessment of the potential for substances to transfer to foods through the gas phase. Taint testing usually involves placing the test material in a sealed vessel together, but not in contact, with a foodstuff such as oil or chocolate. In this instance, the trained panel of assessors samples the foodstuff and scores it for taint against a control sample not exposed to the test material. As for odour testing, this assesses gas phase transfer of substances.

Substances linked with producing odour and taint include short chain aldehydes. In paper and board, these are considered to derive from the degradation of lipids. Pentanal, hexanal, heptanal and nonanal were shown to be volatilised from paper and board materials heated at 60 to 100 °C (Wenzl and Lankmayr, 2002). Other substances were also detected in the headspace above the test samples but were not identified. Whilst transfer to foods was not investigated in these studies, the fact that they were shown

to volatilise from paper and board indicates the potential for gas phase transfer.

Training panels of assessors and carrying out odour and taint testing is labour intensive, time consuming and carries a considerable element of subjectivity. Packaging manufacturers have, therefore, explored possibilities for replacing human testing with testing using instrumentation. Electronic noses were originally developed for assessing food aromas but have obvious applications for assessing odour and taint of packaging materials and have been the subject of several studies.

One such study comparing headspace purge and trap GC-MS, odour tests and an electronic nose showed that the electronic nose could differentiate between unprinted boards and printed and lacquered boards by analysing the vapour phase of the heated boards (Heiniö and Ahvenainen, 2002). Optimum differentiation of materials was achieved when test materials were heated at 60 °C for 20 minutes before sampling. Twenty board samples were studied including one unprinted board. Volatiles detected by headspace GC-MS included hexanal, hexane, heptane, toluene and branched hydrocarbons. The board samples were equilibrated overnight at room temperature in sealed headspace vials.

In another study, three different electronic nose instruments were compared for their ability to evaluate odours of retained solvents in printed packaging (Van Deventer and Mallikarjunan, 2002). Ten film samples commonly used for packaging snack products were analysed including orientated poly(propylene) (OPP), metallised OPP, polyester, low density poly(ethylene) (LDPE) and coated paper. Two of the films included in the studies were considered as 'non-conforming' with regard to retained solvent residues, i.e., they would be considered unacceptable and likely to give rise to product taint if used to package snack products. These samples consisted of an OPP film, rotogravure reverse-printed with approximately 37.5% ink coverage laminated to a layer of LDPE using a water-based adhesive. All three noses tested could differentiate between 'conforming' and 'non-conforming' samples. Analysis by GC indicated the presence of alcohols and ketenes.

The potential for secondary packaging to taint foods via vapour phase transfer of substances was recognised by Tice and Offen (1994) who noted that: 'The transfer of odorous substances from packaging to food may not necessarily involve any direct contact between the packaging and the food. Odorous volatiles released from packaging material into the vapour phase within the packaging can be absorbed by the surface layer of the food and slowly diffuse into the interior.' They noted that cartonboards manufactured using styrene-butadiene or styrene-acrylate copolymer binders have been shown to give rise to volatiles. These included styrene monomer, vinyl cyclohexene and alkyl substituted benzenes including 4-phenyl cyclohexene. Other potential substances identified as giving rise to taint and/or odour included chlorophenol and chloranisoles; aliphatic aldehydes and heterocyclic aldehydes such as furfural produced by oxidation, possibly catalysed by metal ion residues; and printing inks and varnishes including alkyd resins in

lithographic inks which can oxidise to release aldehydes and ketones.

Dahlman and colleagues (Dahlman *et al*., 1999) evaluated laminated packaging material in terms of the potential for release of compounds from the laminate to the gas phase. Whilst it is debatable whether these studies represent a true secondary packaging situation, they do, again, demonstrate the potential for substances to transfer via the gas phase. They used headspace purge and trap GC-MS and a specially constructed test cell to determine substances evolved from a polyethylene/aluminium/paperboard/coated and printed polyethylene (PE) film laminate heated at 30, 60, 90 and 120 °C. The coated and printed PE film was considered as the outer surface of the packaging. Octanal, nonanal and decanal were seen in the headspace from the inner surface indicating transfer across the laminate. They noted that there was increased evolution of substances with increased temperature, with a noted increase in transfer when the temperature was raised from 60 to 100 °C. They also tested a paperboard sample laminated to a poly(propylene) (PP) polymer film. In this instance, transfer of a variety of hydrocarbons was detected including straight and branched chain alkanes and alkenes. These were considered to originate from the PP film.

Two of the substances detected, pentamethyl heptene and tetramethyloctene were considered as substances known to contribute to the odour of extrusion film coatings. The fact that these substances could transfer from the film to the gas phase supported the potential for these substances to give rise to odour problems in foodstuffs. They also impregnated a filter paper with octanal and placed it in the test cell in contact with paperboard laminated to various films including PE, PP, poly(ethylene terephthalate) (PET) and aluminium/PE (Al/PE) (with PE on the outer surface). They monitored transfer of octanal across the material held at 30 °C for 8–10 hours. Transfer was most rapid through uncoated paperboard. Octanal was shown to transfer across PE film laminated to the paperboard within ten minutes. There was no transfer of octanal through PP, Al/PE and PET over ten hours.

Triantafyllou *et al*. (2005), in studies on transfer of potential contaminants from paper and board to food, measured partition coefficients between packaging and air for a range of substances. This was, therefore, an attempt to measure the potential for gas-phase transfer. A mixture of acetophenone (b.p. 203 °C), naphthalene (b.p. 218 °C), benzophenone (b.p. 306 °C), dibutyl phthalate (b.p. 340 °C) and methyl stearate (b.p. 443 °C) was placed in a vial together with samples of test liner made from virgin fibres or triplex board made from 100% recycled fibre. There was no contact between the substances and the paper or board. Vials were sealed and heated at 70 °C or 100 °C and then the paper removed and analysed for uptake of substances. Conclusions from the studies were that:

- The volatile substances partitioned more readily into the vapour phase.
- Acetophenone partitioned more strongly into paper than would be anticipated from its boiling point alone. The authors concluded that this was due to a high affinity between the substance and the fibres, although they did not

offer an explanation for this high affinity.
- Naphthalene partitioned less readily than anticipated. It was hypothesised that electron-rich species such as naphthalene are repelled by the overall negative charge of cellulose fibres due to carboxyl groups from carbohydrates and hydroxyl groups of lignins.
- The thickness of the board plays a role in partitioning, with higher partition coefficients in thicker paperboard materials.
- The total amount of surrogates in the air would be absorbed by the food.
- Higher temperatures pose an increased risk in terms of potential transfer to foods as substances are more likely to partition into the vapour phase at higher temperatures and hence are more likely to transfer to foods.

Studies carried out with the aim of developing models to estimate migration include a study by Aurela and Ketoja (2002). They estimated the diffusion rate of model compounds (butanol, ethanol, butyl acetate and tetrahydrofuran) in air at room temperature. They then measured the diffusion of these substances through papers with different grammages (and hence, porosities) produced from birch Kraft pulp. The model compounds were not in contact with the test papers and hence transferred via the gas phase. They concluded that the diffusion constants determined in air could be used in 'random walk' simulation to predict migration in a fibre network. Random walk simulations are a mathematical means of modelling processes based on probability distribution and are often applied to investigate diffusion processes.

18.5.2 Gas phase transfer to foods

Whilst there is considerable evidence to indicate that substances can volatilise from and/or transfer through packaging materials to the gas phase, there are very few studies on gas phase transfer to foods. Indirect evidence for gas phase transfer to foods was seen in studies by Anderson and Castle (2003) who measured levels of benzophenone in foodstuffs packaged in printed cartonboard materials. Benzophenone is a photoinitiator used in some UV cure inks for the printing of paper and board materials and has been shown to be present in printed paper and board materials indicating that it remains in the paperboard after printing (Johns *et al*., 1995).

Anderson and Castle detected benzophenone in foodstuffs where there was direct contact with the paper and board packaging and also in some foodstuffs where there was indirect food/packaging contact. Intervening materials between the outer board packaging and the food included plastic wrappers, foil/plastic packets, plastic trays and lids and foil trays with plastic wrap. These types of materials are not printed with UV cure inks and hence are unlikely to have been a source of benzophenone. This indicates that the benzophenone transferred from secondary packaging, through primary packaging layers to foods. Analysis of chilled and frozen foods also indicated transfer of benzophenone. It was noted that the average percentage transfer of benzophenone was lower to foods in indirect contact than to foods in

direct contact and even lower to chilled or frozen foods. The mean percentage transfer of benzophenone from cartonboard in direct contact with foods stored at room temperature was 16.1% whereas the mean transfer to foods in indirect contact at room temperature was 2.7%, i.e., a six-fold difference in transfer between direct and indirect contact situations.

A similar reduction in transfer was seen for chilled and frozen foods where the average percentage migration was 2.6% where there was direct contact between the food and packaging compared with 0.4% for indirect contact. It should be stressed that the samples analysed were retail purchases. Hence the types of foodstuffs, packaging and levels of benzophenone were not the same for the direct and indirect contact situations. Caution should therefore be exercised in interpreting the results as they are not a direct comparison of transfer in direct and indirect contact situations. Nevertheless, the results of this study provide evidence that there can be transfer of substances from secondary packaging to foods.

Research by Mariani and co-workers (Mariani *et al.*, 1999) identified transfer of diisopropylnaphthalenes (DIPNs) through the gas phase to rice. Evidence for possible transfer of DIPNs from secondary packaging to food was provided by studies carried out for the UK Food Standards Agency (MAFF, 1999). These substances were detected in a variety of foods. Some of the packaging samples contained an intervening film wrap between the food and the recycled board but this did not contain DIPNs nor appear to influence the migration. This indicated that the DIPNs had transferred to foods from the secondary packaging.

Donetzhuber and co-workers (Donetzhuber *et al.*, 1999) also recognised the potential for gas phase transfer of substances from packaging to foods. They noted that the following parameters could influence transfer: time, temperature, physical state of the foodstuff (e.g. fat and/or water content, dry product), size of packaging, mass of product, handling conditions (e.g. deep freezing versus microwave heating). They used headspace GC-MS analysis to determine substances which transferred to the vapour phase from paper and board samples. Substancs identified included aldehydes, alcohols, ketones, ethers, aromatics (including cyclic compounds), heterocyclic compounds, esters, acids, terpene hydrocarbons and other substances which they categorised as 'substituted compounds'. They carried out quantitative transfer studies, using icing sugar as a test medium. They detected transfer of some substances and concluded that transfer of alkanes, aromatics and terpenes to icing sugar was higher than transfer of alcohols, aldehydes and ketones.

The most extensive studies to date on transfer from secondary packaging to foods have been carried out by Jickells and co-workers (Jickells *et al.*, 2005). These studies used combinations of food and packaging as would be used for retail sale. Cartonboard and corrugated board box were used in the study because they are used widely as secondary packaging materials. Model compounds (benzophenone, diheptyl phthalate, 2,6-diisopropylnaphthalene, 2,2-dimethoxyphenylacetophenone, 2-ethylnaphthalene and 2,4,6-

trichloroanisole) were incorporated into the secondary packaging to provide a potential source of substances whose transfer could be monitored over time. The presence of benzophenone was detected in some of the secondary packaging materials used in the study. For these materials, benzophenone was not incorporated as a model substance. Foods/packaging combinations used are shown in Table 18.1. The experimental set-up for the food storage studies is shown in Fig. 18.1.

Foods were stored for up to 200 days, sampled at known time intervals and then analysed for the model substances. The conclusions of the study were as follows:

- The levels of transfer of benzophenone as an intrinsic migrant in secondary packaging paralleled those of the model substances. This provided a verification of the use of model compounds.
- For all food/packaging combinations studied, there was a higher level of

Table 18.1 Foodstuffs and packaging used for studies investigating factors affecting gas phase transfer (Jickells *et al*., 2004)

Foodstuff	Primary packaging	Secondary packaging
Milk chocolate-coated cream wafer bars	PP film wrapper printed on outer surface with nylon-based resin ink	Corrugated board box
Milk chocolate-coated cream wafer biscuits	Printed cold-seal PP film for individual bars in PP film multipacks	Cartonboard box fully printed on outer surface
Chocolate-coated ice-cream bars	Paper	Cartonboard box fully printed on outer surface
Oatcake biscuits	OPP film (coated on one surface with VdC copolymer) heat-sealed bag	Cartonboard box fully printed on outer surface
Savoury crackers	Heat-sealed PP bag	Cartonboard box fully printed on outer surface
Wheat biscuit breakfast cereal	Paper coated on inner surface (EVA-copolymer?)	Cartonboard box fully printed on outer surface
Wheat biscuit breakfast cereal	PP film	Cartonboard box fully printed on outer surface
Hand-fried type crisps (potato chips)	Metallised PP/PP laminate (outer PP film reverse-printed with nylon-based resin ink) bag	Corrugated board box
Crisps (potato chips)	PP film (fully printed on outer surface) heat-sealed single packs packed in PP film heat-sealed multipack (partially printed on outer surface)	Corrugated board box
Dried raisins	Cartonboard boxes in PP film overwrap (coated on both surfaces with VdC copolymer)	Corrugated board box

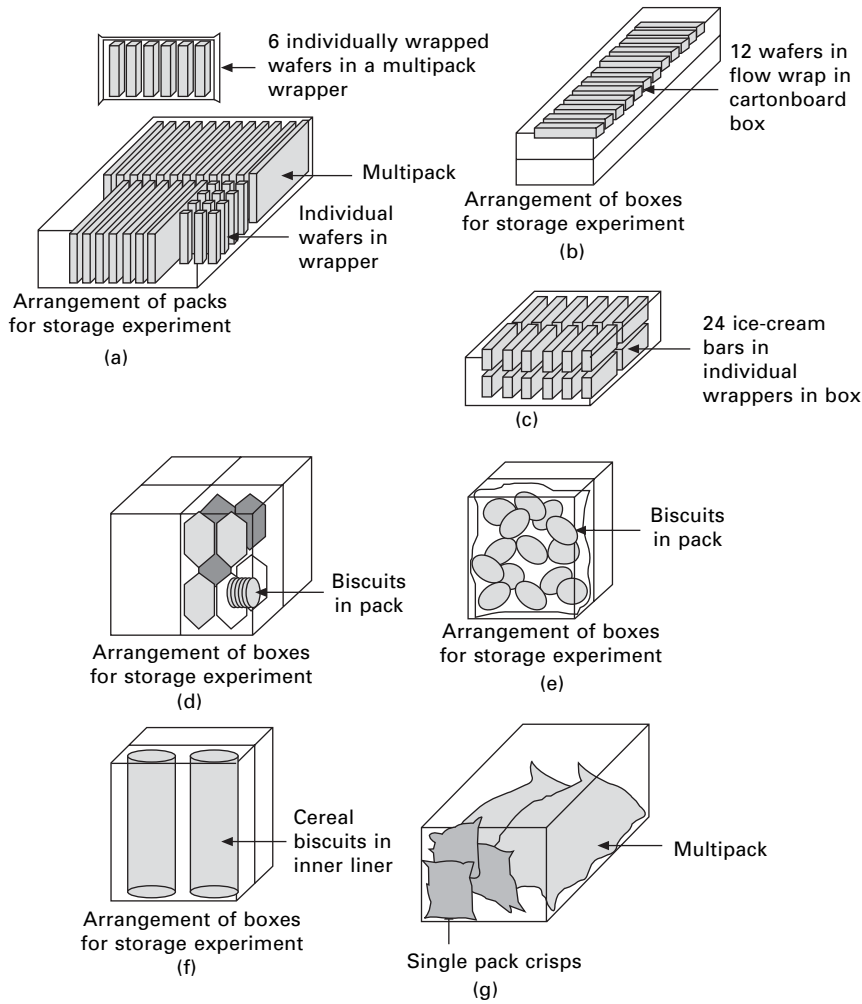

Fig. 18.1 Food/packaging configurations for transfer studies from secondary packaging to foods (Jickells *et al*., 2005): (a) chocolate-coated cream wafer bars single- and multi-pack format in corrugated board box; (b) milk chocolate-coated wafer biscuits in cartonboard boxes; (c) chocolate-coated ice-cream bars in cartonboard box; (d) oatcake biscuits in cartonboard boxes; (e) savoury crackers in cartonboard boxes; (f) wheat biscuit breakfast cereal in cartonboard boxes; (g) crisps (potato chips) in corrugated board box.

transfer of the more volatile test substances compared to those of lower volatility. Transfer of trichloroanisole (b.p. 260 °C) and 2-ethylnaphthalene (b. p. estimated as 252 °C) from secondary packaging was detected into all food and packaging combinations tested. Transfer of benzophenone (b. p. 305 °C) and diisopropylnaphthalene (b. p. 279 °C) to food was detected for seven and ten, respectively, of the 12 food/packaging combinations tested. Transfer of 2,2-dimethoxyphenylacetophenone (b.

p. estimated as 352 °C) was detected for three of the 12 combinations. No transfer of diheptyl phthalate (b. p. estimated as 425 °C) was detected to any foods over the test period (200 days). This indicated that when testing secondary packaging materials for migration, greater attention should be paid to more volatile substances present as these have the greatest propensity to migrate. The data indicated that substances with a boiling point and/or volatility similar to that of diheptyl phthalate have a considerably lower propensity to migrate from secondary packaging. Hence there would be less need to test for these substances in secondary packaging. There is a proviso on this statement regarding concentration. As migration is concentration driven, it is possible that there could be transfer of less volatile substances if they were present at very high concentrations (a maximum level of 0.93 mg/dm^2 diheptyl phthalate was tested in this study).

- Transfer of substances increased with increasing storage time. Transfer was more rapid for substances of lower boiling point and was slower for higher boiling point substances. For some packaging/food combinations, transfer reached a maximum within the test period. Maximum transfer of trichloroanisole to wheat biscuit breakfast cereal occurred at about 90 days. For benzophenone, transfer to the cereal had not reached a maximum at 200 days, illustrating the link between volatility and transfer.
- Percentage transfer varied from 0% to 100%. The highest transfer occurred for 2-ethylnaphthalene from a cartonboard box through a PP wrapper into savoury biscuits, with *ca*. 13.9 mg/kg transferred to the food at 200 days, representing 100% transfer. There was also considerable transfer from a cartonboard box through a paper wrapper to wheat breakfast cereal, again for 2-ethylnaphthalene, with 13 mg/kg transferred to the food at 200 days, representing 50% transfer.
- Paper was shown to be a poor barrier to transfer where there was a relatively narrow air gap between the secondary packaging and the food, i.e., wheat breakfast cereal in a paper wrapper inside a cartonboard box. A PP wrapper in the same situation reduced transfer by between three to 19-fold (three-fold for trichloroanisole and 2-ethylnaphthalene, 7-fold for diisopropylnaphthalene and 19-fold for diisopropylnaphthalene at 200 days).
- Transfer to chocolate-coated ice-cream bars, stored at –20 °C in paper wrappers, was detected from corrugated board secondary packaging, with up to 4.5 mg/kg of trichloroanisole and benzophenone present in the ice-cream bars after 250 days, representing 69% and 26% transfer respectively. This demonstrated that there can be transfer of volatile substances from secondary packaging to foods during freezer storage.
- The presence of an additional layer of film, e.g., as in multipack situations, reduced migration compared to a single layer of film only. For chocolate-coated wafer bars (a confectionery product), transfer to multipacks (two layers of PP film) was approximately four-fold lower than to bars packed

individually in PP film stored in a corrugated board box (secondary packaging). Transfer to crisps in multipacks (two layers of PP film) was approximately two-fold lower than to individual packs stored in a corrugated board box. Transfer to crisps packaged in a single layer of reverse printed (nylon based resin) metallised PP/PP laminate film was reduced 20-fold compared to the individual packs of crisps in PP film.

It should be noted that the food storage studies of Jickells *et al*. (2005) were carried out with the secondary packaging materials over-wrapped with aluminium foil. This over-wrapping will have served to restrict volatilisation of substances to the interior of the secondary packaging. It therefore more closely represents the situation where a corrugated board box (containing food wrapped in primary packaging) is stored in the middle of a stack surrounded by other similar boxes. This is in contrast to the situation where a box is stored alone with no contacting boxes or over-wraps. In such a situation, substances can volatilise both to the interior of the box and to the exterior. Substances volatilising into the airspace around the box will simply diffuse away. This will further force the atmosphere:packaging – substance: food equilibrium towards loss of substance from the packaging and the food to the atmosphere. Hence it is likely that transfer from secondary packaging to foods in this situation will be lower than to foods in boxes stored in the centre of a stack.

Further studies have been carried out by Jickells and co-workers (Jickells *et al*., 2004) to investigate the factors which influence gas phase transfer from secondary packaging materials. Factors investigated were:

- nature of the intervening layer (primary packaging material)
- volatility of the transferring substance
- time/temperature of exposure
- transfer distance between primary and secondary packaging
- humidity
- concentration of substance in the secondary packaging
- nature of the foodstuff.

Cartonboard was used as secondary packaging material for the studies. Model substances were incorporated into the cartonboard to provide potential migrants. Model substances were as listed above for the studies of Jickells *et al*. (2005) but, in addition, benzyloxypropiophenone and benzyl butyl phthalate were also incorporated. The cartonboard was then overlain with primary packaging material and modified polyphenylene oxide (MPPO), used as a receiving matrix, was placed on the primary packaging material (Fig. 18.2). MPPO was used as the receiving matrix for the majority of studies. This is a polymeric material used widely in studies on volatile substances and an officially recognised test medium under EU legislation for plastics materials and articles. Primary packaging materials tested to investigate the nature of the intervening layer on transfer were PP film; reverse-printed metallised PP/PP laminate; PVdC-coated PP; nylon/PP laminate; PET. The effect of an air gap (1 cm or

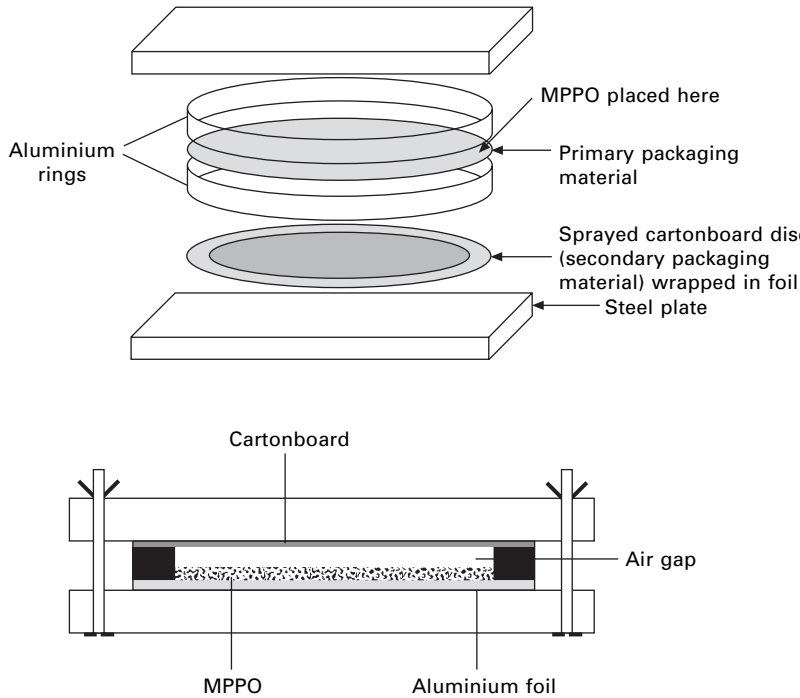

Fig. 18.2 Experimental set-up for studies investigating factors affecting gas phase transfer (Jickells *et al*., 2004): (a) investigating influence of primary packaging material and concentration of substances in secondary packaging material; (b) investigating influence of air gap between primary and secondary packaging material.

2 cm) between the primary and secondary packaging material was also investigated.

For studies carried out investigating the nature of foodstuffs, MPPO was replaced by wheat biscuit breakfast cereal (representing a dry foodstuff with low fat content), savoury biscuits (dry foodstuff with high fat content), butter (fatty foodstuff) or orange juice (acidic foodstuff). PP film was used as the primary packaging material for the studies with foods. Conclusions from the studies were as follows:

- Under the conditions studied, the relative effectiveness of primary packaging materials in terms of reducing transfer of substances from secondary (2°) packaging to MPPO was: PET >nylon> PVdC-coated PP > metallised PP/PP laminate > PP > paper.
- Volatile substances transferred to MPPO more readily than less volatile substances at any given temperature, irrespective of the nature of the primary packaging.
- Transfer of substances increased with increasing temperature and storage time.
- Transfer of benzyloxypropiophenone was detected through paper at

20 °C after 90 days but transfer of benzyl butyl phthalate and diheptyl phthalate was not detected at this time/temperature. This supports the conclusions noted above for studies on the transfer from secondary packaging to foods, i.e., that there appears to be a boiling point or volatility cut-off threshold for transfer at ambient temperature and that the cut-off is above the boiling point/vapour pressure of 2,2-dimethoxyphenyl-acetophenone but below that of benzyl butyl phthalate and diheptyl phthalate.

- The use of an air gap between primary and secondary packaging could reduce transfer of less volatile substances in comparison with situations where there is no air gap but it will not reduce transfer of more volatile substances (e.g. substances with volatility similar to trichloroanisole and 2-ethylnaphthalene). These volatile substances transfer readily at all temperatures, including –20 °C. Using paper or PP as a primary packaging layer in association with an air gap at above ambient temperatures will have minimal effect in reducing transfer.
- For nylon as a primary packaging material, transfer to MPPO under high humidity conditions (90% humidity) increased compared to low humidity conditions. Transfer across PP and PET was not affected by humidity. Results for paper were inconclusive and there was insufficient material to re-test.
- Transfer of substances increased with increasing concentration in the secondary packaging material.

Jickells and co-workers (2004) also evaluated MPPO in terms of migration testing. They concluded that MPPO can be used as a test medium to assess transfer from secondary packaging materials. They proposed a test condition of 6 h at 60 °C but suggested that further studies should be carried out to determine whether the proposed test condition is appropriate for a wider range of food/packaging combinations than those that were tested in their study.

18.6 Improving the safety of secondary packaging materials with regard to chemical migration

In a report detailing research carried out for the UK Food Standards Agency on transfer from secondary packaging to foods, Jickells *et al*. (2004) proposed a set of guidelines on how transfer from secondary packaging could be minimised. The recommendations were as follows:

All persons involved in manufacturing materials intended to be used as secondary packaging for foodstuffs and those involved in supplying food for human consumption should take into consideration secondary packaging used in the storage, transport and distribution of food at all stages of the food production process, including importation of foodstuffs. In order to

minimise transfer, attention should be paid, in particular, to the following aspects.

Residual substances

Manufacturers of secondary packaging, packaging converters and printers, food manufacturers, food distributors and retailers should ensure that the raw materials and processes used in manufacture, food distribution and retail sale do not result in residues of substances in the packaging which could subsequently transfer to foods and pose a risk to human health.

The volatility of a substance is of particular importance in transfer. The more volatile a substance, the more readily it is likely to transfer to foods if it is present in secondary packaging, compared to less volatile substances. This assumes that the substance can transfer through the primary packaging or other intervening layers (see section below on intervening layers).

There are indications that substances with boiling points in excess of about 350 °C do not transfer readily from secondary packaging to foods at ambient temperature (20–25 °C) and below, even at storage periods of up to six months. The research indicated that, provided substances are present at a concentration of 1 mg/dm^2 or below, less attention need be given to minimise residues of substances with boiling points greater than or equal to (≥) 350 °C. Substances with boiling points of less than or equal to (≤) 350 °C were shown to transfer from 2° packaging to foods. In general, the more volatile the substance the more readily it transferred to foods. In particular, substances with boiling points ≤250 °C transferred readily from 2° packaging. Therefore attention should be paid in particular to the presence of substances with boiling point ≤250 °C.

Attention should also be paid to the concentration of substances in the secondary packaging. For any given substance which is sufficiently volatile to transfer from secondary packaging and which can transfer through intervening layers, the higher the concentration in the secondary packaging, the higher the rate of transfer will be. Thus potentially, the higher the concentration in the foodstuff will be. Therefore, if it is not possible to eliminate residues of substances present in secondary packaging, the concentration of the substances in the packaging should be reduced to as low a level as possible to minimise transfer.

Time and temperature

Transfer of substances will also depend on the time and temperature of storage and/or processing or heating of food in 2° packaging. For a given substance, the lower the temperature, the lower the rate of transfer will be and, conversely, the higher the temperature, the higher the rate of transfer.

If substances are present in the secondary packaging material which are sufficiently volatile to transfer under the conditions of storage, there will be a lag period (or delay) before transfer to foods occurs. The length of this lag period will depend on the volatility of the transferring substance, the nature of the primary packaging or other intervening layers, temperature,

concentration of substances in secondary packaging and the nature of the packaged food.

Once transfer to food occurs it will continue until equilibrium is established between the level in the packaging, the level in the food and loss to the surrounding environment. The length of time required to establish equilibrium will be influenced by the volatility of the transferring substance, the nature of the intervening layers, the nature of the foodstuff and the ability of the substance to volatilise into the surrounding environment.

Hence, for a given substance, the longer a foodstuff is stored in a secondary packaging material, the greater the transfer of the substance will be until the equilibrium position is reached. This assumes that equilibration involves the secondary packaging and food only and that there is no possibility for loss to the external environment.

The influence of temperature and time of storage on transfer means that the conditions of use of the secondary packaging must be taken into consideration when assessing suitability of that material.

Intervening layers

The nature of the packaging layers between the secondary packaging and the food will influence transfer. Under the conditions studied in this research, the relative effectiveness of primary packaging materials in reducing transfer of substances from secondary packaging to foods was:

> PET > nylon > VdC-coated PP > metallised PP/PP laminate > PP > paper.

The presence of a second layer of primary packaging material will reduce transfer compared to situations where a single layer only of the material is employed. The use of an air space between primary and secondary packaging could be used to reduce transfer of less volatile substances. It will not reduce transfer of more volatile substances (boiling points ≤250 °C) if these substances can transfer through the primary packaging when there is no air space.

Nature of the foodstuff packaged

If a substance is able to transfer from secondary packaging through the primary packaging layer(s), then the nature of the foodstuff will influence transfer. The order of transfer is:

> fatty food > dry fatty food > dry low fat content food > aqueous, non-fatty foods.

Thus attention should be paid to the type of food to be packed, with particular attention to be paid to fatty foods. However, it should be noted that there can be transfer through some types of primary packaging materials to dry foods of low fat content (e.g. 3% fat) and so it should not be assumed that transfer will not take place to these types of foods. Transfer will occur less readily to aqueous, non-fatty foods.

Humidity
Transfer through some types of primary packaging materials can be affected by humidity. Transfer through PP and PET does not appear to be affected by humidity. Transfer through nylon/PP laminate was higher under high humidity conditions (90%) compared to low humidity (20%) conditions at above ambient temperatures. If nylon materials are to be used under conditions of high humidity, this should be taken into account when evaluating the potential for transfer from secondary packaging through nylon as primary packaging.

Testing
The studies underpinning these guidelines proposed a test condition of 6 h at 60 °C using MPPO as a test medium to assess ambient temperature transfer from secondary packaging to foods. These conditions were found to be appropriate for fatty foods, dry fatty foods and dry foods of low fat content, during their long term storage. Transfer of model substances using these test conditions was generally equal to or more stringent than transfer to these food types stored at ambient temperature for up to 200 days. However, further studies should be carried out to verify that this proposed test condition is appropriate for a wider range of food/packaging combinations than were tested. It was found that these test conditions (of 60 °C for six hours using MPPO) overestimated transfer to aqueous non-fatty foods.

Therefore, on the evidence of this study, if testing is required to evaluate transfer from secondary packaging used for ambient long-term storage of foods other than aqueous non-fatty foods, it is recommended that the test condition of six hours at 60 °C be used. MPPO is suggested as a test medium (4 g/dm^2 of material or article). The material will need to be held in a leak-tight cell to avoid loss of transferring substances. The appropriate primary packaging should be placed between the secondary packaging material and the MPPO, i.e., the primary packaging material which will be used in normal or foreseeable conditions of use of the secondary packaging material. For the testing of aqueous non-fatty food it is suggested that the simulants specified in EU Directives for testing aqueous foods coming into contact with plastics materials and articles should be used in place of MPPO.

With regard to testing, the crucial word in the paragraph above is ‘if’ as in ‘if testing is required’. Whilst there is evidence to indicate that there can be transfer from secondary packaging to foods if substances are present which are sufficiently volatile to transfer to the vapour phase, it is still not clear whether secondary packaging could pose a risk to health in terms of transfer of substances. As noted above, very few studies have been carried out on transfer from secondary packaging to foods and so there is simply insufficient data available on which to form an opinion. However, it would appear prudent that manufacturers and users of secondary packaging materials

should consider the possibility of transfer from their materials. They should take the necessary steps to ensure that their materials comply with the core requirement of EC Regulation No. 1935/2004 regarding inertness and preclusion of transfer of substances to foods in quantities which may endanger human health or produce an unacceptable change in composition or deterioration in organoleptic properties.

18.7 Future trends

18.7.1 Mathematical models

The issue of transfer from secondary packaging to foods and assessing safety-in-use of such materials is in its relative infancy, compared to the situation for transfer from primary packaging materials. For these latter materials and articles, a large body of evidence concerning transfer of substances is available and comprehensive test protocols are in place to assess transfer. In fact, some manufacturers and users of plastics materials and articles for direct food contact use consider that the legislation and testing protocols are too stringent and very onerous. To overcome the problem of onerous testing, a mathematical modelling approach to assessing the potential for migration has been developed and accepted by the EC (Chapter 8). A mathematical modelling approach would seem a natural progression for secondary packaging materials. Aurela and Ketoja (2002) have already started along this route for paper and board materials and Triantafyllou and co-workers (2005) are also seeking to use adsorption isotherms and partition coefficients to evaluate the ability of contaminants to migrate from paperboard to foods or food simulants. Thus far, they have determined partition coefficients to evaluate whether a substance will preferentially transfer to air or packaging.

18.7.2 Use of cut-off threshold for transfer

If, as Jickells *et al*. (2005) have proposed, there is a volatility cut-off threshold for secondary packaging materials it will be exceedingly useful to assign a value for this threshold. This would allow manufacturers and user of packaging materials to evaluate whether substances present in their materials have volatilities above or below the threshold. For substances less volatile than the cut-off threshold, it could be assumed that transfer from the material is likely to be negligible when used as secondary packaging (but see note above regarding the maximum concentration tested in the studies of Jickells *et al*., 2005) and hence that there is no need to carry out any further assessment for these substances.

A key parameter for assessing the potential of a substance to transfer to the gas-phase is the vapour pressure of the substance. The range of substances for which vapour pressure values are available is rather restricted. More importantly, the parameter that really needs to be known is the vapour pressure

in the packaging material. These values are not readily available. However, the research of Triantafyllou *et al*. (2005) has already provided partition coefficient data for substances partitioning between paperboard and air which gives an indication of the propensity of a substance to transfer from packaging to the gas phase. In terms of the cut-off threshold, it would be far simpler if it could be expressed as boiling point, molecular weight or assessed from the chemical structure of a compound because these are much simpler parameters for manufacturers and enforcement laboratories to determine without carrying out experimental work. This would seem to be an important area for study.

18.7.3 Further studies on transfer from secondary packaging

As so little data is available on transfer from secondary packaging to foods it would be useful if more studies were carried out to look at this phenomenon. This would provide a more solid foundation for decisions to be made on whether such materials pose a risk in use and whether further controls are required for these materials in terms of testing.

18.8 Sources of further information and advice

As noted above, the issue of secondary packaging is a relatively unexplored one in terms of applicable legislation and testing required to ensure safety in use. The reader is referred to EC legislation on materials and articles intended to come into contact with foods for general guidance on ensuring the safety-in-use of packaging materials. It is recognised that much of the emphasis is on plastics materials and articles, but the general provisions of the legislation apply to all packaging materials. For paper and board materials, the reader is referred to the Council of Europe Resolution on Paper and Board and associated technical documents (Council of Europe, 2005). These documents have no legislative standing in the UK but give guidance that may be helpful. Although having no recognised legislative or similar standing, the reader is also referred to the guidelines developed by Jickells *et al*. (2004) concerning secondary packaging (see section 18.6).

18.9 References

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19

Case study: Chemical migration from snack and take-away food packaging

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19.1 Introduction

Although the generic material types used to package snack and take-away foods are the same as those used to package other foodstuffs, the food contact conditions are quite different. Snack foods are characterised by a high packaging usage (large surface area of packaging to mass of food ratio) and many have fat present on the surface, which will increase the migration of any fat soluble substances present in the packaging. The material types used to package take-away foods, i.e., paper, cartonboard and plastics, are used in many food contact applications. However, due to the nature of the short-term contact it is not always necessary for these materials to be as durable as those used to package foods for a longer period of time. Although contact time is generally short the majority of take-away foods are served hot, which will accelerate any migration. Like snack foods many take-away foods also have fat on the surface. As a result of these factors, snack and take-away food packagings are considered to warrant special mention over other food packaging materials. In addition, the consumption of both snack and take-away foodstuffs is increasing as consumer eating habits tend towards more convenience foods.

This chapter describes the types of materials and articles that may come into contact with snack and take-away foods, the factors affecting chemical migration into these foods and beverages, and provides examples (not exhaustive) of migration studies carried out. The current legislation applicable to these materials is referred to but is described more fully in other chapters. Sources of additional information are provided.

19.2 Definitions

The *Oxford English Dictionary* definitions of snack and take-away foods are:

Snack – 'small amount of food eaten between meals'. Snack foods are generally considered to be foods designed to be eaten with fingers, not sweetened (confectionery) and not heated (take-away), without further preparation, and usually direct from the packaging.

Take-away food – 'a meal or dish bought from a shop or restaurant to be eaten elsewhere'. Take-away foods may also be referred to as fast food which is defined as 'easily prepared processed food served in snack bars as a quick meal or to be taken away'.

19.3 Usage statistics for snack and take-away foods

19.3.1 Snack foods

Snack foods have been one of the fastest growing sectors of the food market in recent years, with both volume and value consumption increasing. Sales of snack foods in the UK increased by over 10% between 2000 and 2003.[1] A decline of 3.5% occurred in 2004, proposed to be due to public concern regarding rising levels of obesity and the need to follow a healthier and more balanced diet.[1] In 2004 sales of savoury snacks throughout the EU amounted to almost 1,500,000 tonnes, with a retail value of €10.8 billion.[2] Potato chips are by far the largest single category in the EU savoury snacks market accounting for almost 550,000 tonnes, with a retail sales value of over €4 billion (in 2004), and the UK is the largest consumer of savoury snacks in Europe.[2] Other foodstuffs included in the snack foods category are savoury bagged snacks, nuts, and plain and savoury biscuits.

19.3.2 Take-away foods

The take-away food market encompasses outlets such as local roadside caravan stalls through to multi-national chain stores offering a wide variety of hot and cold food and beverages. Take-away foods can include self-serve foods such as obtained from vending machines. Pre-packed sandwiches are also included in this classification because packing can take place locally in small units, although centralised packing and distribution of such items is becoming more commonplace. UK take-away sales grew at 3% in 2003 and 3.9% in 2004 to stand at £8.38 billion, with the UK market being the largest in Europe. The market share in 2004 was sandwiches, 36.5%; burgers, 22.5%; fish and chips, 11.2%; pizza, 10.6%; chicken, 6.3% and 'others', 13.2%.

19.4 Food packaging materials used for snack and take-away foods

19.4.1 Materials used for snack foods

In a study investigating the migration from snack food packaging materials the materials used to package 40 snack foods were determined using Fourier transform infra-red spectroscopy.[3] Foods groups were selected based on market share and the materials found to package these foods are described in Table 19.1. The majority of the samples were packaged in mono- and multi-layer plastics and plastic/board laminates. For these systems migrants may not only originate from the plastic and/or paper but also from the adhesive used in the lamination process. Snack food packaging materials are generally extensively printed to attract consumers to a product.

19.4.2 Materials used for take-away foods

In a recent study in which 180 take-away foodstuffs were purchased[4] and in a follow-up study in which 30 take-away foodstuffs were purchased[3] the packaging materials identified included paper, corrugated board, polyethylene coated board, polyethylene, polypropylene, polystyrene, vinyl acetate/vinyl chloride co-polymers, metallised polypropylene and lacquered aluminium. Details of the packaging materials identified are given in Table 19.2. As mentioned previously the short contact time between the packaging and the foodstuff means that these materials need not be as durable as other packaging systems. For example, the packaging is not usually sealed. Many samples were printed, several of the paper and board samples were treated (grease-proofing agents and/or fluorescent whitening agents and/or wet strength agents were present) and many incorporated recycled fibres.

When purchased by the consumer take-away foods may also have come into contact with other food contact materials. Examples include the packaging in which the food is stored prior to cooking/heating, the metal and/or plastic food contact utensils and the cookware (e.g. metal pans which may have a non-stick coating applied) used in the cooking/heating of the foodstuff at the point of sale. Migration from these materials and articles is not described here.

No food packaging materials are completely inert and any of them may contain chemical substances that have the potential to migrate into the food with which they come into contact. These chemical substances fall into two classes: (i) known ingredients needed to make the packaging and (ii) known or unknown isomers, impurities, reaction products or breakdown products of these ingredients. A large number and variety of chemicals are needed to make packaging materials with the technical properties required and numerous potential migrants exist.

Table 19.1 Materials used to package snack foods[4]

Snack food type	Description of the packaging materials identified for each snack food type
Potato chips	Polypropylene/aluminium/printing inks/polypropylene laminate Printed (external surface) polypropylene Polyethylene/aluminium/cartonboard container laminate printed on the external surface Polyethylene/aluminium/paper laminate with an uncoated metal base
Savoury bagged snacks (such as Twiglets, pork scratchings, Bombay mix, etc.)	Polypropylene/aluminium/printing inks/polypropylene laminate Printed (external surface) polypropylene Polyethylene/printing inks/polyvinylidene chloride laminate Polypropylene/printing inks/polypropylene laminate
Nuts	Polyethylene/aluminium/printing inks/polyester film laminate Polyethylene/aluminium/cartonboard container laminate printed on the external surface Polyethylene/aluminium/paper laminate with an uncoated metal base
Biscuits	Polypropylene/aluminium/printing inks/polypropylene laminate Externally printed polyvinylidene chloride Polyethylene bag within a printed cartonboard box
Processed meat products	Polyethylene bag within a printed cartonboard box Polyethylene/printing inks/polyester laminate Printed polyethylene to which a printed sticky label was applied Polypropylene container to which a printed sticky label was applied with a polystryrene lid
Processed cheese products	Polyethylene/printing inks/polyester laminate Polypropylene container with an aluminium lid coated with an acrylic based resin on the food contact surface and with nitrocellulose resin on the external surface
Salads/olives	Polypropylene container Polyvinyl chloride container
Fruit snacks	Polyethylene/aluminium/printing inks/nitrocellulose coated laminate Polypropylene bag to which a printed sticky label was applied Cartonboard box printed on the external surface

19.5 Chemical migration

As for all food contact materials, chemical migration from materials and articles which come into contact with snack and take-away foods occurs as a result of diffusion processes that are subject to both kinetic and thermodynamic

Table 19.2 Materials used to package take-away foods[3,4]

Take-away food type	Description of the packaging materials identified for each take-away food type
Fish and chips	Grease-proof paper Expanded polystyrene tray Paper bag
Meat pie/vegetable pie/sausage and chips	Brown paper bag Expanded polystyrene tray
Burgers (beef, chicken and vegetarian)	Expanded polystyrene tray Grease-proof coated paper printed on the external surface Paper/polyethylene laminate printed on the external surface Grease-proof coated paper bag printed on the external surface Grease-proof coated paper/board box printed on the external surface
Chicken pieces	Polyethylene coated foil-lined paper bag printed on the external surface Grease-proof coated paper bag
Fries	Grease-proof coated paper bag printed on the external surface Paper/polyethylene laminate printed on the external surface Board printed on the external surface
Indian dishes	Polyethylene coated foil lined paper bag Polypropylene tray and lid Aluminium foil tray with a polyethylene coated paper/board lid Polyvinyl chloride/vinyl acetate container Foiled paper bag
Chinese dishes	Aluminium foil tray with a polyethylene coated paper/board lid Paper bag grease-proof coating on the food contact surface Paper bag Polypropylene tray and lid
Pizza	Corrugated board box printed on the external surface
Sandwiches	Paper bag printed on the external surface; grease-proof coating on the food contact surface PVC container to which a printed sticky label was applied Paper and polypropylene bag Polypropylene container to which a sticky label was attached Polyvinyl chloride/vinyl acetate container to which a sticky label was attached Expanded polystyrene container
Beverages	Board/polyethylene laminate cup printed on the external surface with a moulded polystyrene lid Expanded polystyrene

control. Any migration that takes place will be dependent on the length of time that the food packaging is in contact with the foodstuff, the temperature of the contact, the thickness of the packaging material, the concentration of the migrant in the packaging, the partition coefficient of the migrant between the packaging and the foodstuff and the diffusion coefficient of the migrant in the packaging material.

19.5.1 EU legislation

Although no specific legislation exists in the EU for several of the packaging material types, printing inks and coatings identified as used in snack and take-away food packaging (Tables 19.1 and 19.2) all food contact materials must comply with the Framework Regulation (EC) 1935/2004[5] (see Chapter 3. Similar basic principles are included in the US (Food and Drug Administration) (see Chapter 2) and Japanese laws on chemical migration into foodstuffs.

In the absence of specific legislation for the other (non-plastic) food contact materials used in take-away and snack food packaging then the plastics legislation is used as a guide, although limits are not taken as presumptive standards. Where possible, in the absence of specific migration limits (SMLs), levels found are related back to exposure restrictions such as tolerable daily intake (TDI) or acceptable daily intake (ADI).

19.5.2 Features of snack food packaging that may result in increased migration

When setting SMLs, the food contact ratio of 1 kg of foodstuff packed in 6 dm^2 of plastic packaging is conventionally applied. However, this ratio is not relevant for snack foods in which the ratio of packaging area to the mass of the food can be much greater. For example, for a 30 g bag of crisps the area of packaging may be in excess of 4 dm^2 (equivalent to 1 kg of food in 133 dm^2 – 20 times the conventional ratio). Further the assumption that 1 kg of foodstuff is consumed by a 60 kg adult every day[6] is not applicable to children, whose body weight may be significantly less than the conventional 60 kg and who are considered to have a relatively high intake of snack foods. As a result the conventional ratios may not be applicable for snack foods. It is therefore important to determine the levels migrating into food simulants using the measured food contact ratio or better still into the foodstuff(s) packaged in these materials. In addition, many snack foods are fatty and/or contain fat on the surface.[7] As a result, any lipophilic substances present in the packaging materials will have a high affinity for the foodstuff and the partition coefficient of such substances will be in favour of the foodstuff.

19.5.3 Features of take-away food packaging that may result in increased migration

From a chemical migration perspective, take-away foods assume special importance due to their conditions of use. Although the contact time is generally short, in the order of minutes, the majority of take-away foods are served hot. The diffusion processes involved in the migration from food packaging materials are accelerated at elevated temperature, i.e., a given migrant will be more mobile within the packaging material and the foodstuff

at high temperature. As for snack foods many take-away foods contain fat on the surface and have a large packaging usage. For example, a pizza of mass 600 g is packaged in a cartonboard box of total area 30 dm^2 (equivalent to 1 kg of food in 50 dm^2). Although the direct contact is only 7 dm^2 (in this application) the food contact ratio (equivalent to 1 kg of food in 12 dm^2) is double the conventional food contact ratio. Also, the food is served hot which may result in any volatile substances present in the packaging (even that not in direct contact) being released and if these are lipophilic they may trap onto the fatty (cheese) surface.

19.5.4 Generic studies describing chemical migration from snack food packaging

Only a limited number of studies have been carried out to specifically determine the migration of substances present in snack food packaging into foodstuffs. In a study referred to previously the potential migrants present in the packaging of 40 snack foods were established.[3] An analytical screening exercise was undertaken in which volatile substances were determined by headspace gas chromatography coupled with mass spectrometry (GC-MS), semi-volatile compounds were identified by solvent extraction followed by GC-MS and non-volatile and polar substances were analysed by high-performance liquid chromatography coupled with mass spectrometry (HPLC-MS). The majority of the potential migrants identified derived from the printing inks applied to the outside of the packaging. The worst case migration potential was calculated applying the conventional area:mass food contact ratio as well as the actual food contact ratio for the products. The results of the calculations were then compared with any SML restrictions assigned for plastics or the worst-case exposure was determined and this was compared with the ADI/TDI or other exposure restriction values where they have been assigned.

When applying the conventional food contact ratio the worst-case migration potential did not exceed the SML for any of the substances derived from plastics nor did the calculated worst-case exposure exceed the ADI/TDI or other exposure restriction value in any products. However, when the actual food contact ratio was applied the ADI/TDI or other exposure restriction value of several substances could theoretically be exceeded. The worst-case calculations assume that intimate contact is made with the entire surface of the packaging. This is not the case for the majority of snack foods that are solids or semi-solids and so the actual area of contact made will be less than the total area available for contact (e.g. crisps). The levels of those migrants (diisobutyl phthalate, dicyclohexyl phthalate, dibutyl sebacate, diphenyl 2-ethylhexyl phosphate and 2-ethyl-1-hexanol) that had the potential to exceed the assigned restrictions, assuming 100% migration, were determined in foods. Of the five substances tested for, only one, dicyclohexyl phthalate, was detected in one of the foodstuffs (tortilla corn chips), at a concentration of 0.60 ppm.

Applying the convention that a 60 kg adult consumes 1 kg of foodstuff each day then this equates to an exposure of 0.01 mg/kg body weight. The t-TDI for this substance is 0.1 mg/kg body weight. The majority of the potential migrants detected were associated with the printing inks on the outside of the packaging material, which itself may have provided a barrier to reduce migration. All of the snack foods analysed were rigid or semi-rigid solids which did not make complete and intimate contact with the entire surface of the packaging material. As a result, even where potential migrants were present at comparatively high levels in the packaging the levels migrating into the foodstuffs were reassuringly low. As many of the food packaging materials used for snack foods are multi-layer structures then potential migrants may be derived from the adhesive used to laminate the materials together. The migration from laminating adhesives is described elsewhere in this book (Chapter 16) and therefore is not discussed here.

19.5.5 Specific migration studies in which snack food packaging materials have been investigated

Selected examples of specific migration of substances from snack food packaging are described below. These examples are not intended to be exhaustive but are intended to demonstrate the migration concerns relating to these materials. Printed polypropylene may be used to package bagged snacks. Small labile substances from the printing ink may diffuse through the film(s) to contaminate the food contact layer. For mono-layer materials the rate of the diffusion of a given migrant from the printing ink to the food contact surface will be dependent on the partitioning between the ink and the polymer to which it is applied and the diffusion coefficient within the polymer.

For multi-layer materials one or more layer may act as a functional barrier to migration. For example, a layer of aluminium above a given thickness is considered to act as a functional barrier to the migration of all substances providing no pin holes are present. However, in such cases contamination of the food contact surface can still occur by the process known as set-off. When tightly wound the printed surface is in direct contact with the food contact surface and set-off of the printing ink onto the food contact surface may occur by blocking, peeling or rubbing.[8] Diffusion of any substance between the two layers may also occur. Therefore even in the presence of a functional barrier layer contamination of the food contact surface can occur and this may result in migration into foods. Therefore in all cases it is important to ensure that the residual levels of any substances present in the printed packaging materials are sufficiently low such that any migration that does occur is below the level of concern.

19.5.6 Generic studies describing chemical migration from take-away food packaging

As for snack foods, very few studies have been carried out specifically on the identification and the migration of substances present in take-away food packaging into foodstuffs. The UK Food Standards Agency[3,4] has, in recent years, funded two studies to determine the migration of substances present in take-away food packaging materials into foods. In the first study,[4] a survey carried out in 2000, the identities of any potential migrants in the packaging materials were determined in an analytical screening exercise. The same analytical techniques were used as described for snack foods in section 19.5.4. Several potential migrants were identified. The migration into foods of any of these potential migrants detected, for which the ADI, TDI and/or SML restriction might be exceeded, was determined. Analysis of inorganic species (96 elements were monitored) was achieved by acid digestion followed by inductively coupled plasma-mass spectrometry (ICP-MS). Of the 180 packaging materials analysed in this study, 92 of them were found to have extractable substances above 50 mg/kg. The broad screening yielded expected potential migrants such as styrene and oligomers from polystyrenic (PS) materials, phthalate esters from various products, and alkane hydrocarbons and blowing agents from expanded polystyrene (EPS). Additional substances were also detected in the packaging materials. Analysis of the take-away foods packaged in these materials indicated mainly parts per billion (ppb) levels of contamination, however, there appeared to be very little correlation between observed levels in the packaging and the associated food.

As mentioned previously, contamination of take-away foods may occur not only from the packaging materials in which they are placed at the point of sale but also from any materials and/or articles used to store the foods prior to cooking and/or packaging and any utensils and articles used to prepare the foods for consumption. Therefore the source of the contaminants in the foodstuff could not be proven to have originated from the take-away food packaging itself. To identify the extent of contamination from the take-away food packaging itself a second study was commissioned in which triplicate samples of 30 take-away foods were obtained in the form that the product would normally be sold, i.e., in the relevant food packaging material. A further three samples of each food were obtained wrapped immediately in aluminium foil for solid foodstuffs and in glass bottles for liquid/semi-solid foodstuffs, i.e., no contact with the take-away food packaging occurred. These samples were used as controls. By comparing the levels of given substances in these matched sets of foodstuffs the extent of the contamination of the foods from the take-away packaging could be ascertained. All of the packaging types described in section 19.4.2 were included in this follow-up study.

Screening analysis of the packaging materials, carried out as described for the preliminary study, identified several potential migrants. Twenty-five of the 30 take-away food packaging materials had extractable substances at

concentrations above 10 mg/kg. The worst-case migration potential was calculated applying the conventional area:mass food contact ratio as well as the actual food contact ratio for the products. Of the substances for which a restriction has been assigned either in the form of an SML (for monomers or additives in plastics) or as an ADI/TDI (for substances derived from other sources) only ethylbenzene present in polystyrenic materials (PS lids for cups and EPS cups and trays) had the potential to exceed the limit. The levels of ethylbenzene in the foodstuffs packaged in these materials were measured and compared with the levels in the control foodstuffs. Measurable levels of ethylbenzene were detected in one of the products but only at a concentration of 1 part per billion (ppb) which is much less than the SML of 600 ppb for this substance.

Relatively high levels for the worst-case migration potential for styrene were also calculated (the SML for styrene is currently under review) and the concentration of styrene in the appropriate foodstuffs was determined. Low levels of styrene were measured but in all cases were less than 5 ppb. Thus despite the high contact temperatures between the foodstuff and the packaging, the relatively high packaging area:mass of food ratio and the presence of fat on the food surface, the migration levels observed were low.

19.5.7 Specific migration studies in which take-away food packaging materials have been investigated

As for snack foods, these examples are not intended to cover every migration study that has measured the migration of a given substance from take-away food packaging but is intended to be indicative of the types of studies that have been carried out. In one study[9] the level of styrene migration from PS cups into a variety of foodstuffs was monitored. The highest value for the migration of this monomer was 0.025% of the total styrene detected in the PS cup. Therefore despite the hot contact with the fatty foodstuffs (styrene is fat soluble) only a small percentage of the available styrene migrated into the foodstuff. The level of styrene migrating was found to be dependent on the fat content of the food.

The printed corrugated board samples obtained in the FSA funded study[3] used to package pizza-based foodstuffs contained dibutyl, diisobutyl and di-(2-ethylhexyl) phthalate, diisopropylnaphthalene (DIPN), straight chain alkanes (C12-C18), diethylene glycol dibenzoate and dipropylene glycol dibenzoate. The worst-case exposure of the substances, applying the conventional as well as the measured food contact ratio (a large packaging area:mass of food ratio exists for these foods) and assuming that a 60 kg person consumes 1 kg of this foodstuff a day, was less than the ADI/TDI limits specified for these substances.

Within an investigation to develop rapid test methods to determine the migration from paper and board into food[10] the migration of dibutyl phthalate, diisobutyl phthalate and DIPN from a corrugated board intended for use for

hot pizza packaging was observed. Between 20–40% of these substances present in the corrugated board were found to migrate. Given the relatively high percentage of these substances transferring from the recycled corrugated board samples to the foodstuff, it is important that the recycling process is efficient such that the levels present in the packaging materials themselves do not give rise to the potential for unacceptable migration.

A survey of fluorescent whitening agents (FWAs) in paper and board determined that the highest concentrations of FWAs were found in some of the packaging used for take-away food. Four of the take-away food packaging materials analysed contained FWAs at 430–1160 mg/kg paper.[11] It was concluded that even if all the FWAs in the take-away packaging materials migrated into the food, this would not cause a risk to human health. In practice, only a small proportion would be expected to migrate.

Another survey, again funded by the UK Food Standards Agency, determined the levels of a grease-proofing agent in paper and board.[12] Grease-proofing agents are used to treat paper and board to provide grease and/or water resistance. For example, these agents would be added to paper packaging to prevent it absorbing oil from food during storage or heating. The agents usually used are perfluoroalkyl substances, typically phosphate esters or amine salts. Grease-proofing agents may be added during the early stages of paper production or as a final surface treatment. Samples of paper and board were purchased from supermarkets, independent shops, garage shops and fast-food take-away outlets. The highest concentrations of the grease-proofing agent were found in samples of wrapping from a burger obtained from a fast-food outlet (unheated; 1.8 mg/dm^2 paper) and a microwave chip box (heated; 1.8 mg/dm^2 paper). There is no specific legislation on the use of grease-proofing agents in paper and board. However, the samples did not exceed the recommended levels listed in, for example, the German standards organisation. Further evidence for the use of perfluoro substances as grease-proofing agents for paper and board was described by Begley[13] in which he concluded that 'Paper coatings are potentially a significant source of fluorochemicals. Some paper applications potentially contain 100 μg fluorotelomer/serving.'

It has been suggested[14] that formed plastic containers, used for carry-out foods, should not be reused for microwaving as such containers, if heated, may be subjected to conditions other than those for which they had been safety tested. The authors recommend that for all take-away food packaging, if it has not been tested for repeat use, then labelling should clearly indicate that the foodstuff should not be re-heated in the packaging.

In a study recently carried out in Hong Kong on disposable plastic containers for take-away meals[15] the migration of styrene oligomers, heavy metals and the overall migration from plastic containers and, where present, their lids were determined into food simulants under different test conditions. Results showed that all the disposable plastic container samples met the safety standards for heavy metals and residual styrene monomers. Hence, with the proper use of disposable plastic containers, they would be unlikely to cause a food

safety problem. Most of the plastic materials being tested met the overall migration limits under different testing conditions. In only one PS container sample, when the test condition simulated fatty food use at a temperature of 120 °C, the overall migration exceeded the limit. However, when the test condition was changed to simulate fatty food use at a temperature of 100 °C, the overall migration limit was met. Therefore labelling is recommended to ensure that the take-away food packaging materials are not used under conditions for which their safety has not been confirmed.

Recycled paper used in making board may include carbonless copy paper (also known as self-duplicating paper). DIPNs are used as the solvent for the colour former in carbonless copy paper. Not all of the DIPNs may be removed by the treatment of the recycled fibres. Some may be present in the finished board and thus could migrate into food. Surveillance work reported in 1999[16] analysed the paper/board packaging of 34 retail samples which included ten take-away food packaging materials. DIPNs were detected in all of the take-away food packaging materials. The concentrations in foods packaged in those materials containing the highest concentrations of DIPNs were measured. Of the five take-away foods analysed four contained measurable levels of DIPNs (0.06 to 0.17 mg/kg in the food).

Of the limited studies carried out on the migration of substances present in take-away food packaging materials, in general only low levels of substances have been found to migrate. This is despite the high packaging usage and the high contact temperature between the food and its packaging. Low levels of potential migrants in the packaging materials themselves (these should be kept low to ensure that migration remains at an acceptable level) and the short contact time between the packaging and the food may be important factors.

19.6 Sources of further information and advice

Many of the studies carried out to determine the migration from take-away and snack food packaging have been funded by the UK Food Standards Agency and additional information relating to these studies may be found on the FSA website (www.food.gov.uk). Detailed reports describing all the FSA funded work[3,4] outlined in this chapter are available from the enquiry desk of the FSA library (e-mail: library&info@foodstandards.gsi.gov.uk).

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20

Case study: Poly EthyleneTerephthalate (PET) as a food contact material

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20.1 Introduction

There are plenty of good descriptions of the birth, history, manufacture and use of PET.[1] PET was invented in the early 1940s by Whinfield and Dixon who worked for a company called Calico Printers. This new polymer was used mainly for its fibre forming properties and became a new material for clothing. The manufacturing technology became available for licensing and DuPont obtained a licence for use in the USA and Imperial Chemical Industries (ICI) licensed the technology for the rest of the world. Through the late 1940s and into the early 1950s research and development activities were confined to PET's fibre forming properties. This work resulted in the building of the first full-scale fibre polymer production unit in 1955.

During the late 1950s scientists recognised that PET had other properties that might be commercially useful and so they focused their research on PET's ability to form films by biaxial stretching. The research was successful and in 1959 the first commercial film plant was opened. It follows that researchers never stop researching unless the funds run out. PET was a rising star and as might be expected, funds for research poured in. Research continued apace and in the early 1970s the PET bottle was born. PET has some unique properties which led to it competing with glass as the material of choice. PET bottles were lightweight, shatterproof and held carbonation long enough for PET to become a real competitor in the carbonated soft drinks market.

In 1977 PET bottles were introduced to the USA and from then until approximately 1995 there was rapid growth of PET tonnage into bottle applications. PET bottle applications expanded and as time went by there grew a realisation that there were limitations in the use of PET, the major

limitations being PET's thermal stability and its gas barrier properties, particularly to oxygen. PET thermal limitations were tackled in a physical way by the development of a range of heat-setting processes[2] and its gas barrier properties were tackled using both polymer modification and coating technologies. To date these properties have not really been improved to such an extent that they are commercially acceptable from both a cost and a performance point of view. Research continues into improvements in these very difficult areas.

20.2 PET manufacture

PET is a very clean polymer; essentially it uses two monomers, terephthalic acid (or its methyl variant) and ethylene glycol. To control the manufacture and enhance or control the final properties there are catalysts, co-monomers and process stabilisers. It appears to be a very easy process: one simply takes the monomers, mixes them together and hey presto, PET. Of course this does not happen in reality; there are a lot of processes that need to be carried out in a specific order to manufacture a polymer see Fig. 20.1. In the first stage of PET production the monomers are mixed together to form a paste and this is then heated with a catalyst. Process stabilisers need to be included in the process and the addition points are critical. These stabilisers must be added at the correct time and in the right place in the process or the physical properties of the polymer will be affected. This can affect both the bulk product and downstream processing equipment. Typically hazy polymer can be produced and the polymer chains can degrade, reducing physical strength. Vacuum is applied to remove water and later excess ethylene glycol. Eventually a polymer of lowish molecular weight is formed, which is then cooled, chipped and stored. For the second stage of manufacture the low molecular weight polymer from stage one is further processed in its solid state in a flow-through reactor where the solid polymer continues to polymerise to a much higher molecular weight.

20.3 PET uses

PET resin is converted into three basic forms: a fibre; a film or sheet; and some form of container. Each of the processes for manufacture of the finished article needs a preform of some type, i.e., the processes are all twofold. Fibres are made first with a continuous fibre which is cooled, then reheated and stretched at a fixed temperature (see Fig. 20.2). Film is first extruded into a sheet, cooled, then reheated and stretched in two directions (see Fig. 20.3). Finally a bottle is formed from the reheating of a preform or test-tube-like object and stretched in two directions by physical pushing and by blowing with high pressure air (see Fig.20.4).

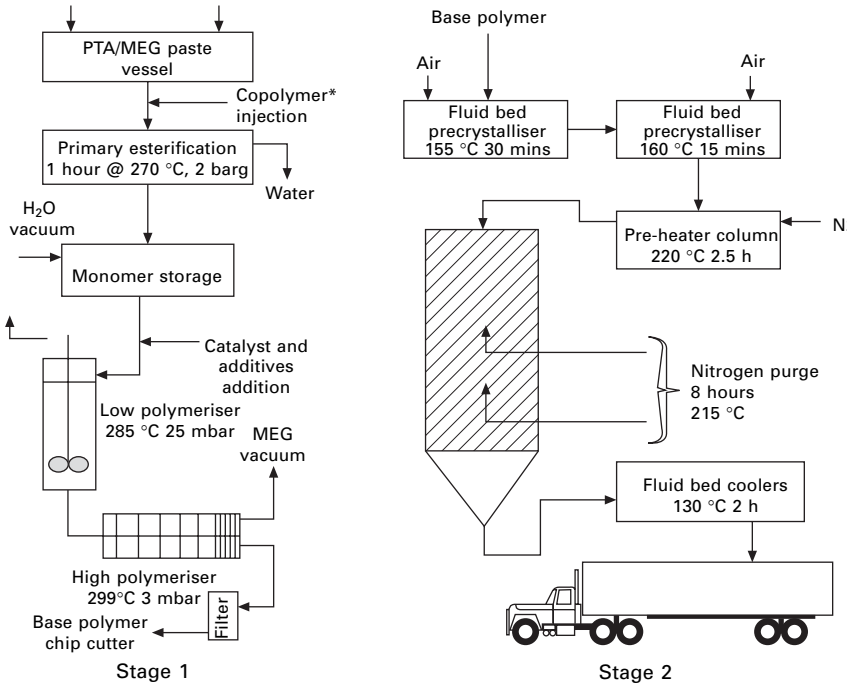


Fig. 20.1 The polymerisation process.

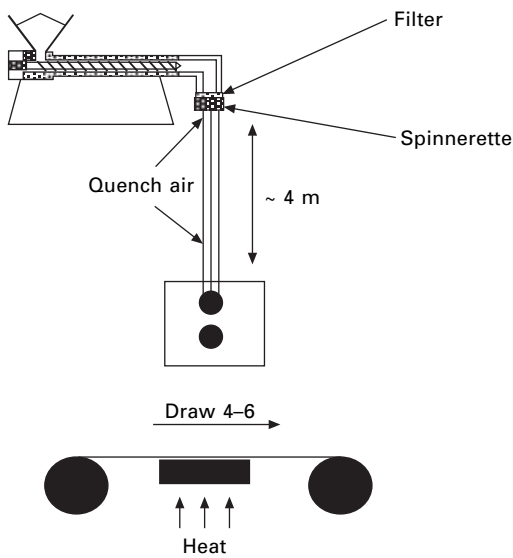


Fig. 20.2 PET fibre production process.

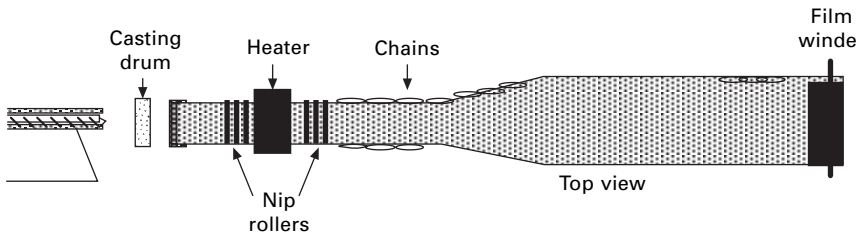
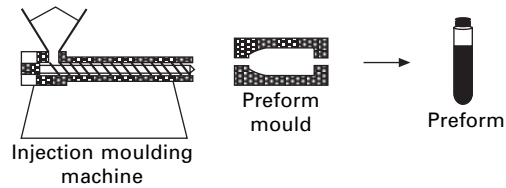


Fig. 20.3 PET film production process.



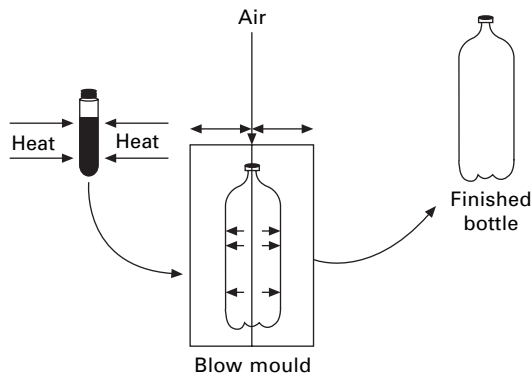


Fig. 20.4 The injection stretch blow moulding process (ISBM).

20.4 Self regulation

As stated earlier in the chapter, PET is a very clean polymer, that is to say there are very few constituents used in the manufacturing and processing processes. PET does not need the stabilisation systems that many other polymers need and generally speaking additives are used for their downstream processing and use effects only. However, before beginning to discuss PET constituents, we need to consider regulations as a whole and why there is application of both self- and legally applied regulation.

The chemical industry has had a very bad press for many years and some of this has been earned. To overcome this image it began its 'Responsible Care'[3] initiative to try to encourage the chemical industry to combat the many allegations being made against it. This initiative demonstrates the year on year improvements in health, safety and environmental performance using

six separate management practices. These are community Awareness and Emergency Response, Pollution Prevention, Process Safety, Distribution, Employee Health and Safety and Product Stewardship. All of these management practices have been and are still being developed using the best expertise that industry can gather. This often causes difficulties and can and should lead to better practices for industry when outside influences demonstrate the need for change. In tackling the Responsible Care initiative a company uses the product stewardship management practice as a sort of adhesive cloud to hold and support the other management practices together. Later in this chapter I refer mainly to food contact regulatory practices; however, it should be remembered that this is only a small section of the product stewardship practice as a whole.

Product stewardship is the management practice by which the health, safety and environmental aspects of designing, manufacturing, marketing, distribution, use, recycling and disposal – in this case of PET packaging – are carefully controlled. Using aspects of this code as a basis for discussion I will extract the relevant parts pertaining to PET and how it is used in conjunction with current food contact regulations.

One final thought before the minefield is tackled: management codes are guidelines only and differing opinions and business pressures can cause considerable discussion inside companies. It is possible for untrained or very focused minds to 'err from the path of righteousness' and for the sake of our industry I urge real caution in this area. There are many examples of both deliberate and accidental errors in the area of food contact application for plastics and none of them are justifiable if the spirit of Responsible Care, product stewardship and consumer safety become, as they should be, the number one priority in a company.

20.4.1 Regulatory aspects of PET – the minefield!

When considering the use of a PET grade (or other polymer grade) for food contact applications, the law in any specific country dictates what, how, when and who has responsibility for the use of that particular PET grade. In considering PET for use in food applications it is important to remember that the PET grade may be used only for a specific application if the law in the country of use allows it to be used. Ignorance is no excuse – I found out that a standard driving practice in the UK was illegal in Thailand where it caused me to receive a very high fine (and a red face!). However, in general, most countries in the world will accept PET and other food polymers provided they comply with either or both the United States of America Code of Federal Regulations from the Food and Drug Administration and European Union Regulations and Directives. It is also worth remembering that both the United States and European Union regulations for food contact articles prescribe the maximum overall migration from containers to foodstuffs. Migration from PET bottles made according to good manufacturing practice (GMP) is usually one or two orders of magnitude lower than the limits.

Most countries have websites where there are up to date copies of the relevant food regulations and often embassies will provide guidance on where to find relevant information. There are many companies, test houses and lawyers around the world who can provide opinion on legal aspects. A word of warning, though: it is important to ensure that the information you receive is fully explained and checked for correctness. I have experienced errors on more than one occasion and would urge individual product stewards to check every piece of information supplied. If the information supplier cannot fully demonstrate their opinion then use another supplier.

20.5 What is PET?

Before going into details on the various components and their uses in the manufacture of PET it is probably useful to talk in general terms about what PET actually is. PET or polyester is essentially a polymeric salt (see Fig. 20.5). In recalling the old school chemistry definitions 'acid plus base equals salt plus water' and 'acid plus organic base equals ester plus water or OH based molecule', PET is usually terephthalic acid plus monoethylene glycol; the two are reacted together and give off water and as the reaction progresses ethylene glycol is also expelled.

20.6 Monomers – the basic building blocks

20.6.1 1,4 benzene dicarboxylic acid – terephthalic acid – TA (PTA)

Terephthalic acid (TA) (diacid) is now the major monomer used in the production of PET. It is produced on a world-wide scale and is available in a number of purities. These can be generally referred to as PTA (pure TA), MTA (medium purity TA) or CTA (crude TA). These descriptions are subjective and used in different ways by manufacturers. The purity of TA is the self-limiting process in PET manufacture. The major impurity in any TA grade is 4-carboxybenzaldehyde and it is a chain growth inhibitor. As the level of impurity increases less reaction can take place. From a food contact point of view the purity or impurities in the TA is important. Both US and EU law state that monomers should be of good technical quality but do not define what that technical quality should be. If no other information is available the

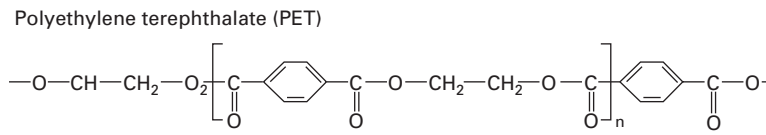


Fig. 20.5 The PET molecule.

product steward will need to give an opinion on the purity of the raw material and at the same time understand the business need to optimise costs. In attempting to lower the purity of the TA a business might decide to submit a petition to the appropriate legal authority, for example using the US FDA premarket notification for food contact substances process.[4]

Most petitions require a dossier of information on the substance and details of how to prepare these dossiers are given in ref. 5 for submission to the US authorities and in ref. 6 for Europe. One issue for both European and US authorities to consider is that although they require similar information to be submitted to the authorities, the information requirement is not the same and this can result in extra and unnecessary costs for the petitioner.

In Europe PTA has been given a specific migration limit (SML) of 7.5 mg/kg. This SML was established on the basis of a temporary tolerable daily intake (tTDI) as at the time of the drawing up of a European wide directive PTA was in common use in the manufacture of PET for food contact applications but did not have a fully prepared dossier and certain information on its safety was missing. During 2000 the European Commission (DG Sanco) told industry that all tTDIs would be removed and that the use of starting materials with tTDIs would be disallowed. Industry has since submitted the missing data to the European Food Safety Authority (EFSA) and has been requested to provide further information. At the time of writing the extra data requested is being generated by industry.

20.6.2 Dimethyl-1,4-benzenedicarboxylate – dimethyl terephthalate – DMT

Dimethylterephthalate (DMT) (ester) is the methyl salt of TA and is the other major monomer used to produce PET. DMT is not as efficient in its use in the production of PET, as at the start of the process an extra ester interchange reaction is required. This extra reaction uses a cobalt or manganese based catalyst and it generates methyl alcohol as a by-product. Methyl alcohol is highly flammable and consequently needs a specially adapted plant to handle this by-product. There are at least two occasions when DMT polymer plants have been destroyed due to accidents with methyl alcohol handling. DMT based polymer is generally more susceptible to yellowing in its downstream processing and has slightly different properties in use. DMT has been available for many years and as a chemical has been fully evaluated for its safety over that time period. There is much data available on DMT demonstrating its safety in use in food contact materials, and because of this and despite its processing difficulties DMT has been fully approved for use in the US and in Europe with its consequent tacit approval for use in food contact applications in the rest of the world.

20.6.3 Ethane-1,2-diol – monoethylene glycol – MEG

As explained above MEG (diol) is an organic base and the other major component of PET along with TA. MEG has been available for use in PET production for food contact for very many years. MEG is listed in the original US FDA regulation for PET (21CFR 177.1630) and has been approved for use in Europe for plastics intended for food contact applications since the first directive 90/128/EC. In Europe it is listed with a specific migration limit of 30 mg/kg; however, this SML must be measured as MEG plus diethylene glycol (DEG) and the total migration of the two materials must not exceed the 30 mg/kg limit.

20.7 Comonomers – the property changers

20.7.1 1,3 benzene dicarboxylic acid – isophthalic acid – IPA

Isophthalic acid (IPA) (diacid) has been used as comonomer in the manufacture of PET since the late 1980s and this use has been restricted somewhat by patents and by production capacity. IPA is mainly used as a comonomer with PTA in PET packaging applications. The IPA disrupts the crystalline nature of the PET polymer and produces a polymer which has better downstream properties for use in the food packaging market. It produces a clearer, lower glass transition temperature (T_g), polymer. From a food contact regulatory point of view, IPA is now fully approved for use in the US and in Europe although this has not always been the case. For many years IPA was approved in the US under 21CFR 177.1630 polyethylene phthalate polymers;[7] however, its use was restricted to up to 3% IPA or from 17% to 23% IPA and with food contact applications it was not allowed for polymers containing 3–17% IPA. This bizarre situation was resolved when the US premarket notification system began, and in March 2000 the then BP Amoco applied for IPA to be used in the range 3–17% and thus closed the regulatory gap. In Europe IPA became fully approved with the fifth revision of 90/128/EC and was allocated a specific migration limit (SML) of 5 mg/kg in food or food simulant; the earlier Directive 90/128/EC had already allowed its use, but only on a provisional basis.

20.7.2 2,6-naphthalene dicarboxylic acid – NDC

This specialist monomer (diacid) is used in various concentrations to increase the T_g of the polyester or to increase its oxygen barrier properties. The stiffness of the naphthalene (two benzene rings) reinforces the backbone of the polyester and inhibits bending at lower temperatures; it also increases the pathway for oxygen molecules and hence provides an increased gas, particularly oxygen, barrier. A fairly new and naturally expensive monomer to manufacture, in the United States it is approved for use for some applications by 21 CFR 177.1637 and for others via the FDA premarket notification system and is

also approved for use in Europe with an SML restriction of 5 mg/kg of foodstuff.

20.7.3 1,4-cyclohexane dimethanol – CHDM

This monomer (diol) is used to broaden the processing window, increase line speeds, slow the crystallisation rate and reduce stress in biaxially orientated structures. It is used in concentrations ranging from 1% up to about 18%. The higher concentration PET is usually referred to as PETG and is mainly used for extrusion blow moulding and sheet extrusion. Polymers from PTA and CHDM are approved in the US by 21 CFR 177.1315; recently the use of CHDM as comonomer in PTA-EG polymers has been listed in the US FDA regulation for PET (21CFR 177.1630). Moreover, the use of CHDM has been approved in Europe for plastics intended for food contact applications since the first directive 90/128/EC.

20.7.4 2,2′-dihydroxyethyl ether – diethylene glycol

Diethylene glycol (diol) is used as a comonomer along with MEG in PET. Small uncontrollable quantities are generated during production providing a background level of DEG in the order of 0.5–1.0%. In the US the presence of low levels of naturally occurring DEG is acceptable under FDA's good manufacturing practice 'suitable purity' clause (21 CFR 174.5), since the safety of the resin was originally demonstrated with samples made with such 'impurities' present in the monomer. In 1995, FDA gave an opinion to an end-user stating their non-objection to the use of up to 1 wt% of DEG for use at room temperature or below. However, increasing the level of DEG by direct addition was not an acceptable practice. Nor was it acceptable to manipulate process conditions to enhance the level of *in situ* DEG, unless such process changes were necessary to effect the polymerisation, for example, to increase production rate. It was also not acceptable to add DEG simply because it improved product properties. However, in October 2000 an industry consortium received a premarket notification to allow the use of DEG and/or IPA in PET up to 10%.

This approval is only for those companies who were part of the consortium. Other polymer manufacturers are restricted to the original conditions as described above. At this point it is probably worth mentioning that as the consortium worked together on this approval they shared the associated costs, a new manufacturer would need to pay the full costs of collecting replica data for the application as an individual company. A new system called the 'registration, evaluation and authorisation of chemicals' (REACH) is currently under discussion within the European Union. In this system it has been proposed that once a chemical has been registered a new entrant or manufacturer would be obliged to contribute towards the original consortium costs and share their data in order to obtain an approval. In Europe DEG is

approved for use and has been since the first food contact directive 90/128/EC. In Europe it is listed with a specific migration limit of 30 mg/kg; however, this SML must be measured as DEG plus ethylene glycol (MEG) and the total migration of the two materials must not exceed the 30 mg/kg limit.

20.8 Other comonomers

There are other opportunities to alter the properties of PET by adding specific quantities of other diacids or diols, e.g., butanediol, pentanediol, and still maintaining the name PET. However, as might be expected, research is still ongoing to find suitable acids and glycols that will affect properties in a cost effective and usually patentable manner. As with all new materials it should be recognised that food approvals will probably not be immediately available and that the researcher will probably need to obtain such approvals. As mentioned earlier, these approvals are best sought using expert guidance from those skilled in this area.

20.9 Additives – production and processing additives

20.9.1 Catalysts

PET cannot be successfully produced commercially without the use of a catalyst. For ester interchange reactions (DMT process) the major catalyst used is a cobalt organic acid salt, or less prevalent are the manganese, calcium and zinc variants. For direct esterfication alkoxides of antimony, germanium and titanium are used. Currently there is no specific regulation covering the use of catalysts; however, in the US they fall under what is known as the basic polymer doctrine.[8] The FDA stated many years ago that a 'basic polymer' is the product that results when a polymerisation process has been carried to commercial completion. Substances such as catalysts, chain regulators, chain transfer agents, and other materials used at low levels (generally 1% or below) and required to produce the resin are considered part of the basic polymer and are not subject to independent regulatory consideration. This principle is often referred to as the 'basic polymer doctrine'. This basic polymer doctrine reflects the practical reality that the US FDA cannot write generic regulations for food packaging materials that specifically clear every substance that might be a trace component or contaminant of packaging materials. Where a substance is used during polymerisation in small quantities and either becomes a part of the resin or is otherwise removed from the resin at the conclusion of polymerisation its potential for migration is minimal. As there is no reasonable expectation of migration the substance is not considered a food additive.

In Europe aids to polymerisation are not yet regulated on a European wide basis and as such are covered by the Framework Regulation 1935/2004, by

legislation in some member states and by guidance documents (i.e. the German Bundesinstitut für Risikobewertung – Empfehlung XVII – Polyterephthalsäurediolester). If there is no member state legislation for a proposed new catalyst then an individual risk assessment on that substance should be carried out. As previously suggested in this chapter, difficult regulatory situations such as this should be discussed with experts in the field. One PET catalyst is regulated at European level and that is antimony trioxide. As antimony performs a useful function in the final polymer, enhancing infra-red reheating of preforms, it is both an additive and a catalyst, and therefore subject to the existing EU legislation on food contact plastics.

Antimony trioxide is widely used in the PET industry and is subject to other EU regulations. To ensure that antimony trioxide could be used in food packaging without hindrance an industry consortium collected the data required and submitted a petition to the EU Scientific Committee on Food (SCF[9]*), which was replaced by the European Food Safety Agency (EFSA[10†]) in 2002. The SCF evaluated the data supplied and gave antimony trioxide an SML of 10 ppb with an analytical tolerance of 10 ppb. This was a disappointing result for the industry consortium who then asked the World Health Organisation (WHO) drinking water group to evaluate the data. The WHO evaluated the data and proposed a tolerable daily intake of 360 ppb of antimony trioxide and a drinking water level of 18 ppb. With this new information the industry consortium approached the newly established EFSA and asked for a re-evaluation. This resulted in a raised SML of 40 ppb for antimony trioxide; the Directive 2005/79/EC of 18/11/2005 confirmed this increase in SML. At the time of writing there is also an EU risk assessment taking place on antimony trioxide and a lot of environmental and human health data is being collected and will soon become available.

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* Answers scientific and technical questions concerning consumer health and food safety associated with the consumption of food products and in particular questions relating to toxicology and hygiene in the entire food production chain, nutrition, and applications of agrifood technologies, as well as those relating to materials coming into contact with foodstuffs, such as packaging.

†Set up provisionally in Brussels in 2002, EFSA provides independent scientific advice on all matters linked to food and feed safety – including animal health and welfare and plant protection – and provides scientific advice on nutrition in relation to Community legislation. The Authority communicates with the public in an open and transparent way on all matters within its remit. EFSA's risk assessments provide risk managers (consisting of EU institutions with political accountability, i.e., European Commission, European Parliament and Council) with a sound scientific basis for defining policy-driven legislative or regulatory measures required to ensure a high level of consumer protection with regards to food safety.

20.9.2 Processing aids

DEG control
Very small amounts (low ppm) of alkali, alkaline earth metal salts or quaternary ammonium compounds are added to the reactors to control the amounts of DEG that are generated in the polymerisation reaction. The use of these materials in the manufacture of polymers for food contact packaging is covered under the basic polymer doctrine for use in the US, by EU legislation and legislation in some member states.

Polycondensation degradation
Melt stabilisers such as phosphoric acid and its salts and esters are added to the polymerisation process to reduce thermal degradation and colour formation (yellow). They also have the added effect of stabilising the polymer when it is being later processed into food packaging. Many of the phosphorus based stabilisers are listed in 2002/72/EC for use in food contact applications and are covered by the basic polymer doctrine of the US FDA.

Colour management
The colour of PET is measured instrumentally on a three-dimensional scale (see Fig. 20.6). The vertical axis is known as the L scale and is generally recorded as Hunter units (Lh) in the US and CIE Lab (L*) in Europe. This scale measures black/whiteness with the higher the number the 'whiter' the polymer. The two horizontal axes measure red/green (ah and a*) with the higher the number the redder the polymer, and blue/yellow (bh and b*) with the higher the number the yellower the polymer. In an ideal world a PET polymer would have a highish L*/Lh (~80), a middle ah/a* (~0) and a slightly negative bh/b* (–1.5),

The manufacturing process for PET can take many hours and as a result the polymer is subjected to high temperatures for extended periods of time.

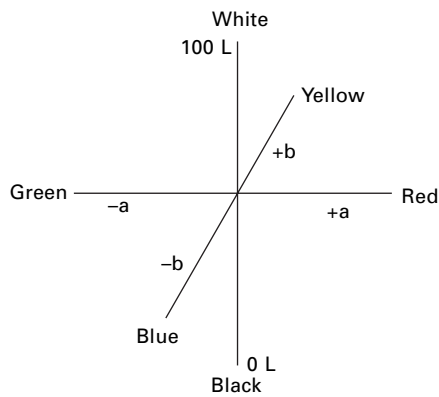

Fig. 20.6 The three dimensions of colour.

It is therefore not surprising that there is degradation in the final polymer. This degradation takes the form of a yellowing of the polymer or an increase in the bh/b* number. To control the yellowness of the polymer low levels of cobalt acetate (blue) or even lower levels of synthetic dyes (blue/red) are added to the polymer. In the US the use of cobalt acetate falls within the US basic polymer doctrine, and in Europe it is covered by a risk assessment using the framework legislation 2004/1935/EC, national legislation and a very low SML which is less than 0.05 mg/kg. The dyes are authorised for use by current US FDA regulations on colorants and by some member states (e.g. the 'French positive list') approvals in Europe. One other aspect of colour management is the use of re-heat substances in the polymer and these are discussed later.

20.10 Effect additives

20.10.1 Scavengers, barriers, temperature resistance and reheat

Effect additives are a much more tricky area when considering regulatory aspects for PET. These tend to be newer, more complex materials with less human health and safety information being available for them. They also tend to be used in quantities that will affect migration and/or the food contact status of PET containing such materials. A major consideration is the economics of the proposed system vs. the return in cash or market share. Regulatory approvals are expensive and obtaining US and EU approvals is both expensive, time consuming and generally needs highly experienced personnel or contractors to guide the process. Some companies market proprietary effect additives and will have obtained (but not always) approvals for use of their products. Good product stewards would check those approvals very carefully before allowing their use in PET to be manufactured or sold by their companies.

20.10.2 Scavengers

Sometimes called active or intelligent packaging systems – are designed to overcome an inherent weakness or provide a competitive edge for PET packaging. Oxygen is the major potential derailer for some forms of PET packaging applications, for instance, beer or oxygen-sensitive foods such as tomato based foods. Another important issue for mineral water is the migration of acetaldehyde from the PET bottle walls. Scavengers tend to be incorporated into the polymer either at the manufacturing stage or afterwards in the conversion to packaging stage. For instance, chemicals that react with oxygen or acetaldehyde and thus prevent their migration to foodstuffs are widely used in more sensitive applications. Great care needs to be taken to ensure that the properties of PET (strength, clarity, stiffness) are not affected unduly by the addition of these materials or that their presence does not hinder the recyclability of PET. In considering a regulatory position these scavengers

(chemicals or polymers), however they are described, are really nothing other than additives and because they are incorporated into the polymer which is used to manufacture a food package are covered under EU and the various member states' legislation. In the US the position may be slightly different in that, if the scavenger is not already approved/listed in the CFRs or is not generally recognised as safe (GRAS[11]) then there is a requirement to use the PMN process.

20.10.3 Barriers

There are many proprietary coating systems to enhance the (oxygen and carbon dioxide) barrier properties of PET and these are generally added downstream of the PET manufacturing process and as such the product stewardship aspects of their use do not concern PET manufacturers. However, they are of concern to the conversion industry. As with scavengers, the majority of the systems in use today are commercially available and manufacturers should have already obtained regulatory approval for use in any particular country. It is very important that these approvals are carefully checked before putting materials on the market.

20.10.4 Temperature resistance

Less known, and possibly more importantly for the PET packaging industry, are additives that will increase the T_g of the polymer. Currently it is possible using heat setting techniques to raise the T_g of PET and this allows its use in hot fill applications. The technique of heat setting requires careful control and requires investment in expensive equipment. The researcher who finds a material to increase T_g will probably be looking at what are currently very expensive molecules that can be reacted into PET's polymeric chain. From a regulatory point of view this could have two effects: one is the simple one of applying for regulatory approval to allow the use of small amounts of the material in PET. The other is more complex: should the material need to be used in large quantities, it is then possible that a new copolymer may be formed and that has implications beyond just food contact approval.

20.10.5 Reheat

As long ago as 1980 it was recognised that there was a shortcoming in PET as a packaging polymer. In almost every application PET polymer is melted and formed via extrusion or injection moulding into what has become known as a 'preform'. This can be an extruded sheet for thermoforming or a test-tube-shaped article used to blow a bottle. After the 'preform' is made it is usually cooled, stored and at a later date recovered, and heated to a suitable temperature for forming, either by physical pressure (plug) or by gas (blown) or by a combination of both. A rate limiting step for these processes is the

speed at which the PET can be 'reheated'. Research led to the simple discovery that 'black bodies' finely dispersed in the polymer matrix could reduce the time taken to get to a temperature at which the PET could be formed.

There have been many reheat processes developed and all are subject to patent protection. All give either increases in machine speeds, which can exceed 25%, or significant energy savings, which again can exceed 25%. The common materials for reheat are metals, metal oxides, mixtures of these oxides, organic molecules that heat in the infra-red range and carbon black. A major difficulty in the use of these materials is that they drive down the Lh/L* of the polymer resulting in a potentially much darker polymer. There is then a balancing act in which the advantages of reheat need to be weighed against consumer acceptance of a darker-coloured bottle. From a regulatory point of view these materials are generally approved for use in the US and in Europe by their use in other polymers. In each case the PET manufacturer has obtained the necessary approvals before marketing these enhanced reheat polymers.

20.11 Recycled PET for food contact applications

Recycled polymers have been the cause of much discussion across the world. Driven by environmental concerns, recycling of all forms of materials has increased in importance and will continue to do so for the foreseeable future. PET is one of the major recycled polymers. Initially all PET was recycled to fibre for clothing, strapping tape, engineering applications, polyols and sheet extrusion. It became obvious that there was a clear commercial and marketing opportunity for recycling of post-consumer PET bottles back to food contact quality and hence remake bottles. Recycling began in the US with a drive to produce the cleanest recyclate possible and with sufficient evidence to convince the US FDA that recycling was both practical and possible. At the same time it was necessary to look at the economics of the processes to ensure commercial viability. Within the US recycling is now well established and produces a range of high-quality PET for bottle manufacture. At the time of writing, approximately 75% of recycle-to-food-contact approvals in the US are for PET.

In Europe the situation is different. There are countries that specifically exclude the use of recycled plastic materials into food contact applications. To be able to recycle back to food contact applications it is generally necessary to obtain approval for each country in which you would like to recycle back to food contact use. However, it is clear that in Europe there is a need for harmonised legislation for recycling plastics back to food contact applications. As a result of two EU sponsored recycling studies, the EU finally decided to regulate the use of recycled plastics back to food contact. An industry task force was formed to help the process of regulation and independent experts within the recycling field were recruited to provide guidance. A draft regulation

was produced and discussions began with member state representatives. The regulation when agreed and published will cover all plastic materials and will require a process approval for recycling of individual polymers and plants. As there is a lot of expertise in the PET recycling field it is likely that PET will be the first polymer to become approved on a Europe-wide basis.

20.12 PET issues

Despite the fact that PET is a very clean polymer there are many issues that arise in using PET in food contact and other applications. Many of these issues are as a result of ignorance. For instance, there is a real misconception that terephthalate equals phthalate and therefore equals suspicion of oestrogenic effects. There has been much research on oestrogenic effects and phthalates and as our knowledge has grown it has become clearer that terephthalates do not cause oestrogenic effects and yet there are still many questions arising on this subject in relation to PET.

There are many more myths that constantly appear such as:

- PET has been claimed to cause cancer if it is stored in a refrigerator.
- PET contains diethyl hexylamine or diethyl hexyl adipate.
- PET contains plasticisers.
- PET contains BSE related substances.

These and other issues are thoroughly discussed and commented upon by expert industry professionals on the website of the American Plastics Council.[12]

There are also well-meaning companies/countries that ban the use of certain substances because they wrongly believe that there is an issue with a particular substance. Many companies/countries ban the use of materials that contain antimony which is used by PET as a catalyst. Yet both the WHO and the EU EFSA group have evaluated antimony and pronounced it to be safe for human consumption albeit with restrictions. There is also an ongoing EU risk assessment on antimony. Given the research into an understanding and evaluation of the safety of antimony, is it reasonable to continue these bans? Over time various issues will arise that will potentially threaten a business, therefore it is wise to have a regulatory crisis management plan in place to deal with these issues if and when they occur. Too often companies are caught out on regulatory matters and are not sufficiently prepared to react quickly to potential disasters.

20.13 Future trends

20.13.1 Harmonisation

In both the US and the EU there are many really good aspects of our regulatory systems as they operate today. Equally, there are many opportunities for

improvements in consumer safety through application, production, range and depth. Regulators in conjunction with industry and governments are making efforts to change the way our food contact plastics are regulated. An example of this type of change was the introduction of the US pre-market notification process (PMN). PMNs have speeded up the ability to get a product on the market whilst maintaining proprietary information and competitive advantage. In my view it would be useful if the maze of regulations were simplified and harmonised. One way for this process to begin is by industry asking the US and European governments to agree that we can harmonise our regulatory processes. The knock-on effect of any harmonisation would spread across the world and lead to improved consumer safety, fewer barriers and better opportunities for commerce.

There will be many opportunities for change in any harmonisation process and it is important that all parties, particularly consumers, are involved and their opinions taken into consideration.

20.13.2 Publicity

Industry is constantly under attack by organisations with their own agenda for change. We are also attacked, sometimes rightly so, for behaving in an illegal manner either deliberately or through ignorance. Our emissions are constantly challenged and the quality of our products and workmanship are questioned incessantly. Our processes are criticised from raw material intake, through manufacture, product production, use, recycling and final destruction of the product. Strong words but essentially true, yet we as an industry, not just locally but globally, allow these words to continue. We make Herculean efforts to ensure our products and their production are to the very best standards available in the world today and we drive innovation to improve these standards. What we fail to do is to tell the world and it is this failure that drives us further and further down the road of rules, regulations and restrictions. One real benefit we could gain as a global industry is to actively pursue our own excellence in production and use it in real, high-quality publicity.

Our products save lives, are energy efficient to the point of being green and provide all nations the support they need to grow and develop. To this end I believe we as an industry should set up some form of publicity machine that will extol the benefits of our industry and promote its safety in use and as a result reduce the rules, regulations and restrictions that stifle our industry.

20.13.3 Risk

Many years ago I started work, as might be expected, at the bottom of the tree. Down there as a wide-eyed young man in a huge laboratory I began to learn things. I learned about the smells that chemicals make, the colours of reactions and those occasional bangs that only research in a big company's

chemical laboratory can teach you. Perhaps one of the best things I learned was all about risk. In those days we did things that would never (thankfully) be allowed now. Our safety officer at that time used to circulate a monthly newsletter. In one of the very early newsletters there was a little risk table. I cannot remember it all but one thing has stuck in my mind for all of these years. 'You are less likely to be killed travelling in an aeroplane than walking as a pedestrian.' Perhaps a silly little thought but it is the basis of something we, as an industry, really do not consider enough. We listen to regulators telling us we leach too many chemicals into food from our packaging. We are told those chemicals kill hundreds of animals having been given huge doses of the same. We spend millions of pounds, dollars and euros on testing and yet the simple fact is our products are hugely safe. Even those packages that contain illegal (i.e. unregulated) additives, monomers, etc., are far less likely to kill, maim, injure or cause permanent damage than the many everyday activities carried out by the human race. We as an industry sit back, do nothing and accept this disproportionate risk.

In areas where the water supply is heavily contaminated, people are far more likely to die from drinking such water than from drinking good clean water from a potentially illegal plastic bottle. How many people become ill with food poisoning due to insect contamination compared to those who become ill from packaging that leaches a few more milligrams of oligomers or additives? Packaging saves many lives, with and without active systems packaging prevents the loss of foodstuffs, packaging provides a means of safe and secure food storage and yet it is still not truly accepted for what it is. I totally accept that safety evaluation of our monomers and additives needs to take place and I am on record as saying that consumer safety must be our absolute first priority, but I truly wonder if additional risk factors going into their hundreds (i.e. a factor of 1:100 or more) and in some cases their thousands (i.e. a factor of 1:1000) are not a bit of overkill in our very risky world.

20.14 Acknowledgements

My thanks go to my wife Sue, to my good friend Claudio D'Angeli and to Richard Sinclair for their help and guidance in compiling this chapter.

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