MIGRESIVES

HORIZONTAL ACTIVITIES INVOLVING SMES

COLL-CT-2006-030309

MIGRESIVES

RESEARCH PROGRAMME ON MIGRATION FROM ADHESIVES IN FOOD PACKAGING MATERIALS IN SUPPORT OF EUROPEAN LEGISLATION AND STANDARDISATION

Collective Research Programme

Final activity report

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Revision 2

Project Homepage: http://www.migresives.eu

Content

1 Publishable executive summary

Between February 2007 and April 2010 the MIGRESIVES project (COLL-CT-2006-030309) was carried out by 21 project partners including seven research institutes, seven industry associations and seven small and medium sized enterprises (SMEs). It was the intention of the project to develop a pragmatic, science based test concept to ensure the safety-in-use of adhesives used in food contact materials. Most food packages and food contact materials are manufactured using adhesives. The EU regulates all food contact materials as migration of their constituents into food should not contaminate the food and not endanger consumer's health. In contrary to plastics, adhesives are not yet covered by a specific regulation which lays down how to implement this overall requirement. On the other hand the demands to document and verify the safety in use of food contact materials including the adhesive layers are increasing in all stages of the production chain up to the food industry. The project outcome may also form a basis for future specific EU legislation and provide industry, especially small and medium sized enterprises, a tool to ensure that migration from adhesives is in compliance with the regulatory requirements.

The concept is built on the following pillars: (i) classification of adhesives according to chemistry and uses, (ii) test strategies based on physico-chemical behaviour of adhesives, (iii) modelling migration/exposure from adhesives, (iv) providing guidelines to integrate the risk assessment approach into the daily life of companies and (v) extensive training and education especially to SMEs and large dissemination to achieve general recognition of the concept in Europe.

Adhesives formulations are often very complex and contain numerous single components. Multiple parameters influence the migration of adhesive compounds through a packaging material into food. These are, apart from the concentration of the compound in the adhesive layer, the adhesive type, the raw material polymer, the used additives in the formulation, the substrates and their barrier properties, the application of the adhesive, the end uses of the adhesive in the packaging and the packaging itself, especially the type of food to be packed and its filling and storage conditions. For the categorisation of adhesive types used in food contact application, adhesives have been classified according to their raw material polymer, the solvent system (solvent free, water based, solvent based) and the curing type (reactive, non-reactive). This way a classification matrix was built based on industry experience from adhesive as well as packaging producers and the most important applications for these adhesive types had been collected. Based on this classification, 23 representative test systems had been defined and selected by the consortium. They can be considered to be typical for adhesives formulations, materials and structures used for food contact materials and include different application and handling conditions, like type of food, type of contact, temperature and storage conditions. The test systems included acrylics, ethylene vinylacetate and vinylacetate ethylene copolymers, polyvinylacetate, natural rubber, synthetic rubber, polyolefins, polyvinylalcohol, polyurethanes and starch. Substrates had been polyolefins, plasticized PVC, paper and board. Furthermore a range of cork stopper applications with polyurethane adhesives were investigated in the project.

Analytical methods for screening and determination of adhesive substances in the materials and their migration have been developed by GC-FID and GC-MS of extracts or migration solutions for volatile and semi-volatile substances, by HS-SPME-GC-MS for volatiles in the material and by HPLC for non-volatiles. For the HPLC method a charged aerosol detector (CAD) was used which allows detecting also substances without chromophores or UV absorbing structures. Furthermore UPLC-MS was used. For the method development a set of more than 50 adhesive related substances was used and calibration curves were established for each of the substances by GC-FID and HPLC-CAD exploring the applicability and the boundaries of the methods especially in relation to screening of unknown compositions.

Applying these methods the adhesives and the finished applications have been screened on their composition including non-intentionally added substances. Using the test systems systematic migration and partitioning studies were performed in order to derive parameters for the prediction of migration. Additional experiments to derive partition coefficients were carried out by fortification of adhesives as well as of paper samples. Furthermore using fluorescence recovery after photobleaching (FRAP) technique, intrinsic diffusion coefficients of fluorescent test substances were determined directly in the adhesive layers.

The data from migration kinetic and concentration profile experiments were evaluated by mathematical modelling using Migratest Exp software. From the experiments more than 1200 migration and diffusion and partition coefficients have been derived at different temperatures in a range of 20 to 70 °C and in different material s by fitting the modelled curve to the experimental data. Partition and diffusion coefficients are the main parameters for the prediction of migration via mathematical modelling. From these data a general estimation of the diffusion coefficients in acrylic, vinylic and rubber adhesives as well as in plastics, paper and board could be derived. Partition coefficients were obtained for 39 substances in 224 conditions. These can be directly used for the migration prediction. For additional substances, reference partition coefficients were proposed for the groups of polar, medium polar and non-polar substances.

For validation purposes and in order to check and broaden the applicability of the modelling approach to additional adhesive formulations from the types under investigation, 45 glued packaging samples from the market had been analysed on their composition and subjected to migration testing on Tenax® (MPPO) at the condition 10 days / 40 °C for all laminates with measurable amounts of migrants. These data were used for comparison with modelling results.. Twenty nine different adhesives were used in the manufacture of the laminates: 9 polyurethanes (PU), 6 acrylics (AC), 2 hotmelts (HM), 1 starch, 5 based on vinyl acetate ethylene (VAE), 4 based on polyvinyl acetate (PVAc), 1 based on polyvinyl alcohol (PVOH) and 1 mixture of vinylic adhesive and starch. The substrates used were cardboard, coated cardboard, corrugated paper, polypropylene, polyethylene, polyamide, polyethylene terephthalate, metallized PET, aluminum and ethylene vinyl alcohol copolymer. Migration from these laminates has been modelled using the reference diffusion parameters and the reference partitioning coefficients as well as the experimentally determined concentrations in the material. The calculated values have been compared then to the experimentally derived ones. After exclusion of analytical artefacts (e.g. higher migration found onto Tenax than possible from the measured concentration in the material), overall 125 data were included into the statistical evaluation, 31 VAE, 35 PVA, 4 PVOH, 8 acrylics, 39 hotmelt and 8 polyurethane data. Most of the calculated data met or overestimated the measured values. The ratios between the modelled values and the measured migration onto Tenax (10 days / 40 °C) were in 93 % of all cases higher than one. T aking the analytical tolerance of the measurements into account from migration and initial content determination as well as layer thickness data, the ratios 0.8 to 1.2 can be considered as that range in which modelling reflects directly the measurement. Thirteen modellings (10 %) were in this range, 2 VAE, 5 PVAc, 1 PVOH, 1 acrylic, 3 hotmelts, 1 polyurethane. Four values were below 0.8 (3 %), 2 VAE and 2 hotmelt. This means that 97 % of all simulations met or overestimated the measured migration, 87 % had a ratio higher than 1.2 between modelled and measured value. These results from the market samples show that the modeling approach including extrapolation to other substances gives reliable results.

The food regulatory evaluation is based on the amount of migration into food. The migration value can be derived by theoretical considerations, analytical measurements or a combination of both. These tools are embedded into a testing concept and a decision tree. The decision tree shall help to find a suitable testing procedure for the specific application. As theoretical calculations are in general less time and working effort consuming than analytical tests, the decision tree was construed such that it checks the possibilities for such estimates and the necessary input data. Experimental migration tests are always an alternative which can be chosen at each level of the decision tree.

A freeware multilayer modelling software was developed further within the project. The link to download this ‘Safe Food Packaging Portal version 3’ (SFPP3) is available on the MIGRESIVES website (www.migresives.eu). The use of the tools and the application of the decision tree are described and explained in a guideline document.

The feasibility of a complementary approach using the bioassays developed within the ‘Biosafepaper’ EU project (QLK1-CT-2001-00930) was investigated. Six laminates (PVOH, PVAC, four Acrylics) and the corresponding paper and adhesives were tested using the following toxicity endpoints: cytotoxicity (RNA synthesis inhibition assay), genotoxicity (comet assay) on HepG2 human cell line and mutagenicity on bacteria (Ames test). Feasibility of the bioassays applied to adhesives extracts was successful in regards to realistic exposure and risk assessment. Laminates extracts were neither genotoxic, nor mutagenic. Some were cytotoxic in the test. The observed cytotoxic effect was never due to the adhesive alone, in one case it could be assigned to the paper, in others only the laminate showed the cytotoxic effect which could not be explained by the analytical data.

Training lessons have been worked out in order improve understanding and awareness of the food regulatory requirements, diffusion and migration processes, use of the Migresives tools and the software. The trainings have been run successfully in Germany, France and Spain. Additionally experts from further European countries have been trained to enable them to give trainings in their countries. The lessons are made available for future use.

Table 1-1: Overview project consortium

No.	Type	Partner	Country
01	RTD	Fraunhofer Institut für Verfahrenstechnik und Verpackung, IVV	DE
02	IAG	FEICA - Association of European Adhesives Manufactures e.V.	BE
03	IAG	Industrieverband Klebstoffe e.V., IVK	DE
04	IAG	Asociación Espanola de Fabricantes de Colas y Adhesivos, ASEFCA	ESP
05	IAG	Association Club "Materiaux pour Contact Alimentaire et Santé" filiere papier/carton, Club MCAS	FRA
06	IAG	IK Industrievereinigung Kunststoffverpackungen	DE
07	IAG	Groupement pour la codification des mesures des bouchons de liège, Codiliège	FRA
08	IAG	Association Française des Industries de Colles, Adhesifs et Mastics, AFICAM	FRA
09	RTD	Institut National de la Recherche Agronomique, INRA	FRA
10	RTD	FABES Forschungs-GmbH für Analytik und Bewertung von Stoffübergängen	DE
11	RTD	Universidad de Zaragoza, Instituto de Investigaciôn en Ingenieria de Aragôn (I 3A), UNIZAR	ESP
12	RTD	Centre technique de la Conservation des Produits Agricoles, CTCPA	FRA
13	RTD	Institut Textile et Chimique de Lyon, ITECH	FRA
14	RTD	Université de Bourgogne-ENSBANA “ERT Sécurité alimentaire-Emballages”, UB	FRA
15	SME	Eukalin Spezial Klebstoff Fabrik GmbH	DE
16	SME	Gludan A/S.	DK
17	SME	Türmerleim GmbH	DE
18	SME	Samtack S.L.	ESP
19	SME	MITOL	SLO
21	SME	Belbo Sugheri, BS	ITA
22	SME	Pietec Corticas SA, Pietec	POR

Explanations: RTD = Research institute, IAG = association, SME = small&medium sized enterprise

Short name of the partner is underlined.

2 Introduction to the project

2.1 Overall project aim and state of the art

Most food packages and food contact materials are manufactured using adhesives. The EU regulates generally food contact materials, as their constituents may not be transferred into food into such amounts that it may contaminate food and endanger consumer's health (Framework Regulation (EC) No. 1935/2004, Article 3). This requirement includes substances from adhesives, but in contrary to plastics which are regulated by positive lists of authorised monomers and additives, adhesives do not have a specific regulation neither on European nor on national level yet. But the EU Commission intends to fill this gap. Simultaneously, the demands to more specifically show and document compliance and safety are increasing driven by legislation but also by food industry. Specifically, such documentation and the need of accompanying conformity certificates is required by Article 16 of the Framework Regulation (EC) No. 1935/2004, at each stage of the production chain of a food contact material in Article 9 of the Plastics Directive 2002/72/EG (in the version of the 4th amendment 2007/19/EC) and also addressed in the Regulation (EC) No. 2023/2006 on good manufacturing practice. Today for evaluation of adhesives existing rules and testing procedures have to be used which are established for other materials (e.g. plastics) and which partly do not satisfy the specific demands of adhesives. This means where by chance another (EU or national) regulation or recommendation made for plastics, dispersions, elastomers, waxes or paper can be used to evaluate a certain compound from an adhesives formulation this possibility is exploited for this purpose as far as applicable.

An enormous amount of knowledge on migration from plastic materials has been accumulated in the last 30 years. Most of these migration studies have been carried out to support national and European food legislation on food contact materials and have led to numerous regulations, guidelines and recommendations and to continued actualization within the European harmonization process. In addition, this interaction between the scientific and the regulatory levels has been accompanied by the development of corresponding European EN standards at the European standardization body (CEN) level (CEN TC194/SC1 and its several working groups: most important CEN standards series: EN 1186 parts 1-15, EN 13130 parts 1- 28 and other). A common feature of all these activities is the fact that adhesives have not been considered as potential migrants from food contact materials into foods. The main reason is the lack of specific regulation as driving force for such work. There is only a small number of published works covering this aspect (Gruner and Piringer 1999), (Lawson, Barkby et al. 1996; Lawson, Bartram et al. 2000) (Lawson, Barkby et al. 2000), (Davies 2003), (Bradley and Castle 2006). Primary aromatic amines from not sufficiently cured laminates on polyurethane basis, found in mozzarella sticks by Danish enforcement laboratories in 2001, gave the initiative to research work on polyurethane adhesives (Brauer and Funke 2002; Brede, Skjevrak et al. 2003; Störmer, Rüter et al. 2005). The food control authorities in the Nordic countries organised a seminar in 2001 where the knowledge on migration from adhesives and the legal situation was collected (Svensson, Binderup et al. 2001). One outcome of this seminar was that 'the development of methods of analysis for migrants from adhesives should be prioritized'. Furthermore 'test methods are needed and development of test methods should be given priority in the EU and be harmonized. There is a need for simple methods that would be well understood in the industry and in the food inspection'. The current regulatory 'deficiency' as well as the non-availability of methodological and conceptual compliance test systems in this area emphasises the strong need to initiate an endeavour to develop a solution and was the motivation for planning the MIGRESIVES project.

A large variety of adhesive systems are used in food packaging materials. Food packaging design is driven by factors such as economics (material minimization), consumer demand (convenience), nutritional aspects and other advanced trends (e.g. active & intelligent packaging). This requires specific adhesive solutions for all those different applications. Adhesives are used in flexible film-to-film lamination, paper-film/cardboard-film combinations, rigid multi-layer packaging systems, boxes, sacks, pouches, labels - in most cases without direct food contact but also in some cases with direct food contact. Other special applications are in refrigerators, microwaves, kitchen furniture or corks for alcoholic beverage bottles.

In contrast to plastics and paper additives, the term 'adhesives' refers to an extremely large and complex pool of compounds which, by nature, are often subjected to changes in their composition and undergo chemical reactions before the finished packaging materials come to the marketplace (Gierenz and Karmann 2001). The adhesives industry uses a large range of raw materials (approx. 2000 chemicals, information from FEICA) and manufactures adhesive formulations which can comprise up to 15 chemicals, even for the simplest systems. On the other hand, adhesives are used only in a relatively low mass fraction (up to 5 %) in food contact materials.

A regulatory solution and tools to verify the compliance to such a solution should consider these characteristics of adhesives and the requirements coming from the industry structure, in particular the large diversity of substances, the small share of adhesive applications in relation to other technical applications of the raw materials and the innovativeness and production of tailor-made adhesive solutions for customers in relatively small batches by SMEs.

For specific regulation of adhesives there are in principal two potential regulatory approaches:

<u>Approach 1</u> would be a positive list system for authorized chemicals in adhesive raw materials in analogy to the current EU system for plastic food contact materials. All other (unlisted) compounds would be excluded then form use. Building up such a positive list would be extremely time consuming and would be an enormous cost burden on the adhesive industry due to the multitude of individual substances. Only about 10 % of the raw material substances are already evaluated by the European Food Safety Authority EFSA. All other substances would need to be evaluated by EFSA and officially authorized, in many cases with specific migration limits. This in turn would necessitate comprehensive migration studies having to be carried out. Toxicological studies would also have to be undertaken on all individual substances. For a given substance, the amount of toxicological data required would depend on the measured migration value. It took industry 20 years to accumulate all the information on 350 monomers and 500 additives for the positive list system for plastics. For an analogous system for adhesives, up to 2000 substances would potentially have to be considered. Such an undertaking would in all likelihood take far longer than 20 years. In contrast to the plastics sector, which is characterized by a relatively small number of large international companies having large turnovers, the adhesive sector involves a large number of SMEs having much lower turnovers. These companies do not have the resources available to invest in petitions for the positive list approach. Furthermore, the functionality and processing of adhesives systems are by nature largely based on chemical reactions and hence the reaction products and by-products would also have to be measured and evaluated, meaning that even more toxicological data and knowledge would be necessary. All told, the positive list approach has more drawbacks than advantages and is not practicable. It should be stressed that the exposure of consumers to contaminants released

by adhesives is much smaller than by plastics (in direct food contact applications). This smaller exposure justifies a different scientific approach to safety assessment.

Approach 2 considers the actually migrating substances and their exposure to the consumer, but not the full list of potential migrants (as per Approach 1). This can be achieved by consideration of the practical applications of adhesives and the parameters influencing the migration of adhesive constituents into foods. This different approach related to the legislation on plastics is in analogy to the functional barrier principle for plastic multilayers as introduced into the Plastics Directive 2002/72/EC by its 4th amendment 2007/19/EC. According to Article 7a of the Plastics Directive, substances which are not in the positive list, may be used in non-food contact layers of a multilayer material if they do not migrate into the food in amounts exceeding 0.01 mg/kg food and if they are not classified as proved or suspect “carcinogenic”, “mutagenic” or “toxic to reproduction”, officially as well as under self-responsibility criteria. Adhesives are in most cases not in direct contact with the foods and are usually separated from the foods by a plastic, paper or cardboard layer. Furthermore, adhesives make up only a very small fraction of the total mass of food contact materials.

The aim of the MIGRESIVES project is to provide the scientific basis and the necessary tools for such an approach. It elaborates a scientific global risk assessment approach to meet current general EU regulatory requirements and as a basis for future specific EU legislation. It will provide SME adhesive industry as well as packaging producers a tool to ensure that adhesives do not endanger consumer health in their packaging application. In the Collective Research Programme of the 6th Framework Programme it specifically considers the needs of the small and medium sized enterprises represented by the associations and a core group of actively involved SMEs.

Thus the following objectives have been formulated for the MIGRESIVES project:

(I) To develop a pragmatic, science based concept to ensure consumer safety related to adhesives used in food contact materials.

(II) To establish European consensus and recognition of the concept by drafting and providing:

- General support of specific European legislation for adhesives.
- Specific solutions to comply with requirements of existing and foreseeable EU legislation on food contact materials.
- Standard test procedures for implementation into European Standards.

(III) To support and strengthen SME competitiveness within the adhesives industry and the added value chain by: To support and strengthen SME competitiveness in the adhesives sector and the added value chain by:

- ensuring product safety through self-evaluation of product compliance
- generating a basis for a legislative approach which does not limit innovation
- generating a basis to save existing and open new markets

(IV) To train industry (especially SMEs) using the tools of the developed concept and to rationalise and disseminate the project outcome as rules and guidelines to the whole food packaging chain.

2.2 Technological/scientific objectives

To support the above mentioned four strategic objectives, the following scientific/technological objectives are set:

(1) Classification of adhesives systems considering chemical types of adhesive formulations, precursor materials and raw materials used, setting mechanism, type and end use (contact conditions) of the food contact material (FCM) and likely migration potentials of adhesive constituents in the FCM.

(2) To establish analytical methods for (i) characterisation of adhesive classes and (ii) (semi)quantification of unknown substances as an essential tool to manage an adhesives inherent problem of dealing with very complex and largely unknown mixtures.

(3) (i) identify the potential migrants classes (technical function of additives, adhesive oligomers, neo-formed reaction products build up in the FCM during and after processing),
(ii) characterize their migration behaviour (kinetic and thermodynamic parameters),
(iii) specify the influence of variables such as time, temperature, humidity, processing & storage conditions
by in depths experimental studies of selected adhesives representative of major classes

(4) Screening programme on the migration potential and actually occurring migration from real FCM market samples.

(5) Methodological basis for the determination of adhesives related migration potentials in FCMs versus actually occurring migration rates from FCMs.

(6) Predictive mathematical tools for the assessment of adhesives related migration from FCM as a core instrument of the new compliance concept for adhesives.

(7) Holistic approach for compliance assessment of complex food packaging systems based on adhesives technology focused.

(8) Investigating into the feasibility of applying bioassay tests developed in another EU project (‘Biosafepaper’) for their potential to serve as possible alternative approaches in the future thus giving added values to both European projects.

(9) Technical descriptions of established test methods in formats suitable for implementation in European standardisation bodies.

(10) Technical descriptions and user-friendly application entries and computer programs for the developed predictive mathematical tools for being used by industry.

(11) Technical education and training programs for implementation of the elaborated test concept into industry.

(12) Develop an approach for safety evaluation of adhesives in interaction with the European Food Safety Authority (EFSA) and DG SANCO

2.3 SME relevance and relevance to European economy

The European adhesive industry has a large proportion of SMEs. This can be gauged by the fact[1] that 65% of the European Adhesives Manufacturing Industry is made up of companies having an annual turnover of less than 20 million Euros. Of the remainder, 26% of companies have a turnover between 20 and 46 million Euros and only 9% have a turnover above 46 million Euros. The adhesive sector in Europe comprises more than 500 SMEs spread throughout the continent with a majority in Germany, France, Italy and Great Britain. Most of these companies are affiliated to the Association of European Adhesives Manufacturers (FEICA, website: www.feica.com) via 15 national member associations. In addition, there are innumerable SMEs from downstream sectors within the packaging industry and food industry food producers concerned. They may add up to figures as high as several thousands. The food industry is of paramount importance to the economy of the EU with a high level of SMEs (small food producers such as groceries, bakeries, confectioneries etc). With 13,4 % of total production value in the manufacturing sector, food industry is ranked first in Europe ahead of motor vehicles and chemicals. In terms of employment it ranks first, illustrating its major economic role at both national and regional level.

To highlight the relevance of the project for the European economy it should also be noted that due to the relatively low mass fraction (up to 5%) of adhesives present in food contact materials (FCMs) and due to the fact that adhesives are used in about 90% of all FCMs, adhesives generate very high added value not only in the FCM production chain but also to a much greater extent to the final users of packaging, the producers of packaged foods. The following table shows EU production data compiled by FEICA which highlight the added value chain and the economic relevance of the project:

Sector	Turnover in 2004 [in billions of Euros]
Adhesives for food-related applications	1.98
Food packages	65
Food industry	>800

2.4 Project partner

21 partner are involved in the project (Table 1-1, page 7) of which are seven associations, seven SMEs and seven research institutes coming from 6 European countries. The associations represent the adhesives industry with the European association FEICA and the national ones in Germany, France and Spain. Furthermore the plastics converter and the producer of paper & board packaging as well as cork stopper producer are represented by an association each. The SME core group consists of five adhesive producer and two retailers of cork stoppers. Thus, the producers as well as the user of adhesives for food contact applications are involved in the project.

[1] Data from the German Industrieverband Klebstoffe e.V., Düsseldorf

2.5 The concept frame

Based on the functional barrier principle, the MIGRESIVES project will elaborate a testing concept and tools for using and applying a classification of adhesive components according to their migration to well defined adhesives and their applications in food contact materials. The tools will comprise of theoretical evaluations, analysis methods and mathematical modelling.

Adhesives components shall be classified into the following five groups:

- Substances which do not migrate.
- Substances which do not migrate at a given functional barrier (application, contact conditions).
- Substances which are evaluated in an EU-list and have a specific migration limit which cannot be exceeded at the intended application.
- Substances which are evaluated in an EU-list and have a specific migration limit which need to be measured.
- Not yet evaluated substances, which can migrate in such amounts that a toxicological evaluation would be necessary.

The approach is not a rupture with the principle of the EU regulation. In Article 7a of the Plastics Directive 2002/72/EC (by Amendment Directive 2007/19/EC) the principle of functional barriers was introduced. Thus in plastic multilayers, non-approved substances may be used in outer layers when migration is reduced by a functional barrier layer to less than 10 ppb in food. Moreover, the question how to handle migrants with low consumer's exposure is also under discussion at the EFSA level.

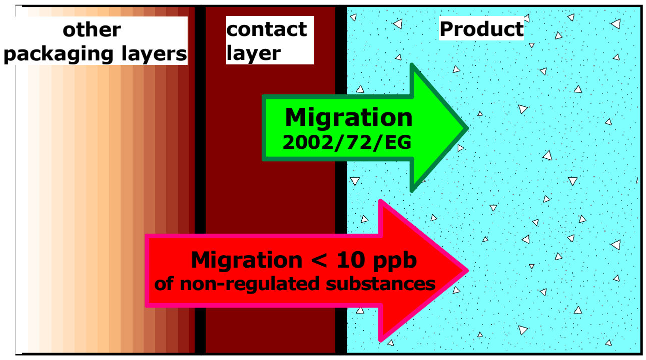


Figure 2-1: Illustration of functional barrier concept in plastic multilayers

3 Project work packages and deliverables

3.1 Overview of the workpackages

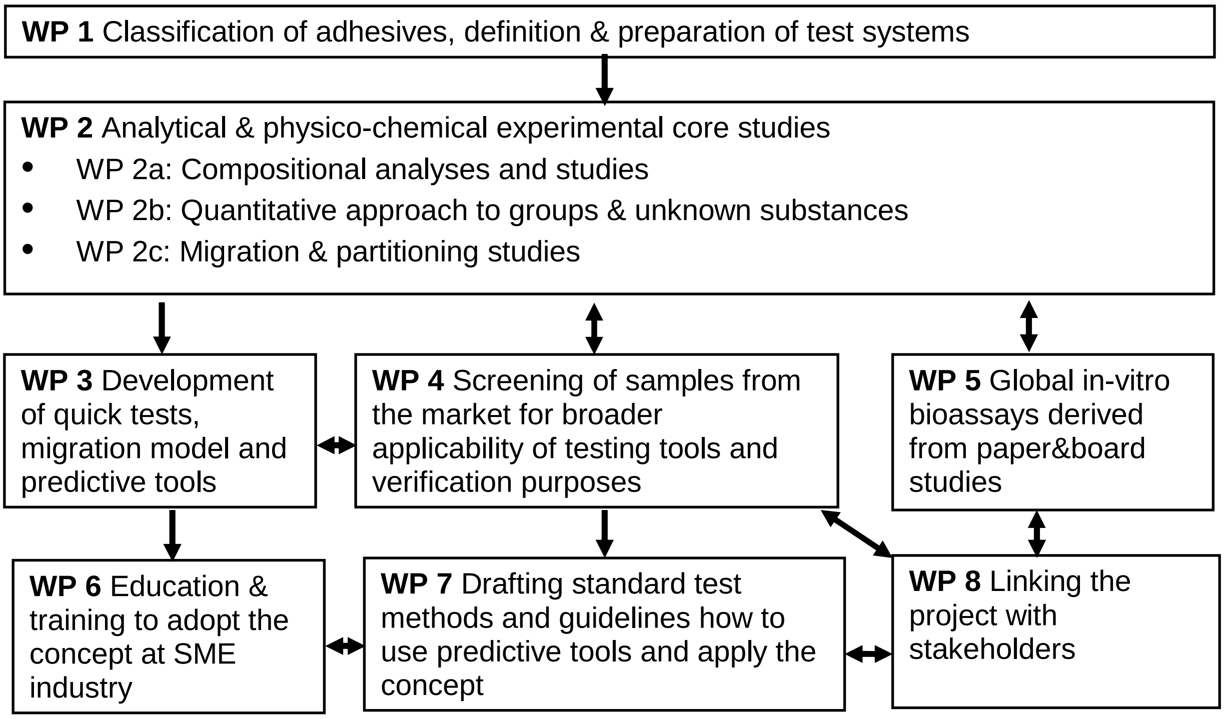


Figure 3-1: Pert diagram of the project

3.2 Overview project deliverables

Table 3-1: Overview of project deliverables

No.	Description, *lead contractor, authors*	WP
D0	Project presentation (website)	0/8
D1.1	Report on the 'Classification of adhesives and definition of test systems' *Fraunhofer IVV. A. Störmer[1]*	1
D1.2	Data base on adhesive FCM applications *Fraunhofer IVV and IVK. A. Störmer[1], A. v. Halteren[2]*	1
D1.3	Data base on adhesive FCM applications (non-confidential) *Fraunhofer IVV and IVK. A. Störmer[1], A. v. Halteren[2]*	1
D2	Summary report on the experimental determination of the migration potential in adhesive test systems from WP1 including an evaluation on the development of the migration potential from a raw material towards a final product Part 1: Investigation of the test systems composition. *Fraunhofer IVV. A. Störmer[1], A. Gruner[1], C.S. Yoon[1], C. Nerin[3], M. Aznar[3], E. Canellas[3], P.Vera[3], P. Saillard[5]* Part 2: Cork samples. *CTCPA. P. Saillard[5]* Part 3: Neoformed substances –the neoformed compounds issue generated from adhesives. *INRA. C. Joly[4]* Part 4: Physicochemical characterisation of adhesives samples. *ITECH. S. Mehlen[6]*	2a
D3	Report on the development of a quantitative determination procedure for chemical groups and unknown substances from adhesives including a detailed method description in a CEN standard format and validation data. *Fraunhofer IVV, C.S. Yoon[1]*	2b
D4	A compilation of data sheets with the experimental results for each of the measured test systems in a standardised format and containing their specifications and intended use conditions as well as non-confidential compositional and migration relevant data. Part 1: Experiments on WP 1 test systems. *Fraunhofer IVV and FABES. A. Störmer[1], A. Gruner[1], C.S. Yoon[1], A. Zülch[7],* Part 2: Experiments on WP 1 test systems (continuing). *UNIZAR. C. Nerin[3], M. Aznar[3], E. Canellas[3], P.Vera[3]* Part 3: Partitioning studies by adding model test substances to selected adhesives and substrates. *INRA. C. Joly[4]* Part 4: Determination of diffusion coefficient D through adhesives. Fluorescence recovery after photobleaching or FRAP experiments. *INRA. C. Joly[4]* Part 5: Migration measurements for determination of diffusion coefficients in paper. *CTCPA, P. Saillard[5]*	2c

Table 3-1: Overview of project deliverables (continuing)

D5.1	Rationale report on the developed compliance test concept and the proposed testing tools. *FABES. P. Mercea*[7], *A. Zülch*[7], *A. Störmer*[1]	3
D5.2	Software to estimate migration from FCM. *INRA. O. Vitrac*[4]	3
D6.1	Review report on the migration potential versus actual migration from market samples including detailed method descriptions. *UNIZAR. C. Nerín*[3], *M. Aznar*[3], *E.Canellas*[3], *P. Vera*[3]	4
D6.2	Review report on the influence of packaging processes on the migration behaviour of adhesives *UNIZAR. C. Nerín*[3], *M. Aznar*[3], *E.Canellas*[3], *P. Vera*[3]	4
D7	Review report on the feasibility study on bioassay approach *UB. I. Severin*[8], *M.C. Chagnon*[8]	5
D8	Training and education concept including training and presentation documents *ITECH. A. Reynier*[6], *N. Forichon*[6]	6
D9	Synthetic report on the development of tools to apply the concept including the adhesive classification, a compilation of standard methods and guideline documents. *CTCPA. P. Saillard*[5]	7
D10	Plan for using and disseminating knowledge *UNIZAR. C. Nerin*[3]	8
D11	Proceedings of the closing conference. *FEICA. B. Ghyoot*[9], *S. De Ridder*[9]	8

[1] Fraunhofer IVV, [2] IVK, [3] UNIZAR, [4] INRA, [5] CTCPA, [6] ITECH, [7] FABES, [8] UB, [9] FEICA

4 Project results

4.1 Classification of adhesives, definition and preparation of test systems (WP1)

4.1.1 Classification of adhesives

A classification of adhesives can typically be made on the basis of chemical composition, setting mechanism, adhesion mechanism and form of application, application temperature and end-uses (Gierenz 2002). A classification according to the setting mechanism is compiled in Ullmans Enzyclopedia (Gierenz 2002; Gruber and Rich 2002) and by (Onusseit 2008). A flexible classification in which each adhesive is characterised and classified according to various features such as chemical basis, form of application, application temperature, thermal behaviour and uses as proposed by Lucke ((Lucke 1967), cited in (Gierenz 2002)) is judged by Gierenz as highly comprehensive (Gierenz 2002). For evaluation of migration, considering a broad range of features from chemistry and composition to applications is necessary as well. The literature as mentioned above relates to all technical applications, none especially to applications for food contact materials. On the basis of common adhesives categories a specific classification is made in the project with respect to the intention of the project which means by considering also the potential of adhesive constituents migration into food. Such a classification is a complex issue and not available today. It required an intensive discussion using the know-how and expertise of the project consortium.

The classification of the adhesives, adhesive compounds, applications and their migration potential should support the following objectives:

- Structuring adhesive compounds, adhesive types, applications as a tool for selection representative test systems (operational objective for the project)
- Collecting information on substance properties, regulations, existing toxicological evaluations, migration potential and on applications needed for
    - Experimental determination
    - Mathematical modelling
    - Choice of a suitable pathway to obtain the migration value by estimation or experimentation.
    - Evaluation of the substance

There are a lot of factors which influence the migration of components from an adhesive layer through substrates into food. Such a multidimensional classification is shown in Figure 4-2. For selection of representative test systems it was agreed within the consortium that it would be the best approach to classify according to the raw material polymer type, the reactivity and the solvent system. Adhesives where the polymer is made from pre-polymers or monomers during curing are compiled as reactive ones and those which cure physically (e. g. by drying or temperature application) as non-reactive. The solution type is divided in three classes. 100 % systems compile all solvent free systems (solvent free reactive systems as well as non-reactive hotmelt systems). The other two classes are the water based and the (organic) solvent based systems (Figure 4-1).

Starting from this classification, the relevant adhesive types for food contact material applications and their applications have been collected. The scheme (Table 4-1) was established within the consortium. This classification reflects the chemistry of the adhesives as well as the complexity arising from numerous parameters in the end use of the system (Substrates, packaging design, means/type of application, etc.). In this scheme the adhesive systems which are included as test samples in the project are marked. Finally the experience of the affected industry, adhesive industry as well as packaging converters of paper&board and plastics was included to obtain an as complete as possible overview on food packaging related adhesive systems and applications and a representative selection of adhesive systems for the research work.

4.1.2 Selection of test systems

Based on the classifications made above, 23 representative test systems had been defined and selected by the consortium with the intention to be typical for adhesives formulations, materials and structures used for food contact materials and to include different application and handling conditions: like type of food, type of contact, temperature and storage conditions (Table 4-2). Furthermore a range of cork stopper applications with polyurethane adhesives are investigated in the project. All these test systems are used for the comprehensive studies within WP 2. Additionally to the project consortium, the selection of test samples has been discussed within the converter associations, partner IK and MCAS, and their input has been considered in order to ensure representativeness.

The samples have been prepared full area coated even if the adhesive was originally intended only small area application e.g. in seams. The laminates were prepared on laboratory scale at the industry facilities or the institutes.

Additionally to the test systems from packaging materials on plastic, paper and board substrates, ten systems for cork stoppers have been investigated. All adhesives for manufacturing the agglomerated cork body were from reactive solvent free polyurethane type with aromatic isocyanates (toluene diisocyanate TDI and/or methylenediphenyldiisocyanate MDI). For gluing a cork disk on the stopper waterbased polyurethane dispersions and one anionic reactive solvent free system were used.

Further 47 market samples, i.e. empty packagings or packaging materials with adhesives have been collected for verification purposes (WP4).

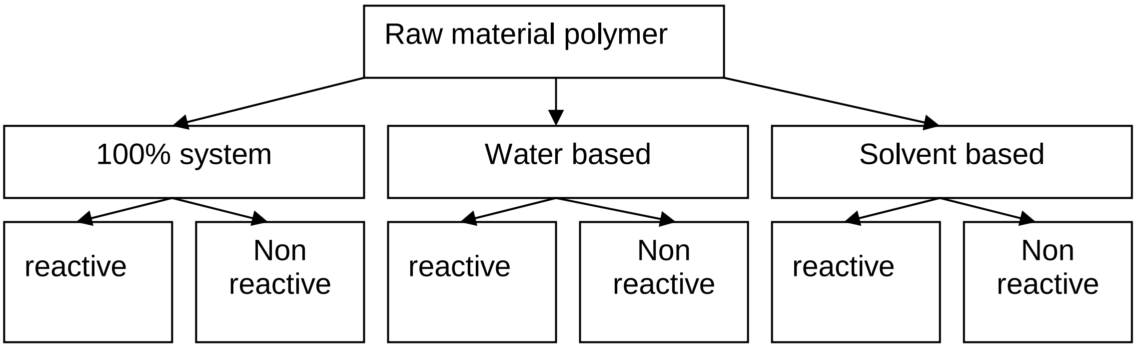


Figure 4-1: Classification of adhesives according to the raw material polymer, reactivity and solution type

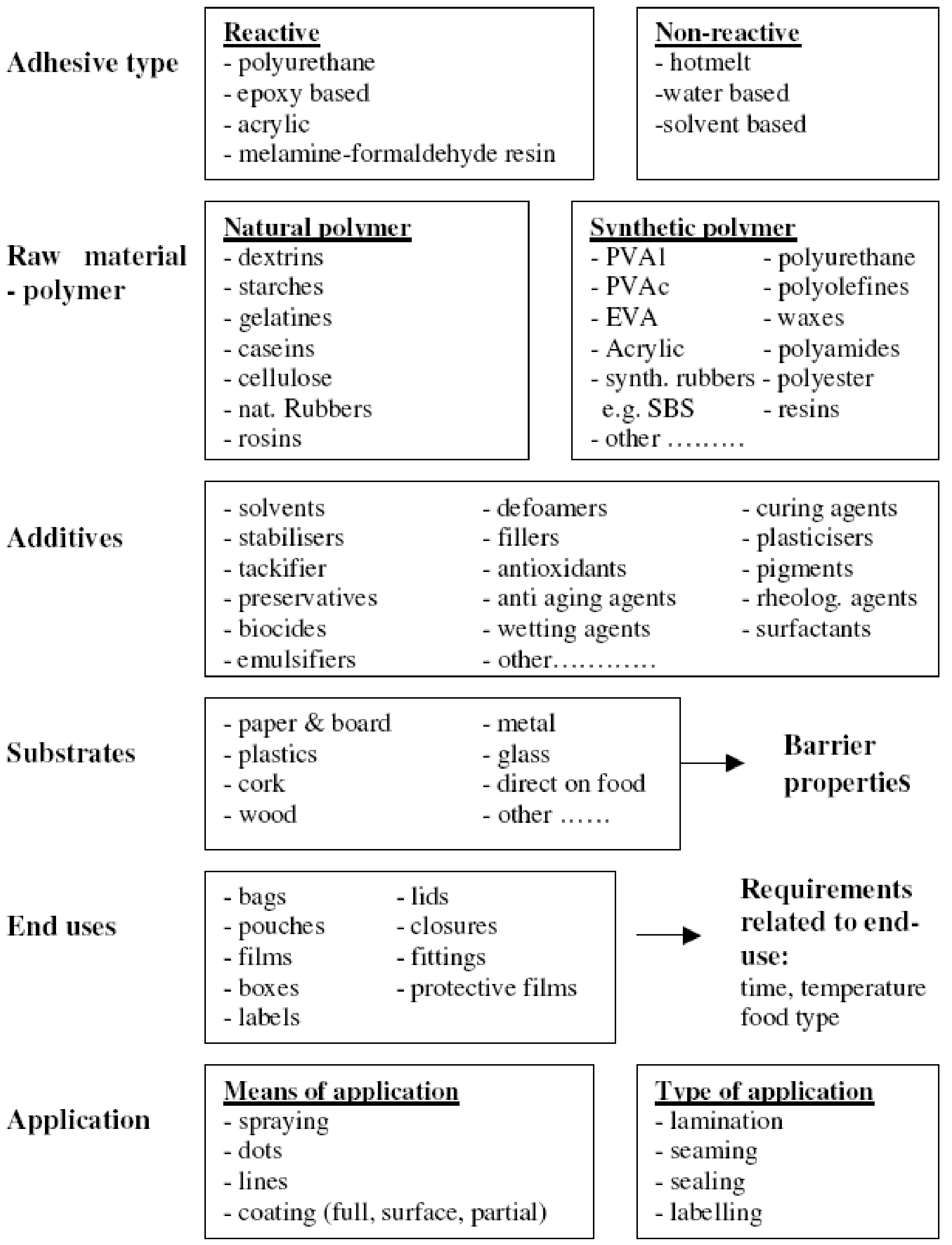


Figure 4-2: Multidimensional classification of adhesives in relation to influence factors on migration of adhesive components.

Table 4-1: Adhesive systems for food packaging applications. Test systems in the project are marked.

Raw material polymer	**100 % system**		**water based**		**solvent based**		Comment
	reactive	non-reactive	reactive	non-reactive	reactive	non-reactive	
Acrylic	x (psa labels, film/film)	x (psa)		x (film/paper)		x (psa, film/film)	
casein				x (labelling, laminating, *cork*)			
cellulose				*x (paper sacks)*			
dextrin				*x (labelling, most packaging, mainly with paper)*			
EVA		x (boxes, labelling, psa)		x (packaging)			
VAE				x (boxes, paper applications)			
(gelatine)				*x (graphical applications, ???)*			
natural rubber				x (cold seals)		x (psa tapes, labels, cork)	
(polyamide)		*x (boxes)*					
(polyester)		*x (textiles)*					
polyolefine		x (boxes, hygiene art., psa, labelling)					
polyurethane	x (film/film, clear boxes, cork)	x (film/paper)	x (film/film, film/paper, cork)	x paper/paper)	x (film/film)		
PVAc				x (paper/paper, wood, cork, packaging)			
PVOH				x (paper/paper, packaging, tissue laminating)			
(resin)		*x (psa, boxes, labelling, hygiene art.)*				*x (psa, boxes)*	*additive*
(rosin)		*x (psa, boxes, labelling, hygiene art.)*				*x (psa, boxes)*	*additive*
starch				x (labelling, paper/paper, corr. board)			
synth rubber		x (hygiene art., boxes, labelling, psa)		x (film/paper, alu/paper)		x (psa)	
('wax?)		*x (paper coating, sealing, boxes)*					*additive*
epoxy based	x (structural applications)						
melamine formaldehyde			x (wood, cork)				
formalehyde condensation products				x (paper/paper)			
PVP		x (labelling)					
polyvinylether				x (labelling)			
glucose				x (paper/paper, tissue)			
water-glass				x (tissue)			
additional systems for cork closures							

psa = Pressure sensitive adhesive, (e.g. adhesive tapes, protective film)
The raw material polymers not used for food contact or only as additives for food contact adhesives are set in brackets and cursive)

Table 4-2: Adhesive test systems for comprehensive studies within WP 2

Test system	Raw material polymer	Description of system	Substrate 1	Substrate 2	End application
Natural Rubber 1	Natural rubber/solvent based/ non-reactive with PUR primer	pressure senstive coating	plastic film	paper	psa tape for closings of folding boxes
Natural Rubber 2	Natural rubber/water-based/ non-reactive	cold seal, system without any fillers	BoPP film	BoPP film	tubular bag
Synthetic Rubber 1	Synth. Rubber/100 % system/ non-reactive	SEBS or SIS polymers, plasticised with mineral oil	paper	plastic film	bag with plastic window
Synthetic Rubber 2	Synth. Rubber/water-based/ non-reactive	SBR emulsion, wet and dry applications	metalised film	cardboard	trays
Acryl 1	Acrylic/ water based/ non-reactive	wet lamination	paper	opp film	bread bags with windows
Acryl 2	Acrylic/ water based/ non-reactive	film print lamination	paper	opp film	folding boxes and tray for food
Acryl 3	Acrylic/ water based/ non-reactive	pure acrylate	label material:	e.g. cling film	psa paper labels
Acryl 4	Acrylic/water-based/ non-reactive	pressure sensitive coating	plastic film	paper	psa tape for folding boxes
EVA 1	EVA/100 % system	injection hot melt	cardboard	(Laminated Opp) cardboard	folding box
VAE 1	VAE/water-based/ non-reactive	VAE plastisized with Triacetin:	cardboard	cardboard	folding box
VAE 2	VAE/water-based/ non-reactive	VAE different plasticizer than TA	cardboard	plastic window	folding box
VAE 3	VAE/water-based/ non-reactive	VAE , plasticiser, antifoam agent, biocide, water	cardboard	cardboard	folding box
VAE 4	VAE/water-based/ non-reactive	VAE plastisized with Triacetin	paper	paper, coated paper	paper bags: side seam
VAE 5	VAE/water-based/ non-reactive	VAE plastisized with Benzoflex	paper	paper, coated paper	paper bags: side seam
PO 1	polyolefines/ 100 % system/non-reactive hot melt	hot melt system	paper	OPP film or polyolefin film	general use
PVAC 1	PVAc/water-based/ non-reactive	PVAc plasticized	cardboard	cardboard	folding boxes side seam
PVAC 2	PVAc/water-based/ non-reactive, plasticised		wood	wood	e.g. kitchen tray, repeated use
PVAC 3	PVAc/water-based/ non-reactive	plastisized PVAc	paper or board	paper	tube winding
PVAC 4	PVAc/water-based/ non-reactive, dispersion	non plastisized PVAc	paper or board	paper	tube winding
PVOH 1	PVOH/water-based/ non-reactive	PVOH solution	paper	paper	paper bags: side seam
Starch 1	Starch	pure starch glue (starch + preservative)	paper	paper	paper bags: bottom seam
Starch 2	Starch	starch glue with VAE-Emulsion	paper	paper	paper bags: base seam
PUR 1	Polyurethane/solvent based/reactive		plastic film	plastic film (PE)	flexible packaging
VAE 6	VAE/water-based/ non-reactive, & acrylic dispersion water-based non-reactive				final application for WP4
Casein	*Casein*				*Label on bottles (Glass,)*
Cork	PU based adhesives		cork		cork stoppers

Note: PVAC2 samples not delivered within project period.
Legend: colour code of laboratories: migration experiments inWP2c at FABES yellow, UNIZAR pink, IVV blue, CTCPA green. White: no substances in sufficient concentrations for migration experiments in the laminate or samples not investigated (see comments)

4.1.3 Database on adhesive compounds

A database with the most important substances used for manufacturing adhesives in food contact materials applications compiled as a tool to provide information on substance properties, regulations and toxicological evaluations (Deliverable 1.2 and 1.3). For all substances the regulatory status in Europe and USA as well as the physico-chemical properties (molecular weight, partition coefficient octanol/water log $P_{O/W}$, solubities, chemical reactivity and, as far as available, analytical method) have been included. The list shall give assistance for evaluation of a substance and provide input data for migration modelling as well as for the selection of appropriate analytical methods or the selection of a suitable pathway to obtain the migration value by estimation or experimentation.

Two lists of substances which are used in adhesive industry have been existing before start of the project. The German TKPV list contains 2130 items (including multiple nominations by different uses). It was established by the industry experts within the Technical Committee Paper and Packaging Adhesives TKPV of the German IVK in the nineties. The list contains substances as well as their regulatory status in Europe, Germany (BfR recommendations) and USA (listing and restrictions in 21 CFR). The list contains only substances which have at least one regulatory reference there. Therefore it is not an inventory list and on the other hand it contains also substances which are not or not anymore used in adhesive applications for food packaging or which are not recommended to be used by the evaluation of the SCF (Scientific Committee for Food of the European Commission). The list was not actualised since more than 10 years also in terms of the legal status of the compounds. Within the project a selection of the actually important substances has been made by the adhesive experts within the project.

The second list had been established within a project of the British Ministry of Agriculture and Food (MAFF Project FS 2223) in cooperation with the De Montfort University in Leicester (Report dated February 1999, (Bonnell and Lawson 1999)). This Montfort list contains about 360 substances and was derived by consultation of industry in UK and more than 160 organisations were approached including trade associations, adhesives and chemical companies, converters, food manufacturers and fruit packagers. There is a broad overlap with the TKPV list but the Montfort list contains also substances which are not present in the TKPV list.

The selection of the TKPV list and the Montfort list have been merged and further substances contributed by project partners have been included, resulting in a list of 437 substances. In the project consortium was no need seen, to have a second list with additional confidential information (Deliverable 1.2).

For analytical purposes in order to establish and validate multimethods for screening and determination of adhesive compounds, a further list of 55 commercially available chemicals which are relevant for adhesive formulations, was established (Deliverable 3).

4.2 Analytical and physico-chemical experimental core studies (WP 2)

The objectives of WP2 are in depths experimental studies of compositional character of selected systems and samples from WP1 in order to generate knowledge on the characterization and migration behavior of adhesive constituents in food contact materials.

4.2.1 Compositional analyses and studies (WP 2a)

The test systems were analytically investigated in order to identify the potential migrants which may be additives (classified by their technological function), monomers and oligomers as well as by-products and neo-formed reaction products build up during production of the adhesive, application, curing and after processing. For this purpose the pure adhesives, cured adhesives on the substrates and the substrates alone had been analysed. The results are compiled in Deliverable D2 part 1.

Analytical procedures were developed for the screening of compounds in both, adhesive and laminate samples. The screening techniques developed and used depended on the compounds volatility. Screening for volatile compounds was carried out by GC-TOF-MS and HS-SPME-GC-MS. SPME allows to have a high sensitivity with low sample handing. The first step of these analysis was the selection of the most appropriate SPME fiber and the optimal extraction conditions depending on the sample studied. Screening for non volatile compounds was carried out by HPLC-MS-MS and HPLC-MS-TOF

Volatile compounds in acrylic adhesives as well as the laminates obtained with them were studied in depth by GC-TOF-MS and HS-SPME-GC-MS techniques providing the data base to start with a list of components present in real adhesives. For the GC-TOF-MS analysis, pure adhesive samples were extracted with acetonitrile. The samples were analysed in both electron impact and chemical ionization modes. With electron impact mode a total of 43 volatiles were detected in the adhesives studied. Even though all the adhesives were acrylic based, only 2 of the volatiles were found in more than one sample. These results showed the variability of adhesive formulations. Chemical ionization (CI) mode allowed identifying 10 compounds previously detected in EI mode, confirming 18 compounds previously identified and identifying some new compounds. HS-SPME-GC-MS technique was used for screening the volatile compounds released by the laminates. Non volatile compounds in acrylic adhesives were analysed by UPLC-TOF-MS and UPLC-Q-TOF-MS in order to identify the compounds presents in the adhesives. Results showed that there was not a common profile of compounds for the pure adhesives. By UPLC-Q-TOF-MS. 13 compounds were detected, all of them were esters.

The hot-melt adhesives were of two different polymer types, one of them based on EVA (HM 1) and the other based on polyolefin (HM 2). The screening of the volatile compounds was carried out by HS-SPME-GC-MS before and after the hotmelting process at 160-180 ºC. In the pure hotmelt 1, 39 compounds were found. Heating had no influence on the substances found but their concentrations changed during the hotmelting process, whereas some of the compounds increased their signal, others decreased.. In the pure HM 2, only 2 compounds were found before and after hotmelting.

A natural rubber adhesive and a synthetic rubber adhesive were investigated by HS-SPME-GC-MS. Only 4 compounds were found in the natural rubber adhesive and 8 in the synthetic rubber adhesive.

These methods have been published in (Nerín, Canellas et al. 2009; Canellas, Nerín et al. 2010).

Five VAE, three PVAC, one PVOH, one natural rubber cold-seal, two starch and one synthetic rubber hotmelt adhesive as well as the corresponding laminated test systems and substrates have been analysed by GC-FID/MS and HPLC-CAD of extracts. In the VAE and the PVAC adhesives mainly the used plasticizing additives have been found. Other substances were in very low concentrations or not detectable. In the PVOH, the cold-seal and the starch adhesives no substances could be detected in amounts which were suitable for systematic migration experiments. In the synthetic rubber hotmelt several, chromatographically non-dissolved peak groups were found which could be assigned to used mineral oil.

Summarizing, mainly the additives, some decomposition or by-products from additives or resin compounds have been identified in the samples. Neo-formation of substances during application could not be detected in the investigated non-reactive systems. Substances present in major concentrations were quantified in order to obtain the initial concentration ($c_{P,0}$) in the material which is a main parameter for migration modeling. The results are laid down in Deliverable D2 part 1.

Polyurethane adhesives for cork stoppers were analysed as non-reacted adhesive, after curing and in the finished cork sample by headspace-GC-MS and GC-MS of extracts. Before polymerisation, most identified chemicals were residual solvents, reactive isocyanates, antioxidants and aliphatic esters. After polymerisation (or drying step for water dispersion) small linear aldehydes, no more reactive isocyanates but still aliphatic esters with long chain were found. In the extracts additionally long chain alkanes and carboxylic acids were detected. In the cork stopper extracts no additional substances from the adhesives were found. The cork stopper studies are described in Deliverable D2 part 2.

The neo-formation of substances was tackled from a theoretical side (Deliverable D2 part 3). As sources for the neoformation of substances during production, application and storage of adhesives or finished articles with adhesives, monomers, antioxidants, antimicrobial substances and plasticizers have been studied. Experimentally none of the predicted neoformed substances could be detected in the investigated adhesives.

For characterization of the adhesives further studies using thermogravimetry, differential scanning calorimetry and infrared spectroscopy were performed (Deliverable D2 part 4).

4.2.2 Quantitative approach to groups and unknown substances (WP 2b)

The substances in adhesives derive from various chemical classes (functional groups) and cover the whole range of physico-chemical properties from volatile to non-volatile, from polar to non-polar. For investigation of these substances, the development of methods is necessary which cover broad ranges of physico-chemical properties so that many compounds can be analysed simultaneously in one analytical run. This is needed for screening analyses and simplifies quantitative determinations by substituting single methods for each analyte.

Extraction methods from pure adhesives as well as glued substrates have been developed and validated. These are described in Deliverable D9.

A selection of 55 adhesive related substances (see chapter 4.1.3) was used to further develop and validate screening GC multimethods. Additional twelve plastics additive were included for developing a HPLC method. The 55 substances were in a range of molecular weights from 72 to 1178 g/mol and covered different polarities and functional groups. The non-volatiles have been underrepresented in the first selection, therefore the additional additives were included although they are not common for adhesives.

Best results for gas chromatographic separation were obtained by using a non-polar polydimethylsiloxane column phase (e. g. DB-1) at a temperature programme from 40 °C to 340 °C. The non- or semi-polar substances were successf ully analyzed with sufficient response, the polar substances like di- and polyalcohols, amines and carboxylic acids showed a bad peak shape and therefore low sensitivity. The method covers substances migrating from packaging materials and adhesives in a molecular range of approximately 80 to 800 g/mol. The substances retention times as well as retention indices correlate well with the molecular weight (Figure 4-3). Thus it can be used for estimating the molecular weight of unidentified compounds. The molecular weight is an important parameter for migration modeling.

Using polar column phases (FFAP, polyethylene glycol-TPA modified or DB wax, polyethylene glycol) the polyalcohols were eluted with a better peak shape and better sensitivity. Because of lower temperature resistance of the phases, higher molecular substances cannot be eluted. For a general screening analysis the polar columns had not so clear advantages that a run with a polar column additionally to the non-polar one would be recommended.

In screening analyses by GC-FID the detection limit and the concentration of the detected substances are estimated in many laboratories by comparison with the peak area of a universal internal standard substance. At Fraunhofer IVV BHA (tert-butylhydroxyanisol) is used as internal standard. Within the project seven level calibrations of 46 substances from the 55 substances list had been measured in the range of 0.1 and 50 mg/l and the relative response factors to BHA had been determined. The calibration curves had been linear. The mean relative response factor was 0.8 ± 0.3 (mean ± standard deviation) or, when excluding the peaks from the four polyalcohols with strong tailing (bad peak shape), 0.9 ± 0.3. This shows the suitability of the approach estimating detection limits and concentrations by BHA as internal standard. Furthermore from the many linear calibration curves of the representative substances it can be concluded that the separation conditions can be used for simultaneous quantification of many adhesive related substances.

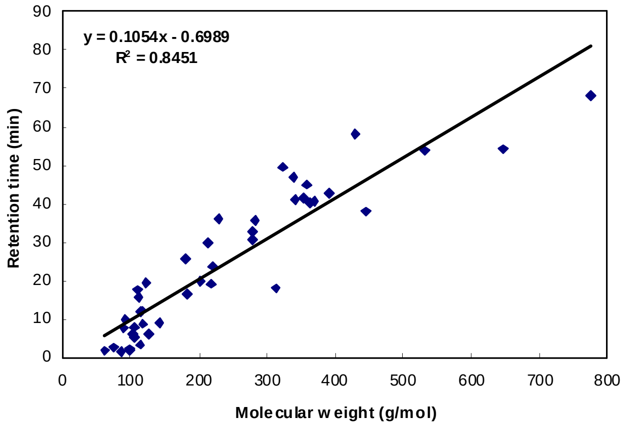


Figure 4-3: Correlation of the retention time with the molecular weight on GC-FID equipped with DB-1 column.

The non-volatile substances from the list have been analysed by HPLC connected with a charged aerosol detector (CAD). The detection mode is independent from chromophore structures (UV or visual light) and should theoretically not be affected by the physico-chemical properties of the substances but only by the number of molecules. 29 substances have been analysed. A acetonitril water gradient starting with 60 % acetonitrile to 100 % turned out to be most suitable. The dicarboxylic acids and other ionic or high polar substances need specific pH adjusted eluents.

For 24 substances calibration curves have been obtained. 2-(2H-benzotriazol-2-yl)-4,6-bis(1-methyl-1 phenylethyl)-phenol (Tinuvin 234) has been used as internal standard. The relative response factors showed a much broader range than GC-FID. The substance properties have a higher influence on the detection than expected from theory. The applicability of estimating concentrations of unknows or detection limits using an universal internal standard is therefore limited, at least a very rough estimate. But the developed method will be useful for simultaneous quantification of non-volatile compounds via calibration with the respective standard substances.

These two approaches of analyzing extracts by GC-FID and HPLC-CAD as well as a feasibility study using two dimensional HPLC are described in detail in Deliverable D3. The method descriptions can also be found in the guideline document Deliverable D9.

4.2.3 Migration and partitioning studies (WP 2c)

Objective of this subworkpackage was to determine key parameters allowing modelling and prediction of the migration behaviour and of barrier properties of food contact material layers (diffusion and partition coefficients).

Substances like additives, stabilizers, plasticizers, etc. from an adhesive, used to glue a multilayer material, may diffuse/migrate through the contact layer of the packaging and contaminate the food. At a certain point in time the level of such a contamination depends on a series of parameters from which the initial concentration, C_{P0}, of the substance/migrant in the adhesive as well as its diffusion coefficients, D_p's and D_f, and partitioning coefficients, K_{pp}'s and K_{pf}, in the multilayer-food system are of outstanding importance (p = packaging and f = food).

The D_p's and D_f, are a measure of the mobility of the diffusing/migrating species in the matrix of the individual layers of the packaging, the adhesive and of the food. The magnitude of these coefficients depends in a complex manner on the working temperature, the chemical nature of the migrant and that of each layer and respectively the food. In the literature there are given several data banks with Dp's. However these sources contain little if any information about diffusion in adhesives. Data banks also lack information about Df's for real foods.

The K_{pp}'s at the interface between two layers of a multilayer material and Kpf at the contact layer-food interface are of thermodynamic nature. These coefficients reflect the ratio of the equilibrium solubility of the migrant in two adjacent layers of the packaging-food system. Because the solubility of a substance in any material usually varies with temperature, T, the K_{pp}'s and K_{pf} also depend on T. Specific information about K_{pp} and K_{pf}'s for multilayer packaging and real food is rather scarce in the literature.

In WP2c the experimental basis for calculation of the partitioning coefficients and diffusion coefficients is laid. The data are used to obtaine the coefficients by mathematical modeling within WP3 (Chapter 4.3.1)

4.2.3.1 Studies using the test systems and their adhesive components

Three different type of studies have been performed using the test samples which had the structure substrate/adhesive/substrate or substrate/adhesive. The adhesive layer was in all cases full area coated.

- 37 Equilibrium experiments at 40 ℃ and 60 ℃ for 10 test systems (Table 4-3)
- 56 Migration kinetics at 20℃, 40℃, 60℃ and 70℃ for 14 test systems (Table 4-4)
- 46 Concentration profiles at 40℃, 60℃ and 70℃ for 13 test systems (Table 4-5)

The details are described in Deliverable D4 part 1.

Table 4-3: Samples and test conditions for equilibrium tests

Test system	Time	Temperature conditions
PVAC1	32 days	60 ℃
	50 days	40 ℃
VAE 2	32 days	60 ℃
	50 days	60 ℃
	71 days	60 ℃
	50 days	40 ℃
VAE 3	60 days	60 ℃
	60 days	60 ℃
	60 days	60 ℃
	60 days	60 ℃
	122 days	60 ℃
	122 days	60 ℃
	122 days	60 ℃
	122 days	60 ℃
	132 days	40 ℃
	132 days	40 ℃
	132 days	40 ℃
	132 days	40 ℃
	87 days	40 ℃
	87 days	40 ℃
	87 days	40 ℃
	87 days	40 ℃

Test system	Time	Temperature conditions
EVA 1	11 days	40℃
	11 days	40℃
	11 days	60℃
	11 days	60℃
Acryl 1	30 days	40℃
	30 days	40℃
Acryl 2	30 days	40℃
	30 days	40℃
Acryl 3	30 days	40℃
Acryl 4	30 days	40℃
	30 days	40℃
Natural Rubber 1	30 days	40℃
	30 days	60℃
Synthetic Rubber 1	30 days	40℃
	30 days	60℃

Legend: Code of laboratories: experiments at FABES yellow, UNIZAR pink, IVV blue, CTCPA green.

In equilibrium experiments enough time must be given to the experimental run to ensure that the process of migrant redistribution between the different layers of the investigated system comes to a halt and equilibrium is reached. Then from the concentrations in the substrate layers and the initial concentration before start of the experiment the partition coefficient can be obtained.

Table 4-4: Samples and test conditions of kinetic migration tests

Test system	Time	Temperature conditions
PVAC 1	2, 5 days	70 °C
	7, 17, 28 days	40 °C
	0,25, 0,7, 1, 2d, 4d, 11d, 25days	60 °C
	1, 2, 5, 12, 25, 32days	40 °C
	3, 5, 11, 21, 28, 49, 60days	20 °C
VAE 2	2, 5 days	70 °C
	7, 17, 27 days	40 °C
	0,125, 0,25, 1, 3 days	20 °C
	0,125, 0,3, 0,67, 2,7, 8, 15days	60 °C
	0,25, 1, 3, 5, 15, 25days	40 °C
	1, 3, 5, 14, 29, 40days	20 °C
VAE 3	2, 4 days	70 °C
	2, 5 days	70 °C
	0,67, 3, 5, 8, 19, 21 days	70 °C
	0,25, 1, 2, 4, 11, 25days	60 °C
	1, 3, 4, 11, 19, 28, 33, 46days	40 °C
	3, 6, 12, 31, 49, 60days	20 °C
VAE 1	2, 4, 5, 16, 24, 24 hours	60 °C
	0.33, 1, 2, 5, 10 days	60 °C
	6, 16, 24, 48h, 5, 10days	40 °C
	2, 4, 5, 16, 24, 24 hours	60 °C
	1, 2, 5, 10, 23, 31 days	40 °C
	12, 20, 30 days	40 °C
	1 day	70 °C
	5 day	70 °C
	10 day	70 °C
VAE 4	4, 7, 20 days	23 °C
	1, 5, 20 days	40 °C
	1, 4, 10 days	70 °C
	1, 5, 10, 15, 20 days	60 °C
	2, 4, 6, 16, 24, 48 hours	60 °C
	2, 4, 6, 16, 24, 48 hours	60 °C
	6, 16h, 1, 2, 5, 10 days	40 °C
VAE 5	1, 4, 7, 10 days	23 °C
	1, 5, 12, 20, 30 days	40 °C
	1, 4, 10 days	70 °C
	0.33, 1, 2, 5, 7 days	40 °C
	0.17, 0.33, 1, 2, 4 days	60 °C
	2, 4, 6, 16, 24, 48 hours, 3 days	60 °C
	2, 4, 6, 16, 24, 48 hours, 3days	60 °C
	6, 16h, 1, 2, 5, 10 days	40 °C
PVAC 3	4, 8 h, 1, 2, 5 days	40 °C
	4, 8 h, 1, 2, 5 days	40 °C
	10, 22 days	60 °C
	10, 22 days	60 °C
PVAC 4	4, 8 h, 1, 2, 5 days	40 °C
	4, 8 h, 1, 2, 5 days	40 °C
	10, 22 days	60 °C
	10, 22 days	60 °C
EVA 1	10 days	40 °C
	10 days	40 °C
Acryl 1	10 days	40 °C
Acryl 2	10 days	40 °C
Acryl 3	10 days	40 °C
Natural Rubber 1	10 days	40 °C
Synthetic Rubber 1	10 days	40 °C

At kinetic tests the concentration in a receptor layer is determined at several timepoints. From the obtained migration curve diffusion coefficients and partitioning coefficients can be calculated.

Table 4-5: Samples and test conditions of concentration profile experiments

Test system	Time	Temperature conditions
PVAC 1	7 days	70 °C
	15 days	40 °C
	3 days	70 °C
VAE 2	7 days	70 °C
	13 days	40 °C
	28 days	20 °C
	3 days	70 °C
VAE 3	2,9 days	70 °C
	7 days	70 °C
	27,1 days	70 °C
	11 days	40 °C
VAE 1	14 days	40 °C
	7 days	70 °C
	33 days	40 °C
Synthetic Rubber 1	1 hour	120 °C
	1 day	40 °C
VAE 4	33 days	40 °C
	1 days	70 °C
	5days	70 °C
	11 days	40 °C
	20 hours	40 °C
	20 hours	40 °C
VAE 5	33 days	40 °C
	11 days	40 °C
EVA 1	24 hours	40 °C
	73 hours	40 °C
	24 hours	60 °C
	73 hours	60 °C
Acryl 1	1 day	40 °C
	2 day	40 °C
	3 day	40 °C
Acryl 2	1 day	40 °C
	2 day	40 °C
	3 day	40 °C
	1 day	40 °C
	2 day	40 °C
	3 day	40 °C
Acryl 3	2 hours	40 °C
Natural Rubber 1	24 hours	40 °C
	48 hours	40 °C
	24 hours	60 °C
	48 hours	60 °C
Synthetic Rubber 1	24 hours	40 °C
	48 hours	40 °C
	24 hours	60 °C
	48 hours	60 °C

In concentration profile experiments, migration into a stack of acceptor layers is determined at a defined temperature-time condition (before reaching the equilibrium). From the concentration profile again partitioning and diffusion coefficients can be obtained. To reduce the number of unknown parameters in most experiments the substrate itself was used as receptor material. In this case K_{34} is equal to 1 in Figure 4-4.

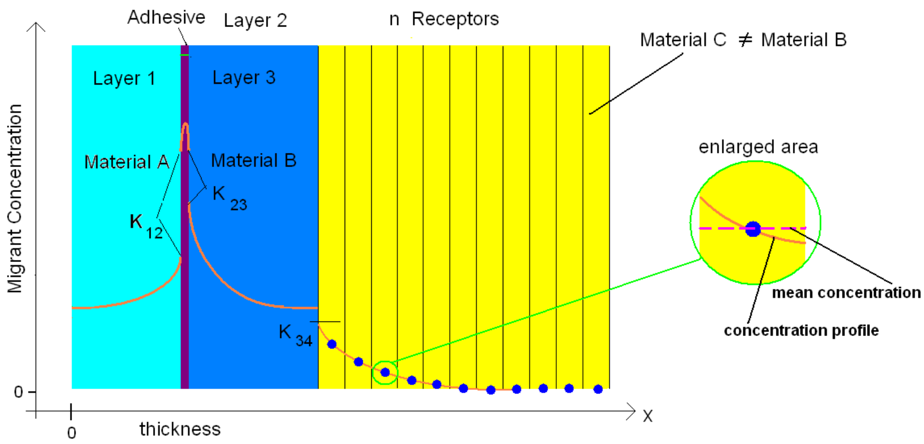


Figure 4-4: Concentration profile for a substance migrating from the glued sample (Material A and B).

4.2.3.2 Partitioning studies using model test substances

Further partitioning experiments have been performed by adding model test substances to selected adhesives and substrates. The objective was to obtain additional information for prediction of partitioning coefficients in dependency of polarity. The strategy was to select a “homogeneous series” of surrogates intentionally added to the selected adhesives, to coat the selected substrates with the doped adhesive, to wait for the equilibrium and then to determine K after peeling the different layers before solvent extraction an analysis from conventional analytical method (GC FID). The model substances are shown in Table 4-6. They have been sorted as a function of their polarity determined from their solubility parameters from literature (Jayasri and Feair 1980), when available, or calculated from the group contribution theory. As substrates an oriented polypropylene film (OPP) and two paper types, silk seminate and parchment substitute has been used. The combinations of adhesives and substrates are shown in Table 4-7.

Table 4-6: series of model migrants for partitioning studies and their solubility parameters

model migrants	CAS number	series	Log P[2]	solubility parameters (MJ m^{-3})
M1 : Octadecane	593-45-3	Apolar series (M1 to M3)	9.50	16.0
M2 : Dioctyl phthalate	84-74-2		8.70	18.2
M3 : Dibutyl Phthalate	117-81-7		4.83	20.2
M4 : Butyl Hydroxybenzoate	1322-01-6	Polar series (M4 to M6)	3.46	26.0
M5 : Methyl Hydroxybenzoate	29468-36-8		1.87	30.1
M6 : Ethylene glycol	107-21-1		-1.69	31.6

Table 4-7: Combination of adhesives and substrates for partitioning studies with model substances

Adhesives + OPP	Adhesives + paper
VAE 1	VAE 4
Acryl 1	VAE 5
Acryl 2	Starch 2
Synthetic rubber 1	PVOH 1
EVA 1	Acryl 1
PO 1	Acryl 2

[2] From Science Finder data base

Model migrants (M1 to M6 see Table 4-6), adhesives (in black rectangle) and substrates (in blue rectangle) were positioned on a polarity scale according their solubility parameter. For adhesives, the solubility parameters can only be estimated from their binders' chemical structure and not for the formulated adhesive. Therefore a rough estimation was made on the basis of compositional information and literature data. The idea is to localize both migrants and substrate. When adhesives and substrates present rather the same solubility parameters, the K value should be near 1 as the migrant will have the same affinity for both of these media (Figure 4-6, first example). When the affinity of the migrant to the adhesive is higher than to the substrate, $K_{adhesive/substrate}$ is expected to be >> 1. Details are described in Deliverable D4 part 2.

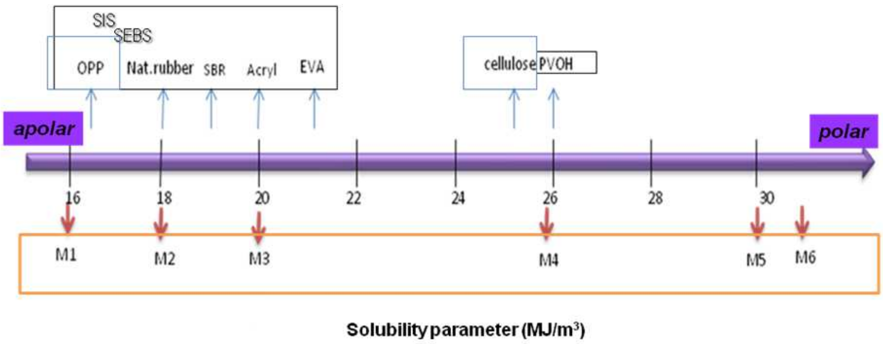


Figure 4-5: Substrates, adhesives and migrants positioned on a polarity scale

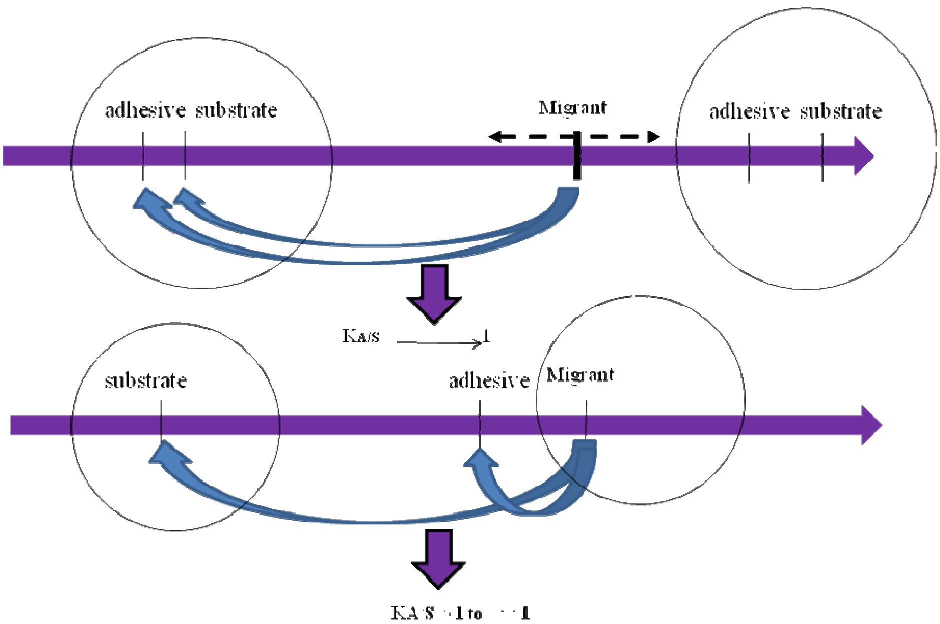


Figure 4-6: : Expected K value as a function of the solubility parameters of the system (substrates and adhesives)

4.2.3.3 In situ determination of diffusion coefficients via fluorescence recovery after photobleaching (FRAP) technique

In the above described kinetic or concentration profile experiments the diffusion coefficients in the adhesive layers are determined indirectly by measuring the concentration changes in substrate or receptor material layers. A complementary approach was to investigate diffusion of fluorescent substances directly in the cured adhesive. For this, adhesives were formulated with a special fluorescent substance which is able to be bleached (or photolysed into a non fluorescent derivative) when a high intensity laser light is applied. A rectangular region is bleached and recovers progressively its fluorescence properties as unbleached dye molecules are migrating from surrounding regions. This recovery is recorded by confocal laser scanning microscopy as a function of intensity and time from which the diffusion coefficient can be calculated. This gives the intrinsic diffusion coefficient without any interaction with the simulant. The technique and the test substances are described in (Pinte, Joly et al. 2008). The results are summarised in Table 4-8. The adhesive PVOH 1 was investigated by Moisan technique where a concentration profile of migration from cured adhesive layers with Uvitex OB and $NBDET_2$ into blank adhesive layers was investigated (Table 4-9). The other adhesives were not available in non-sticky layers which could be de-assembled after a Moisan test.
The details and results are described in Deliverable D4 part 3.

Table 4-8: Diffusion coefficients obtained by FRAP technique at 20 and 40 °C.

Adhesives	Diffusion coefficient of $NBDET_2$ at 20 °C [cm²/s]	Diffusion coefficient of $NBDET_2$ at 40 °C [cm²/s]	Diffusion coefficient of $NBDpip_1$ at 40 °C [cm²/s]
EVA a	5,62E-11		
EVA b	3,16E-11		
EVA c	5,62E-11		
VAE 4	1,027E-11	6,24E-12	3,16E-12
VAE 5	2,12E-11	7,85E-11	
starch 1	1,12E-11	7,72E-12	
acryl 2	8,54E-11	1,72E-10	1,00E-10
nat rubber 2	1,98E-10	2,31E-10	
synth rubber 2	6,26E-13	3,85E-12	3,16E-12
PVAC 1	3,30E-12		

Table 4-9: Diffusion coefficients obtained from MOISAN test (concentration profile of cured adhesive layers) at 20 and 40 °C.

Adhesives	Diffusion coefficient of $NBDET_2$ at 20 °C [cm²/s]	Diffusion coefficient of Uvitex OB at 20 °C [cm²/s]	Diffusion coefficient of Uvitex OB at 40 °C [cm²/s]
PVOH 1	*8,82E-15*	*3,31E-14*	*4,43E-13*

4.3 Development of quick tests, migration model and predictive tools (WP 3)

Aim of work package 3 was to derive an approach for compliance assessment of food packaging in which adhesives are either used to manufacture the multilayered material of that packaging or to bind into a given form the final packaging. Such packaging may contain plastics, cardboard, paper and/or metal layers hold together with special adhesives. The envisaged approach for compliance assessment was thought to link quick and relatively simple experimental procedures (for example: extraction tests or determination of equilibrium solubility in the materials used in the packaging) with a mass transport model through which an estimation of rate of migration from the packaging into the foodstuff can be made.

A core of the compliance concept for adhesives is a mathematical model for the assessment of migration from multilayer materials (including adhesives) into foods or food simulants. This model need to be linked to data bases from which the necessary input parameters for a predictive calculation of the migration rates from the packaging into the foods can be taken. At the starting time of this project numerical migration models for calculating migration from plastics multilayers were available. But information about diffusion in and migration from adhesive layers as well as data of partitioning coefficients between substrate and adhesive layers was rather scarce. Therefore one of the main objectives of this project was to generate new experimental evidence of diffusion in and from various types of adhesives used in the food packaging industry. These data were then used to generate the data bases with the input parameters for the proposed compliance assessment approach.

To check the validity of the compliance assessment approach a series of validation procedures were designed in this project. The core of these procedures is formed by a series of migration experiments done with packaging samples taken from the market (WP 4). The results of these experiments were then compared with predictions made using the proposed theoretical model in conjunction with input data collected from the data bases (generated by the project) with reference values for the diffusion and partition parameters. These validation results are described and discussed in Chapter 4.4 (WP 4).

Furthermore a user-friendly software solution for multilayer modelling including databases and educative elements was developed by INRA as a freeware alternative to the commercial multilayer modelling software solutions.

4.3.1 Calculation of migration parameters from the experiments in WP2c

For fitting the experimental data obtained in WP 2c (Chapter 4.2.3.1) by calculated migration curves, the multilayer modelling software MIGRATEST ® Exp developed by FABES GmbH software was used. The algorithm is based on the solution of the Fick's 2nd law. The methods, equations and results are described in detail in Deliverable D5.1.

Partitioning coefficients at defined temperatures between 20 and 70 °C were derived from the equilibrium experiments (Figure 4-7) and from curve fitting by mathematical modelling of the kinetic and concentration profile experiments.

From Figure 4-8 (b) one can see that diffusion from the adhesive within the multilayer leads to a contamination of the two materials. For a given time $t_1 > 0$ the degree of contamination of each layer depends on the diffusion coefficient of the migrant in that layer, D_1 and D_3, the diffusion coefficient in the adhesive, D_2 and on the partitioning coefficient at the layer-adhesive boundaries, K_{12} and K_{23}. If this diffusion process is left to proceed until equilibrium is reached in the multilayer, $t_1 \rightarrow \infty$, the concentration profiles from Figure 4-8 (b) will become those from Figure 4-7 (b).

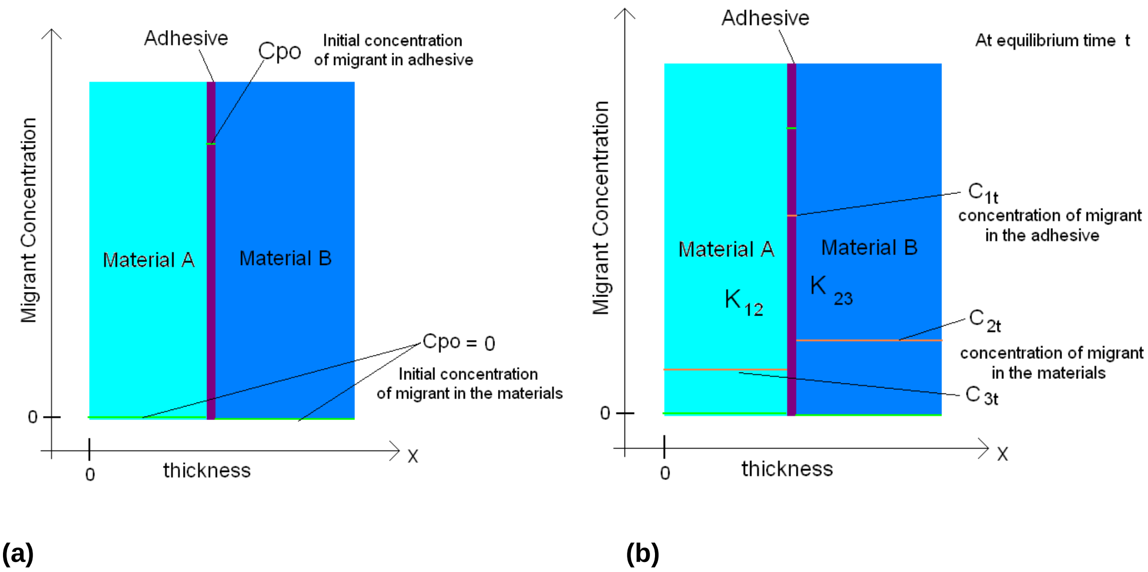


Figure 4-7 (a) and (b): Equilibrium experiment: partitioning processes within a multilayer system at time t=0 (a) and after reaching the equilibrium time t (b).

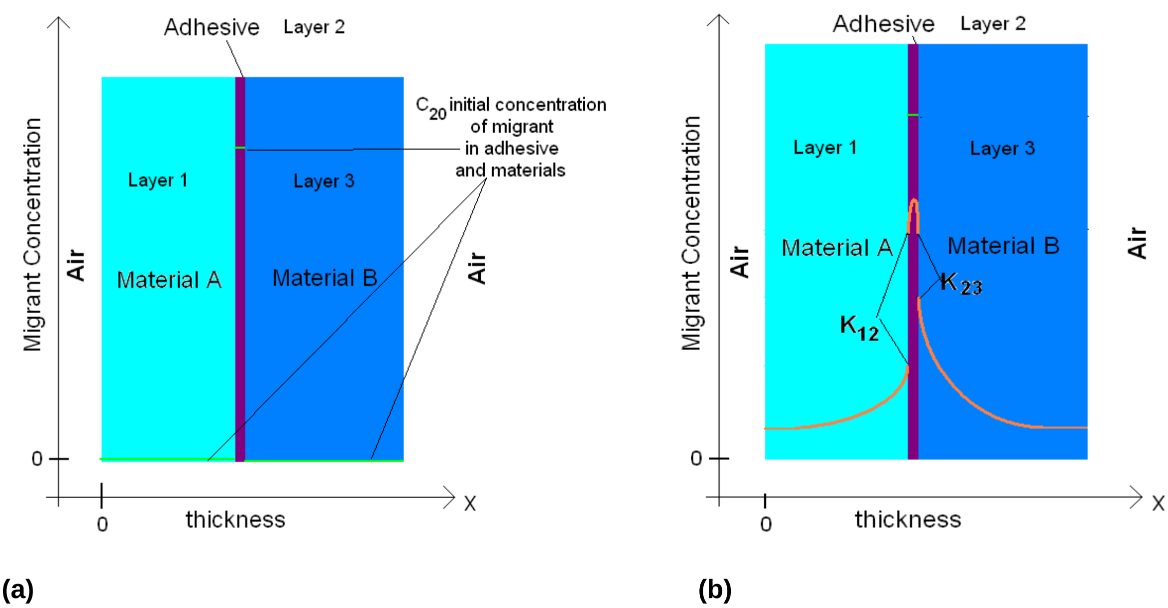
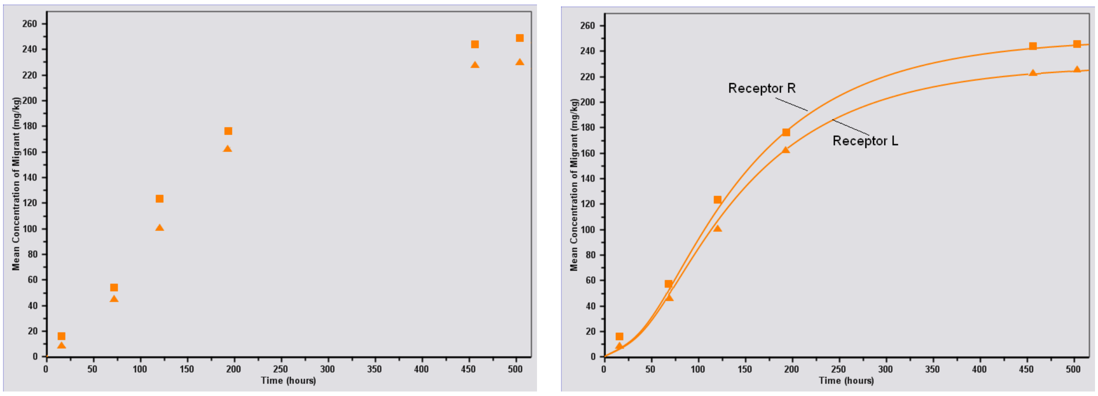


Figure 4-8 (a) and (b): Diffusion processes within a multilayer system at time t=0 (a) and after migration into the sample at time t>0 (b).

For the determination of the diffusion coefficients with the “Kinetic Method” the glued multilayer is exposed at one or both sides to a receptor material. As receptor materials polymers, paper, board and Tenax were used.

Maintaining over a specific period of time, $t_2 > 0$, a tight contact between the multilayer and the receptors, the migrant will diffuse from the multilayer and contaminate the receptors. For a given

t_2 the level of this contamination will depend both on the diffusion coefficients in each layer of the packing and in the receptors as well as on the partitioning coefficients at all interfaces between two adjacent layers. At the end of time t_2 one can separate the receptors from the multilayer, extract the migrant from the donor material and determine with an appropriate analytical method the mean concentration of migrant in each receptor at time t_2 ($<C_{1t2}>$ and $<C_{5t2}>$). Performing such migration experiments for different durations of the contact between the multilayer and receptors, $t_2 < t_3 < t_4 < t_5 < t_6 <$ *etc.,* one obtains eventually a series of results which represent the "mean migrant concentration *versus* time" for each receptor (see Figure 4-9 (a)). This migration process can be simulated using the numerical algorithm described in Deliverable 5.1. By adjusting the diffusion coefficients in the multilayer, D_2, D_3 and D_4, and the partitioning coefficients at the boundaries between the receptors and multilayer, K_{12} and K_{45}, one can obtain a best fit between the experimental and theoretical results (see Figure 4-9 (b)).



(a) **(b)**

Figure 4-9: Kinetic experiment: time dependent migration from a multilayer material into a receptor material (a) and migration modelling "Kinetic Method"– best fit between experimental data (points) and calculated data (curve) (b).

For the determination of the diffusion coefficients from concentration profiles with the "Moisan Method" the glued multilayer is exposed at one or both sides to a stack of receptor materials. As receptor materials polymers, paper and board were used. Before in the system multilayer-medium/receptor the migration equilibrium is reached, a nonlinear decreasing concentration profile in the contact medium exists. The shape and level of this profile depends both on the diffusion coefficient, D_4, of the migrant in the receptor medium and the partitioning coefficient, K_{34}, at the multilayer-medium interface.

To obtain from the experimental results the D's and K's, the experimental results of the experiment were plotted as mean migrant concentration in each of the n sheets of the stack as function of a distance, x, from the boundary with the multilayer. In each sheet the position of x was placed in the middle of the sheet, see for example Figure 4-10. Again the parameters were adjusted to obtain the best fit of the calculated curve to the experimental values.

During production and storage of the samples diffusion processes already occur. These had been considered including the storage conditions before contact with the receptor in the calculation. Hereby further diffusion and partitioning parameters at the respective storage temperatures (20 ℃, 23 ℃, 25 ℃) were obtained.

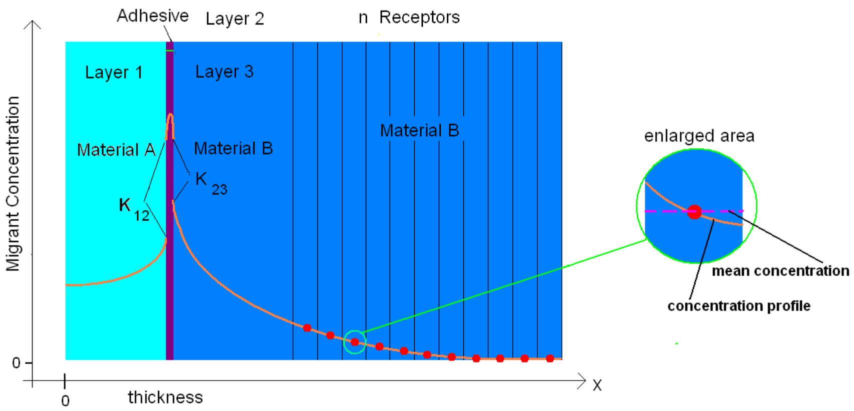


Figure 4-10: Contamination of receptor material B - concentration profile for a substance migrating from the glued sample (Material A and B)

There were more that 400 experimental results (many of them performed in duplicate) from “Equilibrium”, “Kinetic” and respectively “Moisan” experiments. The experiments were performed in the range of 20 to 70 ℃. A series of 15 adhesiv es (polyolefines, rubber, EVA, VAE, PVAc, Acrylic), were used in these experiments to make laminates with different types of substrates (polymers, papers and cardboards). Using these modelling procedures about 1200 new diffusion and partition coefficients were determined.

4.3.2 Reference values for partition and diffusion coefficients

The diffusion and partitioning coefficients determined from experimental results obtained in the framework of this project are related to specific types of adhesives prepared in the lab or obtained from industry and to the substrates used in the project to produce the investigated laminates. These were conceived to cover a broad spectrum of packaging with adhesives used in the food packaging practice. But within such a project only a limited number of samples and applications can be investigated.

Industry is using much more types of adhesives and substrate materials as it was possible to investigate in the time and cost framework of this project. Thus the list of these about 1200 measured parameters must be regarded as a consistent but not exhaustive data base with diffusion and partition coefficients which can be used for migration modeling.

Adhesives from the same type as the investigated ones may differ in the composition which may influence the migration properties e.g. the amount of plasticizer or plasticizing resins. The same is the case for the substrates for example from a different type of cardboard or a different grade of polymer. Modifications of the density and structure of a polymer or a cardboard may lead to sizeable changes of the diffusion coefficient. The same is valid for the partition coefficient: Coating of a cardboard or surface treatment of a polymer may change considerably the interface properties of the material.

Furthermore each analytical measurement and approach has a dedicated uncertainty resulting in the end in a variation of partitioning and diffusion coefficients obtained from repeated analyses or different approaches (e. g. kinetic and concentration profile) for the same substance in the same system. Therefore for compliance assessment purposes it is not useful to calculate with the mean values for partitioning and diffusion coefficients as directly obtained from the evaluation of the experiments but with upperbound values.

The parameters should be applicable to additional substances and a variation of adhesives from the same type as the investigated ones but with different composition. The idea behind the experimental concept of the project is to conceive a limited series of adhesives, substrates and migrants groups to which “upper-bound” or “reference” diffusion and partitioning coefficients are associated. These parameters are derived on the basis of data from the tables with the measured coefficients, but their value is set at a level which ensures a certain overestimation of the migration event. That means that when such “reference” parameters are used for the prediction of migration from an adhesive, substrates, migrants and foods from a certain group, the results are with a high margin of confidence at least as high as an experimental testing would find in the very same situation.

4.3.2.1 Reference Diffusion Coefficients

In plastic materials it is state of knowledge that migration mainly depends on the molecular weight of the migrant and the diffusion properties of the polymer. The empiric equation (Equation 4-1) which describes this relationship is generally acknowledged and included in the guidance documents on migration modelling: (European_Commission 2003) and its update (Simoneau in preparation) which is currently in finalization. The diffusion properties of the polymer are expressed as “diffusion conductance” parameter A_P or, respectively, as temperature independent A_P’ value and the activation energy parameter τ (tau) which describes the temperature dependency of the A_P value (Equation 4-2).

Equation 4-1: $$D_P = D_0 \exp\left(A_P - 0.135 M_W^{2/3} + 0.003 M_w - \frac{10454}{T} \right)$$

With: D_P diffusion coefficient [cm²/s] in the polymer layer P, $D_0 = 10^4$ cm²/s, M_W molecular weight of the migrating substance [g/mol], T temperature [K].

Equation 4-2: $$A_P = A_p^{'} - \frac{\tau}{T}$$

With: A_P polymer specific "diffusion conductance" parameter, A_P' temperature independent diffusion conductance, τ activation energy parameter, T temperature [K].

Equation 4-3: $$E_A = (10454 + \tau) \cdot R$$

Correlation of activation energy E_A [J/mol] and τ: R gas constant (8,314 $Jmol^{-1}K^{-1}$).

First it is assumed that the multilayer material (including an adhesive as a layer) is made of "homogeneous" layers of constant thickness. Here with "homogeneous" one defines a material structure similar to that of a single phase polymer (no crystallites). Such a polymer shows, at a microscopic-level, dense bundles of macromolecules neighboring regions in which there are virtually no macromolecules (the so-called "free-volume" of the polymer). This is in fact a structure where the diffusional movements of a molecule take place mainly through the "free-volumes" of the polymeric matrix. As a result, on a longer-range the diffusion of a molecule in the matrix of the polymer can be quantified with a single parameter (an average diffusion coefficient). One can say that such a polymer is "homogeneous" from the point of view of a mass diffusion process.

The above picture is not completely valid for materials like cardboard and paper which are made of macroscopic fibers, binding materials, "free-volumes" and even fillers. In such a structure the local diffusional motions of a molecule may differ quite strongly in the different components of the material. That means that the overall macroscopic mass diffusion in the material is in fact the result of several diffusion mechanisms occurring in parallel. These mechanisms are quantified by different diffusion coefficients which moreover show different functional dependencies on the nature and concentration of the diffusing species, the temperature and/or pressure. Strictly speaking such a material cannot be regarded as "homogeneous" from the point of view of a mass diffusion process. However when performing migration experiments with cardboards and papers one can measure a net overall mass diffusion through the specimen. The process can then by described with the diffusion/migration model developed for "homogeneous" media by assigning to the cardboard and paper sample an overall "apparent" diffusion coefficient. This diffusion coefficient will be in fact the result of a weighted contribution of diffusion coefficients from the different components of the "non homogeneous" material.

The A_P' and τ values were calculated for all diffusion coefficients obtained in the project. Such the diffusion coefficients were normalized on molecular weights of the migrant and temperature for better comparison and statistical evaluation. In the same manner as done for the plastic materials (Begley, Castle et al. 2005) the "upper-bound" diffusion parameters A_P'* and τ* were calculated (see Table 4-10, Table 4-12) by using the 95 % confidence upper limit of the student t distribution of the experimentally derived values. In case of A_P the higher value, in case of τ the lower value represents the more conservative estimate. The upperbound values are marked with an asterix. From the τ* values the activation energy was calculated (Table 4-11, Table 4-14).

The A_P'* and τ* values can be used to estimate the diffusion coefficient of any substance with known molecular weight at a defined temperature using Equation 4-1 and Equation 4-2 or directly in a migration modeling software by inserting the parameters there. The reference values can be used in a temperature range of about 10 °C to 80 °C. This restriction is necessary as the reference values are based only on experimental data between 20 °C and 70 °C. Structural changes in the polymer at increased temperature e.g. change of crystallinity or melting, may severely alter the migration properties. The substances used for establishing the reference values had a molecular weight between 100 and 400 g/mol.

It was found that polarity of the migrating substance has a certain role in determining the magnitude of the diffusion coefficients, too. A quantitative dependence of the polarity of the migrant on the A_P' and τ of a given adhesive and/or substrate could be derived only for the cardboard substrates. Here the experimental results show that polar substances tend to diffuse much slower than non-polar ones. This can be seen from **Table 4-12** where the A_P'-value for the polar esters and butyldiglycol acetate (BDGA) are smaller than the reference A_P'-value for the non-polar hydrocarbons due to adsorption/desorption processes of the polar substances on the polar fibre surface of cardboard. In paper a dependency of the A_P' value from the polarity of the migrant was noticed, too. But this was much smaller and not statistically significant. In the adhesive layers the migrants' polarity had no perceptible influence on the diffusion coefficient.

4.3.2.2 Reference Diffusion Coefficients for adhesive layers

The mean A_P', τ values, their standard deviations and the upperbound values derived from the student t distribution are shown in Table 4-10 for the investigated adhesive types. The derived temperature independent reference values are compiled in Table 4-11.

From the structures of the polymers it can expected that natural and synthetic rubber layers have similar diffusion properties. This was verified by the experimental data of the test systems. Because of the limited number of diffusion coefficients especially for the natural rubber sample which contained only one measurable migratable substance, natural rubber and synthetic rubber were pooled to a group for which a common upperbound A_P'* and τ* was calculated.

The vinylic adhesives (ethylene vinylacetate copolymer EVA, vinylacetate ethylene copolymer VAE, polyvinylacetate PVAc) showed a similar temperature dependency. Therefore the reference τ* was calculated from the τ values of all systems. The A_P' values decrease with increasing vinylacetate content in the polymer but a mathematical formula describing this relationship could not be obtained from the experimental data. Therefore on conservative reasons the A_P'* obtained for the ethylene vinylacetate copolymer which has the highest diffusion, was used as reference value for the whole group.

From the acrylic type two waterbased dispersions and two pressure sensitive adhesives have been investigated. The two dispersions showed similar diffusion properties whereas the pressure sensitive adhesives were completely different among each other. Therefore for the pressure sensitive acrylic adhesives no reference values can be given, only for the water based dispersions which form a rigid film after drying. The diffusion coefficents or A_P values of acryl PSA adhesives need to be determined for the individual adhesive.

For polyurethanes no migration kinetic or concentration profile data had been obtained within WP2. The parameters for polyurethanes in Table 4-11 have been obtained from theoretical considerations and comparison with the market sample data from WP4 (Chapter 4.4).

Table 4-10: “Upper bound” parameters for the calculation of diffusion coefficients. Adhesive groups.

Adhesive-Group	A_P' value	SD (A_P' value)	upper-bound A_P'* value	τ	SD (τ)	upper-bound τ* value	n	student t (0,05, n-1, single sided)
Natural Rubber	10	0,1	10,3	-313	13	-351	3	2,920
Synthetic Rubber	10,7	0,3	11,2	-376	23	-416	17	1,746
Natural and Synthetic Rubber	10,6	0,4	**11,3**	-366	32	**-421**	20	1,729
EVA	6,3	0,2	**6,6**	-1154	48	-1236	27	1,706
VAE	4,7	0,8	**6,1**	-1090	48	-1172	26	1,708
PVAC	4	0,1	**4,2**	-1056	24	-1112	4	2,353
Vinylics (all)				-1118	91	**-1270**	57	1,674
Acryl-Dispersion	3,3	0,7	**4,5**	191	64	**83**	39	1,690
Acryl-PSA1	3,5	0,2	**3,9**	492	56	**379**	6	2,015
Acryl-PSA2	8,9	0,3	**9,6**	-188	32	**-263**	4	2,353

Table 4-11: “Reference” parameters for the calculation of the diffusion coefficients in Adhesives.

Adhesive-Group	Reference A_P'*	Reference τ*	Activation Energy E_A [kJ/mol]
Natural Rubber	**11,3**	**-421**	**83**
Synthetic Rubber	**11,3**	**-421**	**83**
EVA	**6,6**	**-1270**	**76**
VAE	**6,6**	**-1270**	**76**
PVAC	**6,6**	**-1270**	**76**
Acrylate (from waterbased dispersion)	**4,5**	**83**	**88**
Acryl PSA	none, to be determined individually	none, to be determined individually	
Polyurethanes (reactive for lamination)	4	250	

4.3.2.3 Reference Diffusion Coefficients for substrate layers

The mean A_P', τ values, their standard deviations and the upperbound values derived from the student t distribution are shown in Table 4-12 for the investigated substrates. The derived temperature independent reference values are compiled in Table 4-14.

As already mentioned above, cardboard showed different A_P' values for polar and non-polar migrants. The temperature dependency (τ, activation energy) was similar for all migrants. Therefore a common τ^* was calculated from all cardboard data.

In paper the influence of the polarity on the A_P' was not significant. Experiments with 5 different paper grades at 40 ℃ which were spiked with up to 13 test substances showed that the paper type has a negligible small influence on the value of the diffusion coefficients. These data were not included in the calculation of $A_P'^*$ because there were no data on temperature dependency. But when comparing the upper-bound A_P^* at 40 ℃ of these experiments ($A_P^* = 12,3$) with that derived from the migration experiments with adhesive test systems ($A_P^* = 12,7$), good congruency of the values can be seen. The A_P^* from the adhesive test system experiments includes as slightly more conservative value that of the spiking experiments. Using these additional migration test with paper, the "reference" A_P^* for paper at the temperature of 40℃ could be successfully validated.

The A_P' and $A_P'^*$ values for the plastic layers fit very good to that laid down in the guidance documents for mathematical modelling[3,4] (see Table 4-15). The $A_P'^*$ obtained in the project are slightly overestimated by using the reference values from the guide. In case of plasticized PVC the reference value for 30 % plasticizer was taken as conservative value as the composition of the PVC film was not known.

For calculation of diffusion in plastic substrate layers the values from the guidance document should be taken. That means further that the "reference parameters" listed in that document for other types of polymeric substrates can be used for the calculation of diffusion coefficients in substrates like HDPE, PP, PET, PA and PS.

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[3] European_Commission (2003). Practical Guide „Food Contact Materials“: Estimation of migration by generally recognised diffusion models in support of EU Directive 2002772/EC 'Migration modelling' (Annex I to § 11).

[4] Simoneau, C., Ed. (in preparation). Estimation of specific migration by generally recognised diffusion models in support of EU Directive 2002/72/EC JRC Scientific and Technical Reports.

Table 4-12: "Upper bound" parameters for the calculation of diffusion coefficients. Substrate groups.

Substrate-Group	A_P' (mean)	SD (A_P' value)	upper-bound $A_P'^*$ value	τ (mean)	SD (τ)	upper-bound τ^* value	n	student t (0,05, n-1, single sided)
Paper (from the test systems)	5,6	0,6	**6,6**	-1018	526	**-1902**	49	1,68
Cardboard (polar esters + BDGA)	3,0	0,6	**4,0**	-1247	85	-1391	33	1,70
Cardboard (hydrocarbons)	6,5	0,5	**7,4**	-1387	112	-1578	27	1,71
Cardboard (all)				-1310	120	**-1511**	60	1,67
PVC plast.	10,2	0,9	**12,8**	460	187	**-86**	3	2,92
OPP	9,9	1,1	**11,8**	1595	40	**1527**	25	1,71
LDPE	9,8	0,5	**10,8**	-77	47	**-172**	6	2,02

Table 4-13: Additional migration tests at 40 °C by spiking paper

Substrate-Group	A_P (40 °C)	SD (A_P value)	upper-bound A_P^* (40 °C)	n	student t (0,05, n-1, single sided)
Paper	9,5	1,7	**12,3**	57	1,67

Table 4-14: "Reference" parameters for the calculation of the diffusion coefficients in Substrates.

Substrate Group	Reference $A_P'^*$ value	Reference τ^* value	Activation Energy E_A [kJ/mol]
Paper (from the test systems)	**6,6**	**-1900**	**71**
Cardboard (polar esters + BDGA)	**4,0**	**-1511**	**74**
Cardboard (hydrocarbons)	**7,4**	**-1511**	**74**

Table 4-15: Reference values for plastic layers from mathematical modelling guideline[4]

Substrate-Group	Reference $A_P'^*$ value	Reference tau* value	Activation Energy E_A [kJ/mol]
PVC plast. (30 % plasticizer)	**14,6**	**0**	**87**
OPP	**13,1**	**1577**	**100**
LDPE	**11,5**	**0**	**87**

4.3.2.4 Reference Partition Coefficients

By analyzing the approximately 1200 diffusion and partitioning coefficients derived in this project it was found that polarity of the migrating substance has an important role in determining the magnitude of the partitioning. Therefore the migrants were grouped according to their partition coefficient between octanol and water (log $K_{O/W}$ value) into polar, medium polar and non-polar substances. Migrants with a log $K_{O/W}$ value ≥ 7.5 were classified as non-polar substances, migrants with a log $K_{O/W}$ value between 7.5 > log $K_{O/W}$ ≥ 3 were classified as medium polar substances and migrants with a log $K_{O/W}$ value <3 log $K_{O/W}$ were classified as polar substances (seeTable 4-16). The table contains the substances found in the adhesives as well as the additional substances for the fortification experiments.

All partitioning coefficients obtained by equilibrium, kinetic and concentration profile (Moisan) experiments using adhesive-substrate systems as well as those by adding substances to the adhesives were evaluated according to physico-chemical explanations for the range of the found values. The ranges of partition coefficient values in the experiments are summarized in Deliverable D4 part 1.

However it was not possible to derive, from the available data, a consistent mathematical model for an “exact” relationship between the partition coefficients and the polarity of the migration substance. This is in fact understandable if one takes into account that the partition coefficient of a substance at the boundary between an adhesive and a substrate depends in a complex manner not only on the polarity of the migrant, but also on other structural properties of the substance, the nature and morphology of the substrate and adhesive or on the temperature. Using a further classification in substances with common functional groups, no rules for generalization to other substances could be derived from the available data.

In absence of such quantitative relationships between the polarity of a migrating substance and the partition coefficients in a certain packaging material the concept of “general trends of change with polarity” was used. That means that the pool of migrating substances investigated in this project was categorized according to their polarity and then for these categories different “reference” partition parameters were assigned in the framework of the different groups of adhesives and substrates defined in this project.

The “reference” partition coefficient values for polar, medium polar and non-polar substances at the two temperature ranges, from 10℃ to 40℃ (Low Temperature = LT) and higher than 40℃ up to 80℃ (High Temperature = HT), are summarized in Table 4-17 to Table 4-21. Because of the high scatter of the measured values it was not possible yet to derive “reference” partition coefficients for acrylic adhesives in contact with different types of substrates. The data for the substances from the acrylic adhesives are summarized in Deliverable D5.1.

No reference values were derived for the special application of the adhesive group EVA in contact with P&B coextruded with PP. When comparing the partioning coefficients of the same EVA with pure cardboard and that with the extruded PP layer, the cardboard with PP showed different properties than expected. Especially the partition coefficient ($K_{EVA/substrate}$) of the aromatic hydrocarbons was strongly increased in cardboard with PP compared to pure cardboard. Possibly the extruded layer influences the adsorption properties of the cardboard. Only one type of polyolefin coextruded cardboard was investigated, so that these findings cannot be generalized currently.

Table 4-16: Classification of target migrants according to their polarity.

Target migrant	Log $K_{O/W}$	No.
Non-polar substances		
Tetracosane	12,13	1
Docosane	11,15	2
Eicosane	10,16	3
Octadecane	9,18	4
Hexadecane	8,20	5
Dioctylphthalate (n-octyl or 2-ethylhexyl)	7,60	6
Medium polar substances		
1-methyl-10,18-bisnorabieta-8,11,13-triene	7,31	7
10,18-bisnorabieta-8,11,13-triene	6,85	8
methyldehydroabietate	6,81	9
4b-8-dimethyl-2-isopropylphenanthrene	6,36	10
3,4-divinyl-1-phenylcyclohexane 1	6,35	11
3,4-divinyl-1-phenylcyclohexane 2	6,35	12
3,4-divinyl-1-phenylcyclohexane 3	6,35	13
3,4-divinyl-1-phenylcyclohexane 4	6,35	14
1-methyl-8,7-(1-methylethyl) phenanthrene	6,35	15
1-phenanthrenecarboxaldehyde, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1r-(1a,4aß,10aa)]	6,27	16
1,3,5-triethylbenzene	5,11	17
2,6-Di-t-butylhydroxytoluene (BHT)	5,10	18
benzene-3-cyclohexene	4,59	19
Di-butyl phthalate	4,50	20
9,10-dihydroanthracene	4,25	21
2-ethylhexylacrylate	4,09	22
2,5-di-tert-butyl-1,4-benzoquinone	4,07	23
dipropylene glycol dibenzoate	3,88	24
2-ethylhexylacetate	3,74	25
2,4,7,9-tetramethyl-5-decyne-4,7-diol	3,61	26
Butyl hydroxybenzoate	3,57	27
diethylene glycol dibenzoate	3,04	28
Polar substances		
Butylbutyrate	2,83	29
2-ethyl-1-hexanol	2,73	30
Methyl hydroxybenzoate	1,96	31
4-cyanocyclohexene	1,91	32
Benzaldehyde	1,71	33
2-butoxyethyl acetate	1,57	34
butyldiglycolacetate	1,30	35
dimethyladipate	1,03	36
ethanol, 2-(2butoxyethoxy)	0,56	37
Triacetin	0,25	38
Ethylene glycol	-1,36	39

Fortification experiments with ethylene glycol were not considered because ethylene glycol is not compatible to most of the adhesives.

Within the adhesive groups “natural rubber” and “synthetic rubber” a transfer of reference values of partition coefficients was possible (marked in Table 4-17 to Table 4-21 with the sign **). Some of the values could be assessed by expert judgment (marked in Table 4-17 to Table 4-21 with the sign *). For some adhesive-substrate combinations no or only an insufficient data base for the deviation of reference values was available (marked in Table 4-17 to Table 4-21 with the signs – and #).

Table 4-17: Reference partition coefficients for migrants of the adhesive group „Natural Rubber“.

Adhesive-Group	Migrant	Plastic (non-polar)		Cardboard		Paper	
		LT	HT	LT	HT	LT	HT
Natural Rubber	Non-polar	1**	1*	-	-	-	-
	Medium polar	100	100	-	-	500**	500**
	High polar	-	-	-	-	#	#

LT = Low temperature: 10℃ < LT ≤ 40℃, HT = High temperature: 40℃ < HT < 80℃

** = Transfer from another experiment, * = assessed value, - = no experimental data, # = data base insufficient for the deviation of reference values

Table 4-18: Reference partition coefficients for migrants of the adhesive group „Synthetic Rubber“.

Adhesive-Group	Migrant	Plastic (non-polar)		Cardboard		Paper	
		LT	HT	LT	HT	LT	HT
Synthetic Rubber	Non-polar	1	1*	-	-	-	-
	Medium polar	100**	100**	-	-	500	500
	High polar	-	-	-	-	#	#

LT = Low temperature: 10℃ < LT ≤ 40℃, HT = High temperature: 40℃ < HT < 80℃

** = Transfer from another experiment, * = assessed value, - = no experimental data, # = data base insufficient for the deviation of reference values

Table 4-19: Reference partition coefficients for migrants of the adhesive group „EVA“.

Adhesive-Group	Migrant	Plastic (non-polar)		Cardboard		Paper	
		LT	HT	LT	HT	LT	HT
EVA	Non-polar	5	1*	50	10	-	-
	Medium polar	5	1*	5	1	-	-
	High polar	1	1*	-	-	-	-

LT = Low temperature: 10℃ < LT ≤ 40℃, HT = High temperature: 40℃ < HT < 80℃, * = assessed value

Table 4-20: Reference partition coefficients for migrants of the adhesive group „VAE“.

Adhesive-Group	Migrant	Plastic (non-polar)		Cardboard		Paper	
		LT	HT	LT	HT	LT	HT
VAE	Non-polar	5	1*	-	-	50	10*
	Medium polar	5	1*	10	5	5	1
	High polar	10	5	5	1	5	1

LT = Low temperature: 10°C < LT ≤ 40°C, HT = High temperature: 40°C < HT < 80°C, * = assessed value

Table 4-21: Reference partition coefficients for migrants of the adhesive group „PVAC“.

Adhesive-Group	Migrant	Plastic (non-polar)		Cardboard		Paper	
		LT	HT	LT	HT	LT	HT
PVAC	Non-polar	-	-	-	-	-	-
	Medium polar	-	-	-	-	-	-
	High polar	-	-	10	1	-	-

LT = Low temperature: 10°C < LT ≤ 40°C, HT = High temperature: 40°C < HT < 80°C,

Using these “reference” partition coefficients to simulate, with the proposed theoretical model a migration process may lead to considerable overestimations of the real migration. However this is not a problem for the petitioner as long as the calculated migration level is below the legal limit. In such cases one can state in fact (despite severe migration overestimation) that the packaging is compliant with the law. In cases where the estimated migration is above the legal level an experimental testing of the packaging would be compulsory.

For research and development purposes the migration model proposed in this project can be used with the more “realistic” partition parameters listed in the Deliverable D4 part 1. These tables can be even used to estimate, by using “expert judgment”, partition coefficients for migrants which are similar but not identical to those investigated in this project. However such extrapolations of partitioning behaviors from the available data to situations which differ from the experimental design in this project should be made with care! The partitioning phenomenon is a rather complex one, a series of material and thermodynamic parameters contribute to the final value of the partitioning coefficient at a given interface for a given substance. Therefore even slight modifications of the properties of the materials which generate the interface and/or of the migrant itself may lead to considerable deviations of the magnitude of the partition coefficient.

4.3.3 Partition and diffusion coefficients for the simulant Tenax® (MPPO)

Tenax has a high adsorption capacity. Nearly all substances migrating to the boundary layer are then absorbed from the Tenax. Therefore it is sufficient to have an only very thin layer of simulant on the material in the migration test. The amount of 4 g/dm^2 which was used according to EN 1186-13b corresponds to a thickness of 1.6 mm (density 0.25 g/cm^3). Migration onto Tenax was calculated with an apparent $A_P' = 10$, $\tau = -2500$ and $K_{P,Tenax} = 0.1$. The partitioning coefficient considers the small volume of Tenax related to usual filling volumes.

4.3.4 Decision tree for the evaluation of different adhesive/packaging systems

The food regulatory evaluation is based on the amount of migration into food. The migration value can be derived by theoretical considerations, analytical measurements or a combination of both. The decision tree (Figure 4-11) shall help to find a suitable testing procedure for the specific application. Here only a short overview will be given. The procedures and the decision tree are described in detail in the guideline Deliverable D9. Theoretical calculations are in general less time and working effort consuming than analytical tests. Therefore the decision tree is construed such that it checks the possibilities for such estimates and the necessary input data. Experimental migration tests are always an alternative which can be chosen at each level of the decision tree.

Experimental analytical tests

In general migration tests using suitable test conditions are the absolute way to determine the migration. In case of doubt the analytical migration test is the reference for the conformity evaluation. This means when theoretical considerations give values exceeding the limit or just at the limit, conformity can/should always be verified by an analytical test.

An experimental alternative are quick tests. These are accelerated migration tests at increased temperature or using swelling solvents leading to migration values which are at least as high as the conventional migration test but usually overestimate the real migration. At present stage no general proposals for quick tests especially for materials with adhesives layers can be given.

When using solely theoretical considerations to obtain the migration value, analytical measurements cannot be waived in all cases. For all theoretical approaches the concentration of the target substance in the material must be known. This needs to be measured experimentally if it is not reliably obtainable from the formulation and application data.

Theoretical estimates

For the theoretical estimates a tiered approach is proposed: The more realistic the estimate shall be the more knowledge on the properties of the substance and the layer(s) is necessary. The decision tree is therefore divided into four sections.

The first level is the calculation of total transfer. This is usually highly overestimating. But no knowledge on the migration properties is necessary. The initial concentration in material needs to be known. In this level (green in Figure 4-11) the input data needed also for analytical migration testing are included (knowledge or investigation of relevant target substances, food regulatory status of the target substances, application data of the adhesive and geometry of the packaging).

In the second level the equilibrium concentration will be calculated (pink in Figure 4-11). Here the partitioning coefficients between the layers need to be known additionally or need to be estimated reasonably as described above. The equilibrium concentration is the maximum concentration which can be reached in the food.

The third level is the diffusion modelling (blue in Figure 4-11). Here additionally the kinetics of the mass transfer during storage is simulated. Diffusion (migration) modelling is the estimate which is nearest at the real processes. Here the diffusion coefficients need to be known additionally or need to be estimated reasonably as described above. During storage of a multilayer material before filling with food, mass transfer processes already occur, i.e.

substances from the adhesive diffuse already in the substrate layers. This influences the migration value after filling and needs to be considered. The worse case is equilibrium in all layers.

The forth section is the experimental migration approach (yellow in Figure 4-11).

Depending on the knowledge on the substance and its properties, the amount of substance in the material and the legal or recommended limit for the substance simple calculations (total transfer) are sufficient or more complicated estimates or analytical migration testing are necessary. Total transfer and equilibrium transfer can be calculated by hand or simple calculators, whereas for multilayer diffusion modelling specific software is necessary. Within the project a freeware software tool was developed by INRA (Deliverable D5.2). Commercially available software solutions are MIGRATEST©EXP, FABES ForschungsGmbH, München and AKTS-SML, AKTS AG, 3960 Siders, Switzerland.

4.3.5 Software to estimate migration from food contact materials

Safe Food Packaging Portal version 3 (so-called SFPP3) is a product of the French National Institute for Agricultural Research (INRA), developed mainly by Olivier Vitrac (Chargé de Recherche INRA). Its general purpose is to gather within a same integrated environment databases of properties (transport coefficients and activation energies, regulatory data, etc.), numerical codes to solve migration problems in structures with an arbitrary complexity (thicknesses ranging from few nanometers to centimeters, including 1 up to 10 and more layers, arbitrary jumps in properties, arbitrary temperature variation during migration, arbitrary initial solution to match sequential migrations), decision tools and templates dedicated to multilayer materials and adhesives.

SFPP3 was specifically developed during the Migresives project with the scope of:

- free distribution and modification under an INRA license (almost compatible with Generally Public License version 2);
- installation either as a standalone application (for a single user) or as a server (for multiple users through an intranet/internet) on Windows (32/64 bits) or Linux (32/64 bits);
- a graphical user interface (incl. layout, look and feel) easy modifiable to fit any industrial purpose (labels, corks, co-extruded films, printed parts…) and separated from computational engines;
- easy creation/modification of templates;
- strong traceability requirements (all actions including input data, jobs and simulated results);
- collaborating between workgroups/users via shared/private projects and templates;
- promoting communications with existing tools in the industry and web-feeding from corporate servers (PubChem, NIST, ChemSpider…).

SFPP3 is currently distributed both by the European Association of Sealants and Adhesives FEICA (http://www.feica.com/) and by INRA. The last stable version SFPP3 related to the Migresives project can be downloaded from the INRA research web site “Safe Food Packaging Portal” (http://h29.univ-reims.fr/SFPP3/SFPP3_quick_start/index.html). The reader must note that this website will move to a different domain (agroparistech.fr) by the end of August 2010. The link will be given also on http://www.migresives.eu. The software and its tools are described in Deliverable D5.2.

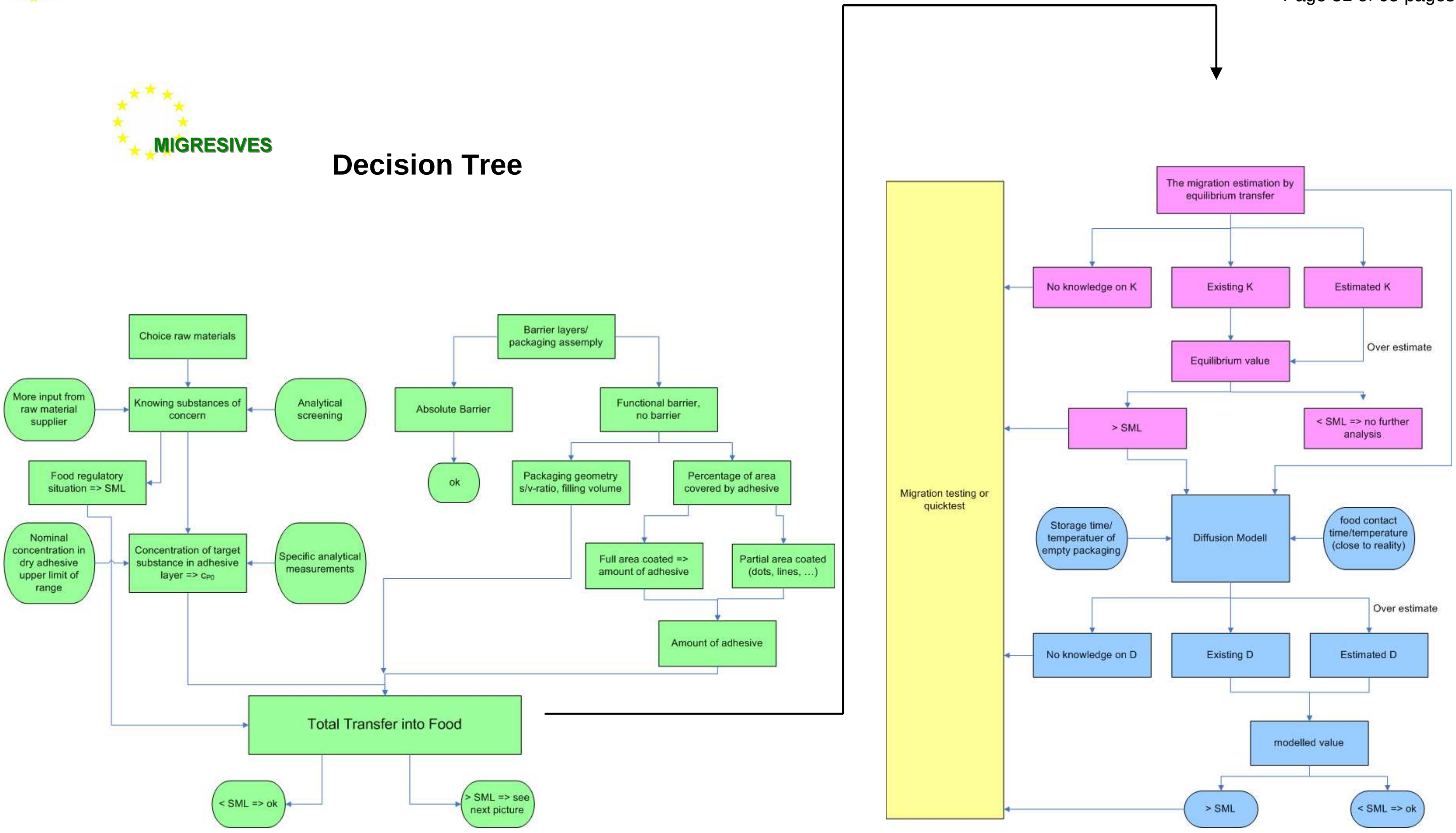

Figure 4-11: Decision tree describing necessary input data and choice of pathways for migration evaluation

4.4 Screening of samples from the market for broader applicability of the testing tools and verification purposes (WP4)

Objective of WP4 was to investigate the applicability of the analytical quick tests and the migration prediction tools developed in WP2 and WP3 to all adhesives types under study and food contact material applications in order to generalise the tools as well as to check the situation of the real market samples in terms of adhesives. A set of 45 samples from the market provided by SME partners and National Associations have been analysed. Most of the compounds found in screening analysis have been identified and quantified.

The samples from the market have been also tested in the whole packaging process in order to study the influence of the processes in the migration values. Thus, the influence of vacuum processes, hot filling or sterilization processes which likely affect the diffusion of migrants from the adhesives layer to the substrates and then to the food in contact with them, that means the migration of adhesives, has been studied. This is on one hand a validation step for WP2 outcome, as many procedures were developed under WP2, and, on the other hand, the experience acquired from additional adhesives and applications in the samples from the market have been used to validate the prediction model.

The materials have been investigated according to the decision tree developed in WP3 (see 4.3.4). This includes in any case a compositional analysis using the tools from WP2a and 2b (see 4.2.2). Quick tests and mathematical migration prediction (from WP3) have been also applied in some cases and compared to conventional migration tests in food simulants including kinetic experiments. This requires a considerable experimental test programme and, therefore, WP4 forms besides WP2 another core study from which many relevant conclusions have been obtained.

The additional materials and applications concerning the samples from the market, which involve adhesives such as polyurethane adhesives, very different from those used in the previous WP, have added new experimental difficulties or interferences compared to that found and solved in WP2. Therefore, the methods have been improved for these applications and the changes have been included in the analytical methods, which will be finally described in WP7. New data on characterisation/identification of unknown substances and its chromatographic and mass spectrometric properties have been obtained in this WP and included in the database established in WP2b. Different technologies have been used for this purpose depending on the nature of the target compounds.

The main aims of this study were:

- To identify the main compounds coming from the adhesives present in 45 multilayer laminates from the market
- To determine the concentration of migrants in the multilayer materials
- To determine the migration of the compounds coming from the adhesives in the simulants, mainly working with Tenax as solid simulant, but not only.
- To validate the prediction model, that means the mathematical modelling, with the experimental migration values obtained in these samples.
- To study the influence of food processes in the migration behaviour of the compounds coming from the adhesives

Table 4-22: Table 1: Samples codes, substrates and adhesives used for the laminates manufacture, dilution factor (dF) and application amount of adhesive (g/m²) in laminates

Sample code	Substrates	Adhesive type	Adhesive code	dF (dm)	g adhesive/ m² laminate
lam_01	CB/CB	VAE	VAE_01	52.3	31.8
lam_02	CB/CB	VAE	VAE_01	52.3	31.8
lam_03	CB/CB	VAE	VAE_01	52.3	31.8
lam_04	CB/CB	VAE	VAE_02	57.6	25.3
lam_05	CB/CB	VAE	VAE_02	30.7	25.3
lam_06	CB/CB	VAE	VAE_02	18.5	25.3
lam_07	CB/CB	VAE	VAE_03	37.1	28.5
lam_08	CB/CB	VAE	VAE_04	63.9	49.1
lam_09	CB/CB	VAE	VAE_04	34.1	49.1
lam_10	CB/CB	VAE	VAE_04	70	49.1
lam_11	CB/CB	VAE	VAE_05	96.7	30.7
lam_12	CB/CB	PVAc	PVAc_01	52.3	101.5
lam_13	CB/CB	PVAc	PVAc_01	52.3	101.5
lam_14	CB/CB	PVAc	PVAc_01	52.3	101.5
lam_15	CB/paper/CB	PVAc	PVAc_02	1.6	na
lam_16	CB/paper/CB	PVAc	PVAc_03	1.6	na
lam_17	CB/paper/CB	PVAc	PVAc_04	1.6	na
lam_18	paper/paper	PVOH	PVOH_01	223.3	38.9
lam_19	paper/paper	PVOH	PVOH_01	74.5	38.9
lam_20	paper/paper	PVOH	PVOH_01	185.6	38.9
lam_21	paper/paper	Starch	Starch_01	97.8	38.9
lam_22	paper/paper	Starch	Starch_01	398.5	38.9
lam_23	paper/PP	Acrylic	AC_01	2604	38.9
lam_24	paper/PP	Acrylic	AC_02	300.5	38.9
lam_25	Al/PE	Acrylic	AC_03	0.17	45
lam_26	paper/PP	Acrylic	AC_04	0.17	18
lam_27	paper/PET	Acrylic	AC_05	0.17	20
lam_28	paper/PP	Acrylic	AC_06	0.17	20
lam_29	paper/corrpaper/paper	Vinylic+Starch	VS_01	0.17	na
lam_30	paper/corrpaper/paper	Vinylic+Starch	VS_01	0.17	na
lam_31	paper/corrpaper/paper	Vinylic+Starch	VS_01	0.17	na
lam_32	CB/CB	Hotmelt	HM_01	0.17	31.28
lam_33	c_CB/c_CB	Hotmelt	HM_01	0.17	31.28
lam_34	CB/CB	Hotmelt	HM_02	8.5	68.2
lam_35	PA/PE	Polyurethane	PU_01	0.17	2.5
lam_36	PA/PE	Polyurethane	PU_02	0.17	2
lam_37	PE/PE	Polyurethane	PU_02	0.17	1.9
lam_38	PET/[PE-EVOH-PE]	Polyurethane	PU_03	0.17	1.8
lam_39	[PA-EVOH-PA]/PE	Polyurethane	PU_04	0.17	1.8
lam_40	PET-met/PE	Polyurethane	PU_05	0.17	1.6
lam_41	PET/Al/PE	Polyurethane	PU_06	0.17	4.3
lam_42	PET/Al/PE	Polyurethane	PU_06	0.17	4.3
lam_43	PET/Al/PE	Polyurethane	PU_07	0.17	5
lam_44	PET-met/PE	Polyurethane	PU_08	0.17	2.5
lam_45	PA/Al/PE	Polyurethane	PU_09	0.17	6.7

Twenty nine different adhesives were used in the manufacture of the laminates: 9 polyurethanes (PU), 6 acrylics (AC), 2 hotmelts (HM), 1 starch, 5 based on vinyl acetate ethylene (VAE), 4 based on polyvinyl acetate (PVAc), 1 based on polyvinyl alcohol (PVOH) and 1 mixture of vinylic adhesive and starch. The substrates used were cardboard (CB), coated cardboard (c_CB), corrugated paper (corrpaper), polypropylene (PP), polyethylene (PE), polyamide (PA), polyethylene terephthalate (PET), metallized PET (PET-met), aluminum (Al) and ethylene vinyl alcohol copolymer (EVOH).

All samples have been subjected to screening analysis of volatiles by HS-SPME-GC-MS. The chromatograms of the laminates were compared to those from the substrates and the pure adhesives. Migrants' initial concentrations were quantified by GC-MS of extracts. Migration testing was carried out onto Tenax at the condition 10 days / 40 ℃ for all laminates with measurable amounts of migrants. These data were used for comparison with modelling results. Polyurethanes were additionally investigated for migration into isooctane at the substitute condition 2 days / 20 ℃. The results are summarised in Deliverable D6.1.

Deliverable 6.2 shows the results of studying the influence of different packaging conditions on migration of compounds present in adhesives to food. Packaging conditions selected were vacuum, pasteurization and a combination of both since they were the most commonly used for the laminates studied. Migration was studied using Tenax as food simulant and two plastic multilayers containing PU adhesives: polyester 14 µm/polyurethane/PE 60 µm and PET 12 µm-Al 7 µm/polyurethane/PE 85 µm. Four different packaging conditions were studied with each sample:

- Usual conditions (UC): sachets filled with Tenax and sealed
- Vacuum conditions (VC): sachets filled with Tenax were vacuum packed and sealed
- Pasteurization conditions (PC): sachets filled with Tenax and sealed were undergone to pasteurization conditions (70ºC, 10 minutes)
- Vacuum and pasteurization conditions (VPC): sachets filled with Tenax were vacuum packed and sealed and finally undergone to pasteurization conditions (70ºC, 10 minutes)

All samples were stored after the pre-treatment in an oven at 40ºC during 10 days. For the laminates studied no influence on migration to Tenax was observed for any of the packaging conditions studied (vacuum or pasteurization).

4.5 Validation of approach for compliance modelling (WP 3)

As already discussed in Chapter 4.3, the parameters for migration modeling have been derived from a limited number of samples and systems but shall be extrapolated to other adhesive related substances as well as to other adhesive formulations from the investigated types. For validation purposes therefore the 45 market samples (laminates or glued samples from type Acrylic, polyvinylalcohol (PVOH), polyvinylacetate (PVA), vinylacetate-ethylene copolymer (VAE), hotmelt, polyurethane (PU) and rubber) have been modelled using the reference diffusion parameters and the reference partitioning coefficients described in chapter 4.3.2 and the experimental data from WP 4. The hotmelts have not been further specified regarding adhesive class. For hotmelts a A_P' of 1000 and a τ of -1000 was used. The modelled data were compared to the measured migration onto Tenax at the condition 10 day / 40 °C. The final result of the experiments have been about 150 migration results of different types of migrants in the above mentioned adhesive types. Experimental and calculated data are compiled in Deliverable D5.1.

Most of the calculated data met or overestimated the measured values. In 8 laminates no migration onto Tenax® was detectable. In both rubber adhesives higher migration onto Tenax® was found than theoretically from the measured initial concentration was possible by total transfer. The same was the case for one substance in an acrylic adhesive (Lam. 47). These data were excluded from evaluation because of obvious analytical errors. In two cases modeling resulted in values below 0.2 the measured value. Both were derived from polyvinylacetate adhesives and the target substance was a small trace of the same plasticizer which was not intentionally used in these adhesives but in another one. These data were considered as analytical artifact by carry over and also disregarded for statistical evaluation. Thus overall 125 data were included into the statistical evaluation, 31 VAE, 35 PVA, 4 PVOH, 8 acrylics, 39 hotmelt and 8 polyurethane data.

A graphical presentation of the ratios between the calculated and experimental results is shown in Figure 4-12 and the frequency distribution of the ratios between modelled values and measured migration onto Tenax (10 days / 40 °C) in was in 93 % of all cases higher than one. Taking the analytical tolerance of the measurements into account from migration and initial content determination as well as layer thickness data, the ratios 0.8 to 1.2 can be considered as that range in which modelling reflects directly the measurement. Thirteen modellings (10 %) were in this range, 2 VAE, 5 PVA, 1 PVOH, 1 acrylic, 3 hotmelts, 1 polyurethane. Four values were below 0.8 (3 %), 2 VAE and 2 hotmelt. This means that 97 % of all simulations met or overestimated the measured migration, 87 % had a ratio higher than 1.2 between modelled and measured value.

These results from the market samples show that the modeling approach including extrapolation to other substances gives reliable results.

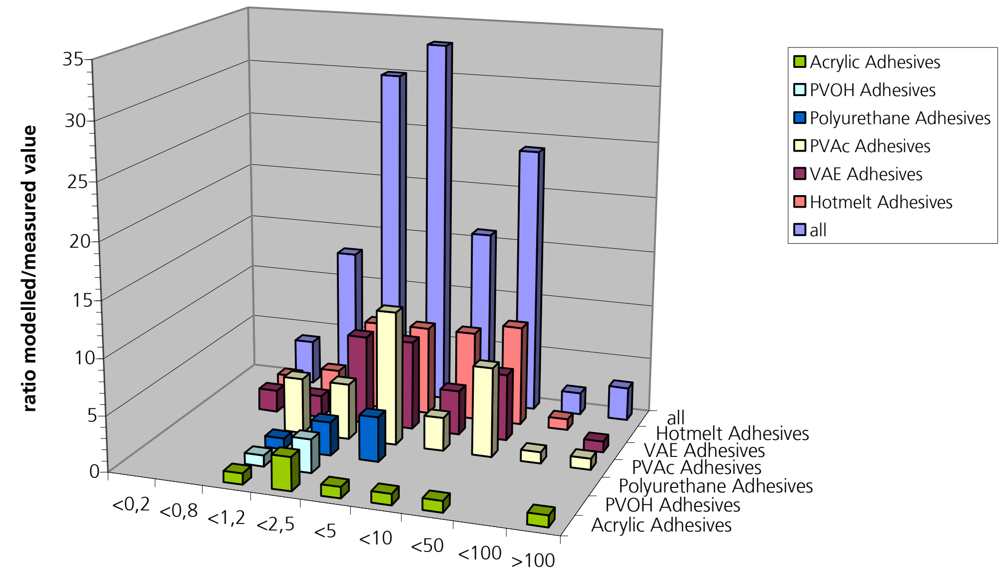

Figure 4-12: Ratios of calculated versus experimental migration values for migration from 41 laminates onto Tenax, 10 days @ 40℃.

Table 4-23: Frequency distribution of the ratios between modelled values and measured migration onto Tenax (10 days / 40 ℃), statistical ly evaluation of the derived classes.

	ADHESIVES							
classes	VAE Adhesives	PVAC Adhesives	PVOH Adhesives	Acrylic Adhesives	Hotmelt Adhesives	PU (Polyurethane)	All	% of All
>0,2	0	0	0	0	0	0	0	0 %
0,2-0,8	2	0	0	0	2	0	4	3 %
0,8-1,2	2	5	1	1	3	1	13	10 %
1,2-2,5	8	5	3	3	8	3	30	24 %
2,5-5	8	12	0	1	8	4	33	26 %
5-10	4	3	0	1	8	0	16	13 %
10-50	6	8	0	1	9	0	24	19 %
50-100	0	1	0	0	1	0	2	2 %
> 100	1	1	0	1	0	0	3	2 %
< 1	3	2	0	0	3	1	9	
≥ 1	28	33	4	8	36	7	116	
all	31	35	4	8	39	8	125	
ratio ≥ 1	**0,9**	**0,94**	**1**	**1,00**	**0,92**	**0,88**	**0,93**	
≥ 0,8							121	
ratio ≥ 0,8							**0,97**	
		without outliner		outliner (migr.>c_{P0}) removed				

4.6 Feasibility of global in vitro bioassays derived from paper&board studies (WP 5)

The EU project 'Biosafepaper' (QLK1-CT-2001-00930, project duration 1.12.2001-30.11.2005) has developed bioassays for paper&board as alternative approach for safety assessment of these materials compared to investigation of single substances (Honkalampi-Hämäläinen, Bradley et al. 2010). In that project a test battery of different *in-vitro* toxicological tests with different endpoints has been selected as basis for a decision tree approach in safety evaluation, appropriate extraction methods for paper&board were developed and the data were scientifically evaluated in order to translate the toxicological data into risk assessment. Actually, the test battery is including two types of tests corresponding to two different toxicities: RNA synthesis inhibition test is dedicated to an assessment of general cytotoxicity, the Ames test and the Comet assay are used for examination of genotoxic potential. The advantage of such an approach will be to have a sum of toxicological endpoints for a global evaluation of the sum of migrating substances. Like paper&boards contain adhesives different substances as potential migrants.

In this project the feasibility of applying these tests to samples with adhesives should be investigated. The methods and results are described in detail in Deliverable D7. Six laminates (PVOH1, PVAC1, Acryl 1, 2, 3 and 4) and the corresponding paper and adhesives used were tested. Samples extracts in 95 % ethanol were prepared by WP2. The extraction procedure was harmonized according to EN 15519, in order to mimic the foreseeable conditions of use with food. Several toxicity endpoints were measured; cytotoxicity (RNA synthesis inhibition assay) and genotoxicity (comet assay) on HepG2 human cell line and mutagenicity on bacteria (Ames test, OCDE n°471). F easibility of the bioassays applied to adhesives extracts was successful in regards to realistic exposure and risk assessment, as long as we respect a non cytotoxic quantity of solvent (ethanol). Furthermore, a concentration step was necessary to give acceptable sensitivity. The dissolution of the adhesive extract in the culture medium was suitable. Laminates extracts were neither genotoxic, nor mutagenic. In contrast, some of them (4/6) were cytotoxic for the HepG2 cell line. The observed cytotoxic effect was never due to the adhesive alone, but sometimes, it was also present in the paper alone (PVAC1). For Acryl 1, 2 and 4, the cytotoxic effect was only present in the laminate extracts. These results raise some questions as analytical data could not fully explain the cytotoxic effect. The discussion given in detail in deliverable D7 includes recent advances in toxicology: mixture effects, low-dose and epigenetic effects. It clearly emphasizes the importance of testing the whole extract of the finished packaging for toxicity using bioassays for a better safety assessment, as well as considering the individual substances. Then, this global approach appears to be pertinent in regards to new toxicology paradigms.

4.7 Education and training to adopt the concept at SME industry level

The assurance of safety in use for food packaging adhesives is a complex issue which needs not only to be disseminated to the adhesive SME's but requires that the stakeholders of the food packaging industry are educated and trained to be able to properly use and adapt the concept developed in the project to their products and their quality assurance system. They have an interest to also be able to explain this added value of their products to their customers. Safety in use of adhesives for food packaging is strictly related to the finished packaging material while the food packer/ distributor have the responsibility for food regulatory compliance of the package. Adhesive producer must therefore know about all influences which relate to adhesive migration components into food to also ensure in the future its safe use in application. To match this target, a training concept and lessons were developed and trainings were carried out.

4.7.1 Converting the output of the project into training lessons

The objectives of the training were:

- o To raise awareness among stakeholders of the food packaging industry to regulatory constraints on food contact materials and more specifically adhesives. Understanding the MIGRESIVES project objectives in this regulatory context.
- o To understand the major principles of migration and diffusion to appropriate use and easy collaboration with specialized laboratories
- o To understand the principles of the tools developed in Migresives: Decision tree, migration simulation software

Training lessons for a 1.5 days training were developed. A first approach for a 1 days training figured out that there was a need of additional explanations. The training is built up in four modules.

Module 1: Legislation. The first module tackles the legislative background and gives a introduction in the objectives of the MIGRESIVES project. A short introduction of migration and the relevant limits is given, further more on adhesives from the view of possible migration. The various legislative sources as well as recommendations and other sources which can be used for food regulator evaluation are described and set in the context of their relevance. Using two examples the applicability of these legislative sources is demonstrated. The functional barrier principle is explained.

Module 2: Diffusion modeling theory. The objective of this module is to understand the major principles of diffusion model for relevant use and easy collaboration with specialized laboratories. It explains diffusion, how diffusion can be calculated by modeling, what are the parameters involved, how this parameters influence the diffusion, how to choose values for the parameters. This theoretical background is then transferred to the general case for adhesives in food packaging.

• Module 3: Global strategy of control of the migration. This module is divided in two parts: Part 1 tackles the effects of the scattering of knowledge in packaging industry. It shows the impact and the importance of a good communication between stakeholders in the food packaging industry. Using an example it explains the results of migration modeling and subsequently it illustrates the impact of changes made by various players in the chain to the final packaging and the food manufacturer on the migration value of this example. It provides understanding what minimum information is needed for a realistic migration modeling. In part 2 the decision tree (Chapter 4.3.4) usable with gradual knowledge is described an explained.

Module 4: MIGRESIVE's migration software. In part 1 the use of MIGRESIVE's migration modeling software Safe Food Packaging Portal version 3 (SFPP3) is presented. In part 2 examples of application are given for using the decision tree and the software.

The modules are compiled in Deliverable D8 and are available as Powerpoint presentations for further use after the project end. Module 4 is integrated as helping tool into the migration modeling software SFPP3.

4.7.2 Train the trainer concept and the realisation of trainings

In order to further spread out the trainings beyond the national associations in the project and to provide the chance of participating in such trainings to additional adhesive SMEs or to packaging producers within the supply chain, all national adhesive associations have been asked via the European adhesive association FEICA to send experienced members for a special training to become able to give trainings in their countries using the training modules and to translate them into their home languages. Germany provided 2 trainers, France 2, Spain 1, Denmark 1, Holland 1, Italy 1, UK 1. The training was organized in REIMS on October 15, 2009, in the afternoon to October 16 until noon. The training lessons were given by N. Forichon and A. Reynier, who wrote the training lessons. Additionally to the trainers from industry, the training was also attended by the RTD's IVV and Unizar. As a result of the experiences made in the training, the lessons were refined, extended from three to four modules and from one day or two half days to 1.5 days in order to spend more time on the interpretation of the results and the practical training of the software.

The National Associations organized the following training sessions in their country, in local language:

Germany: IVK: 1 session (January 2010)	→ 30 participants,
Spain: ASEFCA: 2 sessions (Q1 2010)	→ 25 participants,
France: AFICAM: 2 sessions (Q1 2010)	→ 15 participants,
outside the project financation: :	
UK: BASA: 1 session (Q2 2010)	→ 30 participants (est.).
Germany IVK (June 2010)	→ 35 participants
In preparation in IT, DK, NL Associations	→ 25 participants (est.).

Audiences have been adhesive SME's and packaging converters. The trainings were headed by the trainers trained in Reims in October 2009. The training sessions were typically of 1,5 day.

Although the objectives set by the WP8 are met, both FEICA and the National Associations are of the opinion that the education job is not completed and there shall be given additional opportunities for trainings in the future.

4.8 Drafting standard test methods and guidelines how to use predictive tools and apply the concept (WP 7)

In order to enable industry and laboratories to use the concept and the tools a guideline document is prepared (Deliverable D9). It contains a description of the concept for the practitioner, a description of the decision tree, explanation of the procedure using examples, the analytical methods and a training documentation concerning the software.

4.9 Linking the project with the stakeholders (WP 8)

The objective of this workpackage is to present the intention of the project and later on results and the concept at several areas, at meetings of associations (adhesives, raw material producer, downstream user), public conferences and workshops. DG Sanco and EFSA are kept informed via such public channels and case by case directly. At the end of the project all stakeholders were informed and involved in a conference where the output of the project was presented and discussed.

4.9.1 Dissemination and exploitation of project results at all stakeholders level

From the beginning, the MIGRESIVES project has found high attention in the public domain at the level of all interested or concerned parties and potential stakeholders. The projects intention and later results and conclusions have been presented in many occasions. The associations informed their members, discussed the project outcome as well as current questions within their boards and brought the input back to the consortium. The project was presented at various conferences on industry, educational and scientific level.

A highlight on scientific level was the invitation to two oral presentations (A. Störmer, C. Nerin) and two posters (IVV) at the ILSI 4th International Symposium on Food Packaging - Scientific Developments supporting Safety and Quality, Prague, 19.-21. November 2008 and 2 oral presentations at the 15th and 16th IAPRI World Conference (Bankgkok, 2008 and Grernville, USA 2009) (UNIZAR) and 1 poster presentation in the SLIM Shelf Life International meeting (Spain, 2010) (UNIZAR). One oral presentation will also be given in the 17th IAPRI conference in October 2010 (UNIZAR).

The project was presented at industry meetings e. g. FEICA Conference, 13 Sept. 2007, CEFIC-FCA General Assembly, 17 Oct. 2007, Brussels, CEPI CONTAINERBOARD meeting of the Food Contact Committee, 25 Oct. 25, 2007, San Sebastian, MCAS Seminaire, 6 Dec. 2007, European Coatings Conference -Food Contact Coatings, 13 June 2008 Berlin, International Adhesives Conference WAC, April 2008, Miami, Spanish Conferences on Adhesion and Adhesives, 25-26 Sept. 2008. Feica Conference 2008, Sept. 2008, Marseille, Eurocoat Congress, 10 Feb. 2008, Pira Conference Plastics & Polymers in Contact with Foodstuffs, 11/12 Dec. 2008, Conference 3rd international workshop “Cold-Chain-Management”, 2008, Bonn, FEICA Conference, Sept. 2009, Helsinki, Pira Conference Plastics & Polymers in Contact with Foodstuffs, 10/11 Dec. 2009, 6th IK Food Packaging conference, 21/22 April 2010, Bad Homburg.

All events and activities are listed in Deliverable D10.

4.9.2 Closing conference 27 and 28 April 2010 in Ljubljana

The MIGRESIVES project consortium had presented and discussed the results of more than 3 years of research work at the closing conference. The conference was held on 27 and 28 April in Ljubljana organised by FEICA. 150 participants from all over Europe, USA, Japan and Saudi Arabia joint the conference.

The presentation of the project work and results was set into the frame of the expectations towards the project and implications of the outcome to the legislator, the adhesive SMEs and associations as well as all other stakeholders especially the packaging converters, food industry, surveillance laboratories and the food safety authorities. In the introductory session Dr. Annette Schäfer from the European Commission, DG Sanco pointed out the food regulatory situation of adhesives in food contact materials and her expectations towards the project. The main part of the first day was the scientific presentation of the project outcome performed by the R&D partners Fraunhofer IVV, FABES, INRA, University of Zaragoza and CTCPA: analytical methods for screening and determination of adhesive substances in the materials and the migration, systematic migration and partitioning studies in order to derive parameters for the prediction of migration, the evaluation of the data and the mathematical modelling. The use of the tools and the application of the decision tree were presented on the second day, as well as the multilayer modelling software developed by INRA. Furthermore the training lessons have been presented by ITECH. The feasibility study for a complementary approach using bioassays was presented by the University of Burgundy.

The implications and expectations to the project were highlighted by representatives of the packaging converters (O. Bosetti, Goglio), food industry (C. de la Cruz, Nestlé), EFSA (A. Feigenbaum), the adhesives associations (A. v. Halteren, IVK) and the surveillance laboratories (V. Golja, NRL Slovenia/C. Simoneau, CRL Ispra).

The results especially the applicability of mathematical modelling to adhesive layers, to paper and board for prediction of migration into food and simulants met high interest in the conference.

The proceedings of the conference are compiled in Deliverable D11.

4.9.3 Publications in scientific journals

Störmer, A. and R. Franz (2009). MIGRESIVES: a research project on migration from adhesives in food-packaging materials in support of European legislation and standardization." Food Additives & Contaminants: Part A: 26(12): 1581 - 1591 (IVV)

C.Nerín, E.Canellas, M.Aznar and P. Silcock (2009). Screening of potential volatile migrants from adhesives used in food contact materials. Food Additives and Contaminants 2009 (26) 1592-1601 (UNIZAR)

E. Canellas, C. Nerín, R. Moore and P. Silcock (2010). New UPLC-MS approaches for the identification of non-volatile compounds as potential migrants from adhesives used in food packaging materials. Anal. Chim. Acta (666) 62-69 (UNIZAR)

E. Canellas, M. Aznar, C. Nerín and P. Mercea (2010). Partition and diffusion of volatile compounds from acrylic adhesives used for food packaging multilayers manufacturing. J. Mater. Chem. 2010, DOI:10.1039/C0JM00514B (UNIZAR and FABES)

4.9.4 Publications in progress

P. Vera, M. Aznar, C. Nerín and P. Mercea. "Chemical study of hot melt adhesives used in food packaging multilayer laminates. Evaluation of the main factors affecting migration to food" (in redaction process), (UNIZAR and FABES)

M. Aznar, E. Canellas, P. Vera, J. Gaspar, C. Nerín and P. Mercea. "Adhesive composition of multilayer materials used in food packaging market samples. Migration studies to food and influence of food packaging processes in migration" (in redaction process). (UNIZAR and FABES)

J. Gaspar, M. Aznar, C. Nerín and P. Mercea. "Screening of natural and synthetic rubber adhesives used in food packaging multilayer materials. Partition, diffusion and migration studies" (in redaction process). (UNIZAR and FABES)

Two publications planned on the analytical methods and 1 publication to the overall results and modeling by IVV

4.9.5 Works presented at Symposiums, Conferences, Meetings and Workshops:

C.Nerín, E.Canellas, M.Aznar and P. Silcock (2009). Screening of potential volatile migrants from adhesives used in food contact materials. Oral presentation at ILSI 4th International Symposium on Food Packaging - Scientific Developments supporting Safety and Quality. Prague, 19.-21. November 2008.

E. Canellas, C. Nerín. Migration from adhesives in food packaging materials.Oral presentation in 16th IAPRI World Conference on Packaging, 8-12 June 2008, Bangkok, Thailand

Störmer, A. and R. Franz (2009). MIGRESIVES: a research project on migration from adhesives in food-packaging materials in support of European legislation and standardization." Oral presentation at ILSI 4th International Symposium on Food Packaging - Scientific Developments supporting Safety and Quality. Prague, 19.-21. November 2008.

Yoon, C. S., J. Ungewiss, et al. (2008). Semi-quantitative determination of potential migrants in food packaging materials - Part 3: Non-volatile compounds. Poster at ILSI 4th International Symposium on Food Packaging - Scientific Developments supporting Safety and Quality. Prague, 19.-21. November 2008.

Gruner, A., C. S. Yoon, et al. (2008). Semi-quantitative determination of potential migrants in food packaging materials - Part 2: Semi-volatile compounds. Poster at ILSI 4th International Symposium on Food Packaging - Scientific Developments supporting Safety and Quality. Prague, 19.-21. November 2008.

Franz, R. (2008). Adhesives regulation in Europe & the MIGRESIVES project. 25th PIRA International Conference Plastics & Polymers in Contact with Foodstuffs, Brussels, 10&11 December 2008.

P. Vera, M. Aznar, C. Nerín "Diffusion and migration from hot-melt adhesives in food packaging materials" IAPRI Symposium, Greenville (EEUU), 2009 (UNIZAR).

P. Vera, M. Aznar, C. Nerín "Caracterización química de adhesivos hot-melt utilizados en envases alimentarios" X Jornadas de Adhesivos, Alicante (Spain), 2009 (UNIZAR)

M. Aznar, E. Canellas, C. Gaspar and C. Nerín "Migration from food packaging laminates based on polyurethane" 4th Shelf life International Meeting (SLIM), Zaragoza (Spain), 2010 (UNIZAR)

Störmer A. (2010): EU-Migresives Projekt – aktueller Stand.
Mercea P: MIGRESIVES Modelling Software.
Eukalin Informationsveranstaltung MIGRATION UND EU-LEBENSMITTELRECHT-Rechnen statt Messen. 25. Februar 2010, Frankfurt am Main

Störmer A. (2010) Europäisches Forschungsprojekt MIGRESIVES: Migration aus Klebstoffen – Entwicklung von Konzepten und Methoden zur Konformitätsprüfung. IK Lebensmittelverpackungstagung, 21.22.4.2010, Bad Homburg

P. Mercea "Migrationsberechnung statt Prüfung" 6th Session of the German Food Packaging Association, Bad-Homburg, 21.-22.04.2010

P. Mercea "Migration from Multilayer Packaging into Foods", TWG-Meeting, Paris, 16.06.2010

P. Mercea. "Modelling Migration from Adhesives into Foods", Food Contact Plastics, Conference, Brussels, 16-17.06.2010

C. Nerin. The role of adhesives in food packaging - Challenges and results of the EU project – MIGRESIVES, Food Contact Plastics, Conference, Brussels, 16-17.06.2010

4.9.6 Planned presentations in the next months

C. Nerín, M. Aznar, E. Canellas, P. Vera, J. Gaspar "Migration from food packaging laminates", 17th IAPRI World Conference on Packaging, Tianjin (Chine), 2010 (accepted)

M. Aznar, E. Canellas, P. Vera, C. Nerín. Herramientas analíticas para el análisis de migrantes en adhesivos. XI Jornadas de Adhesivos, Madrid (Spain), 2010 (accepted)

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