EXTERNAL SCIENTIFIC REPORT

Study on implications on the requirements for submission of toxicological information, restrictions and administrative consequences of the draft revised guideline on Food Contact Material (FCM)[1, 2]

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ABSTRACT

The CEF Panel considered it appropriate to revise the current guidelines taking into account new developments in science and the experience gained by EFSA from the safety assessment of substances used in food contact materials and in related areas. The main differences between the draft revised guidelines and the current guidelines concern the exposure assessment approach, the tiered thresholds triggering the need for more toxicological information and the toxicological data required. The objective of this study was to assess the possible implications triggered by the revision of the guidelines on the data requirements and on the restrictions of use by applying the revised guidelines to a set of 73 model substances which had already been evaluated by the AFC/CEF Panel. The toxicological data requirements and the restrictions according to the current and the revised guidelines were compared; differences were identified and further analysed. Afterwards, indicators to identify substances for which the application of the draft revised guideline resulted in different data requirements or restrictions were proposed. Finally, the proposed indicators were applied to the substances listed in Annex I of the Regulation (EC) 10/2011. For 97% of the substances present in Annex I, no more adequate migration data or toxicological data will be required according to the revised guidelines. It should however be noted that this extrapolation contains some uncertainties. The impact on the data requirements of the remaining 3% of the substances of the Union list should also be further evaluated. In addition, the revised guidelines will have an influence on most of the restrictions of substances covered by a migration limit. Lastly, it should be emphasized that this study, the impact assessment and the conclusions, have used the information that was provided by applicants for

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[2] EFSA would like to specify that this report is provided for information in view of EFSA's work in the area of FCM. It was finalised in September 2014 prior to the availability of the draft opinion for public consultation (May 2015) and EFSA CEF Panel's adoption of the scientific opinion on "Recent developments in the risk assessment of chemicals in food and their potential impact on the safety assessment of substances used in food contact materials" in December 2015. Calculation of the exposure, food consumption categories and related values considered in this study are the same as those presented in the draft opinion subject to public consultation (http://www.efsa.europa.eu/en/consultations/call/150707). The tiered approach for toxicological data requirement was also the same with the exception of the upper threshold value of the second tier. The publication of this report was timed to coincide with publication of the above mentioned EFSA CEF Panel scientific opinion. Report's annexes are not published as they contain information from applications submitted that is confidential.

substances within the framework of the existing guidelines. It seems likely that the impact (if any, where identified for particular substances) may change – probably lessened but could in principle increase – if the specific uses of the materials and their substances were in the future, better defined and thus realigned to the proposed new guidelines by the producers or users of those substances and materials.

SUMMARY

The Scientific Committee on Food (SCF) established in 2001 the first guidelines for the presentation of the application for safety assessment of substances to be used in food contact materials (FCM) prior to authorisation. In 2011, the CEF Panel considered it appropriate to revise the current guidelines taking into account new developments in science and the experience gained by EFSA from the safety assessment of substances used in FCM and in related areas such as genotoxicity, nanoscience/nanotechnology, and the application of thresholds of toxicological concern. The draft revised guidelines are currently being discussed by the CEF Panel. EFSA considered it necessary to assess the possible implications triggered by the draft revised guidelines on the requirements for submission of toxicological information and restrictions of use as well as to evaluate the administrative consequences by estimating the possible number of re-evaluations of already evaluated substances. To evaluate the impact of the revision of the guidelines EFSA issued The Call for proposals GP/EFSA/FIP/2013/01.

The evaluation of the impact of the revision of the guidelines was done by applying the current and revised guidelines to a set of 73 model substances which have already been evaluated by the AFC or CEF Panel. Hence, for these substances Scientific Opinions, Summary Datasheets, Petitioner Summary Datasheets and full technical dossiers were available.

First, a database was developed that summarised relevant information from the different data sources. The database contained, amongst others, information related to the type of FCM, the technological function, the intended contact food, migration data (specific migration data, overall migration data, data obtained by total mass transfer calculations or migration modelling) and the available toxicological data, and was used as a working tool during the project.

Second, the restrictions defined by the current guidelines were interpreted for each of the 73 model substances. In the current guidelines, the restriction for an FCM substance is derived from the toxicological data on the FCM substance and its related migrants provided by the applicant. The type and amount of toxicological data required are in their turn triggered by the migration data submitted in the dossier. Consequently, the interpretation of the restriction of the 73 model substances according to the current guidelines was deduced from the migration and toxicological data provided.

The migration data available in the dossiers of the 73 model substances were obtained by different methodologies including specific migration using simulants, overall migration, total mass transfer calculations based on residual content or nominal amount and migration modelling using residual content or nominal amount. For most of the 73 model substances and related migrants, specific migration data were provided by the applicant. In case no specific migration data were available, total mass transfer or modelling was applied by the applicant to estimate migration. Overall migration was

never used as a single technique for the determination of the migration, but rather as an indication for the migration of the low molecular weight fraction.

Based on the migration data, the toxicological information provided in the dossiers of the 73 model substances was discussed. Toxicological dataset requirements in the current guidelines are following a tiered approach, based on the principle 'the greater the migration, the more toxicological information that will be required'. For substances classified in Tier 3, the core set of toxicological sets is required including genotoxicity tests, subchronic toxicity studies, studies on absorption, distribution, metabolism and excretion, studies on reproduction and developmental toxicity and long-term toxicity/carcinogenicity studies. This core set of tests can be reduced for substances classified in Tier 2 and can even be limited to genotoxicity tests for Tier 1 substances. Most of the 73 model substances and there related migrants were allocated to Tier 1, followed by Tier 2. Only seven out of the 73 model substances were classified as Tier 3.

Once the migration and toxicological data had been collected and discussed, the rationale behind the restriction of each of the 73 model substances was clarified. In general, two categories of restrictions were distinguished: substances covered by a migration limit and substances covered by a restricted use. Some substances were covered by both a migration limit and a restricted use. Substances covered by a migration limit could further be divided into substances covered by the generic migration limit and substances covered by a specific migration limit. Based on the value of the SML, the latter group could be further subdivided in three categories: (i) substances with an SML $\leq$ 0.05 mg/kg (ii) substances with 0.05 mg/kg < SML $\leq$ 5 mg/kg and (iii) substances with 5 mg/kg < SML $\leq$ 60 mg/kg. Most of the substances had an SML higher than 0.05 and lower than or equal to 5 mg/kg. Different types of restrictions could be distinguished for substances covered by a restricted use: (i) restrictions excluding certain types of food, (ii) restrictions on the concentration used and (iii) restrictions on the type of plastic. For the majority of the substances only covered by a restricted use, restrictions were based on the type of plastic, whereas for most substances covered both by a migration limit and a restricted use, restrictions were related to the intended contact food. Many of the substances covered by a restricted use were polymeric additives composed of authorised monomers. For all 73 model substances, the migration and toxicological data allowed to clarify the rationale behind the restrictions according to the current guidelines.

Third, the restriction according to the revised guidelines was defined for each of the 73 model substances. In the revised guidelines, the restriction is still derived from the toxicological data provided. The type and amount of toxicological information required depends however on the exposure and not solely on the migration of the FCM substance and its related migrants. Indeed, based on the progress made over the last years in tools for exposure assessment, the CEF Panel proposes in the revised guidelines to take into account the specific consumption data of subgroups of the population such as infants and toddlers and, to this extent, standardised consumption data for three food group categories are established. An overview of the different food group categories and the corresponding food consumption data to be considered for the estimation of the exposure are given in Table 1.

Table 1: Food consumption values to calculate dietary exposure as a function of the three food group categories

Food group category	*Foodstuffs*	*Population driving the consumption*	*Food consumption used for the estimation of the exposure*
1	Water and other liquids such as milk formula consumed by babies and infants up to 12 months old	Infants	150 g/kg bw/day
2	Beverages, such as non-alcoholic or alcoholic beverages, milk or milk products	Toddlers	80 g/kg bw/day
3	Foodstuffs not covered by Categories 1 and 2	Toddlers	20 g/kg bw/day

For each of the 73 model substances, exposure was calculated by combining the predicted level of the FCM substance in food, obtained from migration data, with the consumption data for each food group category covered by the intended uses of the FCM. For most of the substances, the intended contact foods could only be covered by a combination of all three food group categories. Only for two substances, not all food group categories were necessary to cover the intended contact foods: i.e. i.e. fresh fruit was covered by food group category 3 and all foodstuffs except beer and beverages was covered by food group category 1 and 3.

Once the food group categories that cover the intended contact food were identified, migration data could be selected. In most cases, specific migration data were used to calculate exposure. However, each food group category may be covered by different simulants as is illustrated in Table 2.

Table 2: Food group categories defined in the revised guidelines and corresponding food simulants as described in Regulation (EU) 10/2011

Food group category		**Type of simulant**						
1	Water and other liquids such as milk formula consumed by babies and infants up to 12 months old	Water				D1		
2	Beverages, such as non-alcoholic or alcoholic beverages, milk or milk products			B	C	D1		
3	Foodstuffs not covered by Categories 1 and 2		A	B	C	D1	D2 95% EtOH Isooctane	E

Simulant A: 10% EtOH, B: 3% Acetic acid, C: 20% EtOH, D1: 50% EtOH and D2: Vegetable oil, E: Tenax®

Consequently, migration data obtained with an adequate simulant (i.e. a simulant mentioned for the specific food group category in the table above) were preferred. When migration data obtained with more than one adequate simulant for the same food group category were available, the highest migration value was retained. If no migration experiments were performed with simulants adequate for the food group category under investigation, the highest specific migration value obtained with the non-adequate simulants was selected. If no specific migration study was performed, modelling data were selected. When no data on specific migration nor on modelling were available, total mass

transfer data were chosen over overall migration data. It should be noted that since an adequate simulant for all requested food group categories was only available for a minority of the 73 model substances and related migrants, the calculated exposure was overestimated for many of the model substances. This was further taken into account for the interpretation of the impact of the application of the revised guidelines.

Afterwards, the highest estimated exposure value was identified to determine the toxicological data required, on the basis that 'the greater the exposure to the substance through migration into food, the more toxicological information will be required'. For most of the 73 FCM substances, the highest exposure value was found in food group category 1. However, this could be explained by the absence of adequate migration data for most of the models substances, since in that case the highest migration (and thus with an non-adequate simulant) was used for the calculation of the exposure.

As for the current guidelines, a tiered approach determined the toxicological requirements, in which Tier 3 was associated with the highest amount of toxicological data. However, the threshold values of these tiers were different from those of the current guidelines and expressed as µg/kg bw/day. According to the revised guidelines, the three dietary exposure tiers included: (i) < 1.5 µg/kg bw/day, (ii) 1.5 ≤ exposure ≤ 100 µg/kg bw/day and (iii) > 100 µg/kg bw/day. Based on the highest calculated exposure value obtained according to the revised guidelines, most substances and their related migrants were allocated to Tier 2, followed by Tier 3. Only sixteen substances were classified as Tier 1. Compared to the tier-allocations according to the current guidelines, a change in tier was observed for 49% of the model substances (i.e. for the substance itself and/or one or more of its related migrants). Most of the substances and/or the related migrants, shifted from Tier 1 to Tier 2. No shift from Tier 1 to Tier 3 was observed. For many substances that shifted in tier, exposure was calculated using migration data that significantly overestimated the migration. Factors contributing to overestimation of migration include the type of migration experiments, the adequacy of the simulants, the migration conditions and the use of a limit of detection to calculate exposure.

Based on the tier according to the revised guidelines and the understanding of the restriction according to the current guidelines, the impact of the revision of the guidelines on the restriction of the FCM substance was evaluated. Substances covered by a migration limit according to the current guidelines will be covered by an exposure limit according to the revised guidelines. However, the exposure limits need to be translated in migration per kg of food by applying the consumption value for the food group category that contained the highest exposure value for the substance. In contrast to the current guidelines, each tier is thus not associated with one but with three SML values as illustrated in

Table 3.

Table 3: Overview of the restrictions according to the revised guidelines

	Tier 1 *(< 1.5 µg/kg bw/day)*	***Tier 2*** *(1.5-100 µg/kg bw/day)*	***Tier 3*** *(> 100 µg/kg bw/day)*
Food group category 1 *(150 g/kg bw/day)*	0.010 mg/kg	0.67 mg/kg	6.67 mg/kg
Food group category 2 *(80 g/kg bw/day)*	0.019 mg/kg	1.25 mg/kg	12.5 mg/kg
Food group category 3 *(20 g/kg bw/day)*	0.075 mg/kg	5 mg/kg	50 mg/kg

Consequently, most of the substances covered by a migration limit received a different restriction according to the revised guidelines, regardless a change in tier. For substances without a change in tier, no additional toxicological data were required to set the new restriction. The value of the new restriction depended on the food group category containing the highest exposure value. For all substances covered by an SML ≤ 0.05 mg/kg without a change in tier, the new SML was set at 0.01 mg/kg as the highest exposure value was in all cases found in food group category 1. For most of the substances covered by a 0.05 mg/kg < SML < 5 mg/kg, , the highest exposure value was also found in food group category 1 and consequently, the new SML value was set at 0.67 mg/kg. Only for one substance, the SML remained at 5 mg/kg since for this substance, the third food group category delivered the highest exposure value. Finally, none of the substances covered by a migration limit > 5 mg/kg, changed in tier and consequently, the new migration limit could just be set by identifying the food group category containing the highest exposure value. For all substances in this category, an SML of 6.67 mg/kg was set as category 1 was responsible for the highest exposure. For substances with a change in tier, additional toxicological data were required to set the restriction. Revision of the guidelines had however no effect on the toxicological requirements of substances allocated to SCF-list 0 or 1 as for these substances an ADI did not need to be established or a previously established ADI or equivalent value was considered acceptable. For the other substances that changed in tier, exposure calculations were often performed with data overestimating migration. Only for the substance 3,3',5,5'-tetrakis(tert-butyl)- 2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4- hydroxy-5-methylphenyl)propyl] oxyphosphonous acid (EFSA-Q-2008-678, FCM No. 792), migration data were expected to be adequate.

For substances covered by a restricted use without a change in tier, no additional toxicological data were required and the restriction did not change. In contrast, for substances with a change in tier, additional toxicological data were required to evaluate if the restricted use could be maintained according to the revised guidelines. Again, for substances allocated to SCF-list 0 or 1, no more toxicological information was needed as for these substances an ADI did not need to be established or a previously established ADI or equivalent value was considered acceptable. In addition, for the

substances covered by a migration limit, exposure calculations were often performed with data overestimating migration.

Analysis and comparison of the data requirements and restrictions according to the current and the revised guidelines revealed that two factors had an important impact on the outcome of the application of the revised guidelines: (i) the migration data used to calculate exposure and (ii) the intended contact food of the FCM substance. For most substances, the migration data used for the exposure calculations might have significantly overestimated real migration, e.g. migration data obtained by total mass transfer, modelling or specific migration data with non-adequate simulants. The use of overestimated migration data could have triggered a change in tier and subsequently a change in restriction, which might not occur when adequate migration data (obtained from specific migration experiments with adequate simulants under appropriate migration conditions) were used. Interestingly, for most of the substances covered by adequate migration data, no change in toxicological requirements was observed when the revised guidelines were applied. The intended contact food on the other hand determines the food group categories for exposure calculations, and so indirectly the restriction of the substance. For some substances, combination of the migration data with consumption values of food group category 1 or 2 may result in different toxicological requirements compared to those triggered by food group category 3. In case these substances are covered by a migration limit, the value of the SML will be different. Furthermore, for substances covered by a restricted use, the intended contact food should be considered when setting the restriction.

In a next step, an attempt was made to propose indicators to identify substances for which the application of the draft revised guideline resulted in different data requirements or restrictions. Substances with adequate specific migration data obtained under appropriate conditions were considered most relevant to define such indicators. However, the number of substances with adequate specific migration data obtained under appropriate migration conditions for which more toxicological data were required was limited to one out of 15. This substance, i.e. 3,3',5,5'-tetrakis(tert-butyl)-2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert- butyl-4-hydroxy-5- methylphenyl)propyl] oxyphosphonous acid (EFSA-Q-2008-678, FCM No. 792), was an additive only to be used in polypropylene, intended to be in contact with all foodstuffs. Based on the characteristics of one substance, indicators for substances that will require more toxicological data when the revised guidelines are applied could not be defined. In contrast, the results of the evaluation of the 73 model substances allowed to propose some indicators for substances for which application of the revised guidelines will not affect the toxicological data requirements. These indicators included (i) substances for which an ADI did not need to be established or for which a previously established ADI or equivalent value was considered acceptable, (ii) substances with SML = Not detected and (iii) substances covered by SML > 5 mg/kg or GML.

As for most of the substances, the change in toxicological requirements was due to the lack of adequate migration data, a second attempt was made to set indicators to identify substances for which more adequate migration will be needed according to the revised guidelines. In order to facilitate extrapolation to the database, the proposed indicators were based on some straightforward characteristics of the FCM substances. However, no reliable indicators to identify substances for which the application of the revised guidelines will change the data requirements and/or restrictions,

could be defined. For this reason, indicators containing a certain degree of uncertainty ('indecisive') were proposed to further identify substances for which the application of the revised will not require more adequate migration data.

An indecisive indicator to identify substances for which the application of the revised guidelines will not require more adequate migration data could be defined, i.e. substances covered by an SML $\leq$ 0.05 mg/kg. This indicator contained a certain degree of uncertainty as it was based on two assumptions:

- The real migration of substances for which a too high LOD was used to calculate exposure substances was assumed to be low enough to ensure that no additional toxicological data were required.
- The real migration of substances for which the exposure values were close to the lower threshold of the toxicological tier was assumed to be low enough to ensure that no additional toxicological data were required.

For the model substances covered by an SML $\leq$ 0.05 mg/kg that changed in tier, the change in tier was indeed triggered by the use of a too high LOD for exposure calculations (or a result of the migration expressed as 'smaller than') or the calculated exposure value was very close to the threshold values.

If an additional degree of uncertainty would be allowed, a second indecisive indicator to identify substances for which the application of the revised guidelines will not require more toxicological data could be defined, i.e. substances covered by an SML between 0.05 and 5 mg/kg. This indicator contained a higher degree of uncertainty as it was based on the assumption that no direct toxicological concern occurs when the SML according to the revised guidelines is applied. The assumption was based on the observation that the NOAELs of all model substances with an SML between 0.05 and 5 mg/kg that changed in tier allowed to set the SML according to the revised guidelines. This is not surprising as the SML of 6.67 mg/kg of food group category 1 combined with Tier 3 is close to the maximum migration limit that could be set for substances classified in Tier 2 according to the current guidelines, i.e. 5 mg/kg. Indecisive indicators should be applied with caution as they contain a certain amount of uncertainty.

Finally, the proposed indicators were applied to the substances listed in the Union list in Annex I of the Regulation (EC) 10/2011 and the substances for which application of the revised guidelines will have an impact on the different data requirements were identified. When only the reliable indicators were applied, 65% of the substances present in the Union list will not require more toxicological and/or migration data after the application of the revised guidelines. The remaining 35% could further be decreased by applying the indecisive indicators. Finally, for 97% of the substances present in the Union list in EU Regulation 10/2011, no more adequate migration data or toxicological data will be required according to the revised guidelines. It should however be noted that this extrapolation contains some uncertainties. The impact on the data requirements of the remaining 3% of the substances of the Union list should also be further evaluated. In addition, the revised guidelines will have an influence on most of the restrictions of substances covered by a migration limit and for substances covered by a restricted use, the intended contact food should be considered when the restriction according to the revised guidelines is set.

Lastly, it should be emphasized that this study, the impact assessment and the conclusions, have used the information that was provided by applicants for substances within the framework of the existing guidelines. It seems likely that the impact (if any, where identified for particular substances) may change – probably lessened but could in principle increase – if the specific uses of the materials and their substances were in the future, better defined and thus realigned to the proposed new guidelines by the producers or users of those substances and materials.

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CONTEXT

As food contact materials (FCM) are intended to come into contact with food, migration of hazardous chemical substances from FCM into the food can occur. To protect the consumer's health, substances intended to be used in FCM must comply with the general provisions of the Framework Regulation 1935/2004 describing the safety assessment of a substance for its use in FCM. At present, a more specific regulation is only available for substances that can be used in plastic materials and articles. Commission Regulation (EU) 10/2011 sets out in its Annex I a Union list of authorised substances that can be used in plastic materials and articles. Anyone seeking an authorisation for a substance not yet included in that list shall submit an application in accordance with Article 9(1) of Regulation (EC) No 1935/2004. Article 9(1) requires – *inter alia* – that an applicant shall submit a technical dossier containing the information specified in the guidelines for the safety assessment of a substance. EFSA shall subsequently express its opinion as set out by Article 10 before the European Commission and, where appropriate, authorise the substance by adding it to the list. Authorisation is not specific to an applicant and once it is added to the Union list, the substance can be used by anyone wishing to use it in a plastic material or article. The Scientific Committee on Food (SCF) provided in 2001 the first guidelines for the presentation of the application for safety assessment of a substance to be used in FCM prior to authorisation. These guidelines have been endorsed by the EFSA Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) in its second meeting in 2003. On July 10th,2008, the Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel) was set and continued to use these FCM guidelines.

In the light of developments in science and alignment of the guidelines with opinions issued by EFSA on threshold of toxicological concern (TTC), nanoscience and nanotechnologies, and genotoxicity as well as the experience gained from the safety evaluations of many substances to date, the CEF Panel considered it appropriate to revisit the current guidelines and asked for self-tasking in 2011 (EFSA-Q-2011-00107). The draft revised guidelines are currently being discussed by the CEF Panel and are expected to be published in 2014. In its safety evaluation, EFSA assesses the risks originating from the migration of substances from FCM into food. In the draft revised guidelines, the EFSA CEF Panel proposes to carry out an exposure assessment using a harmonised methodology of EFSA and to take into account the specific consumption of subgroups of the population such as infants and toddlers rather than the current approach which use a single default assumption. Based on the Comprehensive European Food Consumption Database released in 2011 by EFSA (EFSA, 2011) and the level of water consumption in infants set by the World Health Organization (WHO) in 2003 (WHO, 2003), the CEF Panel proposes to set standardised consumption data for a number of food group categories. Such an exposure-based approach may lead to the requirement of different toxicological data compared to the current approach and consequently may lead to the proposal by EFSA of different restrictions on the use of a substance.

EFSA issued The Call for proposals GP/EFSA/FIP/2013/01 to evaluate the impact of the revision of the guidelines, by applying the current and the revised guidelines on a selection of 73 model substances listed in Annex II of the Call. Specific attention was paid to the influence of the exposure-based model on the amount and type of toxicological information required and the influence of the

imposed restrictions on the use of a substance. Finally, the substances that already had been evaluated by the AFC/CEF Panel, but needed to be revised based on the requirements of the revised guidelines, were selected and their characteristics responsible for the re-evaluation were identified. These indicators were then used on all the substances in the Union list of the European Regulation 10/2011 on plastic materials in order to predict the number of re-evaluations caused by the application of the revised guidelines. It is however important to note that the aim of the project was not to re-evaluate the FCM substances according to the current guidelines. In addition, evaluation of the impact of migration conditions prescribed in EU Reg. 10/2011 (e.g. the change in t/T conditions of 10d @40°C into 10d @ 60°C for long term storage at room temperature) was also outside the scope of this project.

METHODOLOGY

The project can be divided in 6 different tasks as shown in Figure 1.

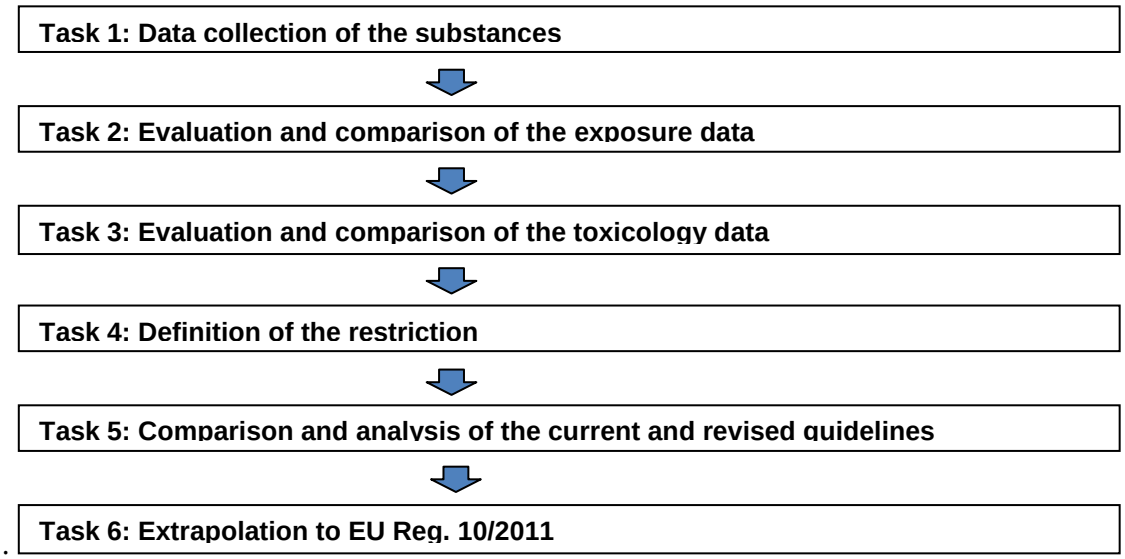

Figure 1: Overview of the different tasks of the project

Note: Annex II of the Call for proposals lists 74 substances. However, one substance, 'glass powder, ground, made from postconsumer recycled glass (up to 100%)' (EFSA-Q-2008-001) was negatively evaluated by the CEF Panel. Therefore, this substance was considered not suited as a model substance to evaluate the impact of the revised guidelines. This substance was excluded and the evaluation was done with 73 instead of the initially proposed 74 substances. An overview of the substances is given in Annex A.

1. DATA COLLECTION OF THE SUBSTANCES

As food contact materials are intended to come into contact with food, migration of hazardous chemical substances into the food can occur. To protect the consumer, substances intended to be used in FCM must therefore comply with the general provisions of the Framework Regulation 1935/2004 describing the safety assessment of a substance for its use in food contact materials. Article 9(1) of this Regulation refers to the guidelines for the presentation of the application for safety assessment of a substance to be used in Food Contact Materials (FCM) prior to authorisation provided by the Scientific Committee on Food (SCF) in 2001. Afterwards a note for guidance was prepared by EFSA to explain the practical aspects of the administrative procedure to be followed by an applicant requiring the evaluation of substance (EFSA, 2008).

The 73 model substances that are subject of this call, have already been evaluated by the AFC or CEF Panel. Hence, for these substances Scientific Opinions, Summary Datasheets, Petitioner Summary Datasheets and full technical dossiers are available. First, a database was constructed that structurally summarises relevant information present in these extensive data sources. The scope of the database

was to facilitate the evaluation and comparison of the exposure and toxicological data. Furthermore, the database served as a tool to perform all requested calculations in the project.

The data sources for the 73 model substances were carefully analysed and the information on different predefined parameters was extracted and inserted into the database. The applications for these substances have been introduced based on the current guidelines. Hence, information on the substances was expected to be present according to Annex 6 of the 'Note for guidance for petitioners presenting an application for the safety assessment of a substance to be used in food contact materials prior to its authorisation' (EFSA, 2008). The relevant data from the Scientific Opinions were inserted in the appropriate column of the database. In addition, the conclusion of the Scientific Opinions and, if applicable, information on the substances present in the Union list of EU Reg. 10/2011 was also included in the database.

In order to avoid confusion when referring to a particular substance, the name of each substance was proceeded by the EFSA-Q-number. 'A substance' can however be an individual chemical compound or an entity of several compounds. Substances usually fall into one of the following categories:

- Individual chemical compound
- Defined mixture of compounds
- Non-defined mixture of compounds
- Polymer used as additive
- Biobased polymer

In case the substance is not an individual compound, additional information has to be provided by the applicant:

- Defined mixtures of compounds (e.g. Copper hydroxide phosphate – EFSA-Q-2010-708, FCM No 972): information on every compound in the mixture has to be provided, independently of its concentration in the mixture.
- Non-defined mixtures of compounds (e.g. Sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salt – EFSA-Q-2005-151, FCM No 813): information should be provided according to one of the three following options: (i) information on the different individual components of the mixture which are not yet included in the EU lists has to be provided; (ii) information on the total mixture has to be submitted or (iii) data on one or several representative compounds of the mixture has to be provided.
- Polymers used as additives (e.g. 2-Phenyl-3,3-bis (4-hydroxyphenyl)phthalimidine – EFSA-Q-2009-834, FCM No 872): information on the monomers or starting materials and on the low molecular weight fraction (MW below 1000 Da) has to be provided.

Furthermore, for each FCM substance, data on potential impurities such as residual starting products (e.g. alpha-Alkenes (C20-C24) maleic anhydride-4-amino-2,2,6,6- tetramethylpiperidine, polymer - EFSA-Q-2006-171, FCM No 803) or oxidation or hydrolysis products (e.g. 1,3-bis(isocyanatomethyl) benzene – EFSA-Q-2012-062, FCM No 988) should also be submitted by the applicant.

Both the additional information required for mixtures and polymers and the data on potential impurities are important for the evaluation of an FCM substance. Consequently, this information also needed to be included in the database. Data on constituents, reference compounds or potential

impurities ('related migrants') were inserted in separate rows. Information on one substance can thus be displayed over several successive lines, although all proceeded by the same EFSA Q-number.

The following paragraph comprehensively describes the layout of the database:

- **Identity of the substance(s)**
  - Chemical name
  - Constituents, reference compounds and related migrants:
    Includes, if applicable, the chemical names of constituents, reference compounds and/or related migrants.
  - PM/Ref number
  - FCM number
  - CAS number
  - Molecular mass range
  - Components with molecular mass < 1000 Da (%)
  - Molecular and structural formula
  - Molecular weight
  - Other information

- **Physical and chemical properties of substance**
  - Octanol/water partition (Log Po/w)
  - Other information related to lipophilicity
  - Thermal stability
  - Reactivity
- **Intended application of the substance**
  - Food contact material:
    Describes the type of food contact material in which the substance will be used and is an important parameter to estimate the real exposure; a very restricted or a very broad field of application may influence the final authorisation and the restrictions of the substance.
  - Technological function:
    Demonstrates the functionality of the substance in the production process and/or in the final product.
  - Contact food:
    Indicates any typical or all types of foodstuff to be in contact with the finished products. Migration tests should be carried out accordingly.
  - Time and temperature
    Describes the time and temperature conditions of contact in practice and any restriction if applicable.
  - Surface to volume ratio.
    For general application, the ratio of 6 dm^2 food contact materials to 1 kg of food is used.
- **Data on migration of the substance**
  Specific migration
  - Test sample:

Should always represent the worst case situation (highest concentration of additive or co-monomer, thickness) e.g. selection of the material or polymer representing the worst case situation in the migration testing (if polyolefins: LDPE may be sufficient).

- Test food(s)/food simulants:
  Describes the test food(s)/food simulants used in the migration experiments. Selection of foodstuff(s) or food simulant(s) used in migration testing should be in accordance with EU Reg. 10/2011.
- Migration conditions:
  Describes how the contact with the simulants was achieved (e.g.: cell, pouch, total immersion), if the test was performed on one or both sides of the test specimen (used in the calculation of the contact area) and the duration of the test and the test temperature.
- Surface to volume ratio:
  Describes the actual contact surface to volume ratio applied in the migration test and is calculated as the dm^2 test sample that is used per kg food or per L simulant. Conventionally the ratio is 6 dm^2/kg simulant, but can deviate often for analytical reasons (in that case should be carefully considered because using a higher ratio of area to volume could influence the final migration due to saturation of the simulant).
- Results mg/kg:
  Summarises the results of the individual migration experiments with sufficient details to interpret the final results.

Overall migration (for the description of the parameters, see 'specific migration)

- Test sample
- Food simulant
- Contact mode
- Migration conditions
- Surface to volume ratio
- Results mg/dm^2
- Results mg/kg

Residual content of the substance in the food contact material

- Test sample:
  Should be - when relevant - equivalent to the test sample used in the migration experiments. In other situations, the sample should represent a worst case situation. In case of different polymers, they should be examined for the residual content of the substance. However, if it is properly argued, only determination of the residual content in a polymer representing the worst case can be acceptable. Criteria of selection will depend on the substance and the manufacturing process.
- Results
- Calculated migration (worst case):
  Sets out calculation of migration of the substance assuming total migration. In case worst case calculation is acceptable, an analytical method for analysis has to be provided.
- Residual contact versus specific migration:
  Reflects the relationship between residual content and specific migration, if determined.

Data obtained by modelling

- Test sample

- Methodology:
  Summarises the different parameters (thickness, contact mode, type of material, t/T° test conditions), close to the intended situation of use, that are introduced in modelling software for estimation of migration taking account the worst case conditions.
- Results

- **Toxicological data**

Summarises the toxicological data used for the evaluation of the substance. An indication was provided if toxicological data were provided by the applicant (performed), collected from previous evaluations (previously evaluated) or obtained from literature (literature data).

General information on toxicity

Contains general information related to the toxicological data e.g. reference to previous evaluations or additional read-across information. In case no toxicological data were required, the statement 'no toxicological data required' together with the rationale behind this decision was included in this column.

Genotoxicity

Provides information on the different genotoxicity tests. For most substances, in vitro genotoxicity tests were performed in the absence and presence of a metabolic activation system (S9), respectively referred to as '–S9' and '+S9'. The outcome of the tests (negative, positive or inconclusive/equivocal) was included. If relevant, additional information on the experimental design was provided, e.g., further specification of the test, cell type/animal species.

- Gene mutation test in bacteria
- In vitro mammalian cell gene mutation test
- In vitro mammalian chromosome aberration test
- In vitro mammalian micronucleus test
- In vivo follow-up
- Other information

General toxicity

Summarises information related to the general toxicity tests. No observed (adverse) effect levels (NO(A)EL) or lowest observed (adverse) effect levels (LO(A)EL) values are provided, together with the animal species and the effects that were used to establish the NO(A)EL/LO(A)EL values.

- Subchronic (90d) oral toxicity
- Chronic toxicity/carcinogenicity
- Reproduction/developmental toxicity
- Other information

Metabolism

Contains information on ADME studies and, when available, 'other considerations' that were used to evaluate the absence of the potential for accumulation in man.

- Absorption, distribution, biotransformation and excretion
- Accumulation in man
- Other information

Miscellaneous

- Effects on immune system
- Neurotoxicity
- Induction on peroxisome proliferation
- Other information

- **Conclusion of the Scientific Opinion**
  - SCF-list
  - Restriction

- **EU Regulation 10/2011**
  - Present in EU Reg. 10/2011:
    Indicates if the substances are listed in the Union list of EU Regulation 10/2011. If this is the case, 'yes' is displayed.
  - Use as additive or polymer production aid:
    Indicates if the substance is authorised to be used as additive or polymer production aid (yes) or if the substance is not authorised to be used as additive or polymer production aid (no). For substances that are only authorised as polymer production aid, 'yes' is displayed in this column but under the specifications a statement is inserted that the use is restricted to polymer production aid.
  - Use as monomer or other starting substance or macromolecule obtained from microbial fermentation:
    Indicates if the substance is authorised to be used as monomer or other starting substance or macromolecule obtained from microbial fermentation (yes) or if the substance is not authorised to be used as monomer or other starting substance or macromolecule obtained from microbial fermentation (no). For substances that are authorised as macromolecule obtained from microbial fermentation 'yes' is displayed in this column but under the specifications a statement is inserted that the substance is a macromolecule obtained from microbial fermentation.
  - FRF applicable:
    Indicates if for the substance the migration results can be corrected by the Fat Consumption Reduction Factor (FRF) (yes) or if they cannot be corrected by the FRF (no).
  - Specific Migration Limit (SML) (mg/kg):
    Indicates the maximum permitted amount of a given substance released from a material or article into food or food simulants, expressed in mg/kg of food or food simulant.
  - Remark
    Contains more information on the use, the maximum permitted level of the substance, polymerisation of a specific type of polymer, oxidation products, direct or indirect contact...

Grouping of the substances into at least 50 different categories was not performed considering the limited number of substances that were subject of the Call, i.e. 73. Consequently, the impact of the revision of the guidelines was evaluated for each of the 73 model substances.

2. INTERPRETATION OF THE RESTRICTIONS DEFINED BY THE CURRENT GUIDELINES

For the 73 model substances, the restrictions defined by the current guidelines were interpreted based on the migration and toxicological data provided by the applicant and the information available in the Scientific Opinions. However, the aim of the project was not to re-evaluate the FCM substances according to the current guidelines but instead to understand the rationale behind the restrictions set by the AFC/CEF Panel.

2.1. Migration data

The safety assessment of substances used in FCM requires the combination of toxicological data indicating the potential hazard (see 2.2) with likely human exposure data. For FCM, exposure is determined by the level of migration of a substance into the food and the consumption of the respective food. However, as human exposure data were not readily available when the current guidelines were established, a default assumption is used to estimate exposure. The default assumption states that a person of 60 kg may consume daily up to 1 kg of food packed in the relevant food contact material. Consequently, selection of migration data for the substance and related migrants was sufficient to calculate exposure according to the current guidelines.

The migration potential of an FCM substance can be assessed with different methodologies, namely, specific migration using simulants, overall migration, total mass transfer calculations based on residual content or nominal amount and modelling using residual content or nominal amount. Migration data are not only required for the substance itself but also for its related migrants. Hence, dossiers often contain a substantial amount of migration data. In the project, the migration data of the 73 selected substances were collected from the different data sources and summarised in the database. To calculate exposure according to the current guidelines, a selection of the provided migration data for each substance and its related migrants, was made. The selection of migration data was based on the following principle: if specific migration data were available, the highest reported value was used. If not, data from migration modelling, total mass transfer and overall migration were used. This principle was also followed by the AFC/CEF Panel. Since the 73 model substances have already been evaluated by the AFC/CEF Panel, the conditions (choice of simulant and time/temperature conditions) of the migration experiments performed were considered sufficiently severe to cover the intended contact foods of the FCM substance. Therefore, possible underestimation of the migration of the substance and related migrants was not taken into account, while overestimation of the migration of the substance and related migrants often occurred.

The selected migration data were then used to set the toxicological requirements.

2.2. Toxicological data

In the current guidelines the toxicological dataset requirements depend on the migration potential of the substance and related migrants. The greater the migration, the more toxicological information that

will be required. The rationale is based on the principle of conventional dose-response relationship of toxic effects according to which at low levels of exposure the likelihood and variety of adverse effects will diminish, and on ethical reasons regarding the reduction of animal studies. Based on the migration data, three different tiers, each associated with different toxicological requirements, can be distinguished (Table 4).

Table 4: Overview of the thresholds of the different tiers and the associated toxicological requirements according to the current guidelines

Threshold values		Toxicological requirements
Tier 1	< 0.05 mg/kg	• 3 mutagenicity tests in vitro
Tier 2	0.05 mg/kg ≤ migr ≤ 5 mg/kg	• 3 mutagenicity tests in vitro • 90 day oral toxicity study • Data to demonstrate the absence of potential for accumulation in man
Tier 3	5 mg/kg < migr ≤ 60 mg/kg	• 3 mutagenicity tests in vitro • 90 day oral toxicity study • Studies on absorption, distribution, metabolism and excretion • Studies on reproduction in one species, developmental toxicity, normally in two species • Studies on long-term toxicity / carcinogenicity

It should however be noted that in some cases, the petitioner may deviate from these requirements based on knowledge for example related to the identity, use of and potential exposure to the substance requested. Such deviations are allowed in case the provided reasons are judged scientifically valid. On the other hand, the petitioner should always provide all available data, relevant for the evaluation.

For each of the 73 model substances and related migrants, the toxicological information considered in the Scientific Opinion and/or provided in the SDS was compared to the data required according to the corresponding tier. In case data were lacking or provided additionally, the (possible) rationale for this deviation was discussed.

2.3. Interpretation of the restriction

The results of the toxicological tests were used by the AFC/CEF Panel to set a restriction. In general, two types of restrictions are used: (i) a specific or generic migration limit and (ii) a restriction related to the use of the substance. Some substances can be covered both by a migration limit and a restricted use.

Substances covered by a migration limit (SML or GML)

For substances with migration values higher than 5 mg/kg (classified as Tier 3), the restriction is based on the results of the complete core set of toxicological tests. For non-genotoxic substances, usually a dose causing no observed adverse effects in laboratory animals (NOAEL) can be determined. This NOAEL value can then be used to calculate the tolerable daily intake (TDI) for man, expressed in mg/kg bw/day, by applying a safety factor, usually 100. The SML is obtained by multiplying the TDI value by a factor of 60. This factor is derived from the convention that a person of 60 kg could daily consume up to 1 kg of foodstuffs in contact with a plastic article always containing the considered substance at a concentration corresponding to the SML. Migration of a substance should however always be lower than 60 mg/kg in order to be compliant with the relevant requirements set out in Article 3 of EU Regulation 1935/2004. Indeed, in case migration exceeds 60 mg/kg the material can no longer be considered inert, since the migrating substances can lead to unacceptable changes in the composition of the food. However, in case there is not sufficient data to establish a TDI or when the safety factor is considered insufficient, a lower SML can be set depending on the amount and type of toxicological data provided and the NOAEL values obtained in the toxicological studies.

For the substances with migration values equal to or between 0.05 and 5 mg/kg (classified as Tier 2), the SML can be less or equal to 5 mg/kg. These restrictions are set based on a reduced set of toxicological data including genotoxicity data, the results of a 90 day oral toxicity study and data to demonstrate the absence of potential for accumulation in man. In case the substance does not have genotoxic effects or the potential to accumulate in man and the available toxicological data give an estimated TDI which allows migration of the substance up to 5 mg/kg (and probably much higher), the SML is fixed at 5 mg/kg. A lower SML can be set when required data are lacking or the safety factor is considered insufficient.

Substances with migration values below 0.05 mg/kg (classified as Tier 1), can obtain a restriction below or equal to 0.05 mg/kg with the important condition that the genotoxicity data provided did not indicate a potential genotoxic effect.

Substances covered by a restricted use.

Substances that are evaluated by the AFC/CEF Panel for a specific type of plastic or for only one type of use, are mostly covered by a ‘restricted use’ and not by a migration limit. The amount and type of toxicological data required for these substances also depends on the migration data. In case sufficient data are provided and these data did not indicate a toxicological concern at the detected migration level, the substance is included in the positive list with a restricted use.

For each of the 73 model substances, the restriction set by the AFC/CEF Panel was identified and the (possible) rationale behind the restriction was discussed.

3. DETERMINATION OF THE RESTRICTIONS ACCORDING TO THE REVISED GUIDELINES

3.1. Exposure calculations according to the revised guidelines

In the revised guidelines, exposure assessment is no longer based on the default assumption that a person of 60 kg may consume daily up to 1 kg of food in contact with the relevant food contact material. Instead consumption scenarios are set for three default food group categories based on a harmonised methodology of EFSA which takes into account subgroup populations and their corresponding weight. Each food group category has a consumption value driven by the subpopulation giving the worst case scenario. The three food group categories with the associated default food consumption are summarised in Table 5.

Table 5: Food consumption values to calculate dietary exposure as a function of the three food group categories

Food group category	***Foodstuffs***	***Population driving the consumption***	***Food consumption used for the estimation of the exposure***
1	Water and other liquids such as milk formula consumed by babies and infants up to 12 months old	Infants	150 g/kg bw/day
2	Beverages, such as non-alcoholic or alcoholic beverages, milk or milk products	Toddlers	80 g/kg bw/day
3	Foodstuffs not covered by Categories 1 and 2	Toddlers	20 g/kg bw/day

Exposure can then be calculated by combining the predicted level of the FCM substance in food, obtained from migration data, with the consumption data for each food group category covered by the intended uses of the FCM. The highest estimated exposure will determine the toxicological data required, on the basis that the greater the exposure to the substance through migration into food, the more toxicological information will be required.

For each of the 73 model substances, the exposure was calculated according to these revised guidelines. First, the consumption data for each substance were selected as a function of its intended contact food. Since a distinction between three different food group categories is made in the revised guidelines, the information on the intended contact food present in the database had to be translated to the corresponding food group categories. For example, when a substance was used in an FCM destined for 'all foodstuffs', the three food group categories needed to be considered, while for 'Fresh fruit' only the third category was taken into account for the exposure assessment. It is however important to note that the intended contact foods were not those requested by the applicant, but the contact foods for which the FCM substance was positively evaluated by the AFC/CEF Panel.

In a second step, specific migration data corresponding to the intended contact foods were identified for each of the 73 model substances and related migrants. Specific migration levels can be estimated in a stepwise approach using results of different types of experiments, starting from worst-case conditions down to, if needed, specific migration measurements in foodstuffs themselves. However, for most substances migration measurements in representative foods are not available. Specific migration tests using appropriate food simulants under proper test conditions are acceptable too. An

overview of the simulants to be chosen for the different types of foods is provided in Annex III, Table 2 in the EU Regulation 10/2011.

In the revised guidelines, different types of foods are grouped in the same food group category. Consequently, each food group category may cover foods requiring different simulants. For each of the three food group categories, the corresponding simulants were identified and summarised in Table 6.

Table 6: Food group categories defined in the revised guidelines and corresponding food simulants as described in Regulation (EU) 10/2011

Food group category		**Type of simulant**						
1	Water and other liquids such as milk formula consumed by babies and infants up to 12 months old	Water				D1		
2	Beverages, such as non-alcoholic or alcoholic beverages, milk or milk products			B	C	D1		
3	Foodstuffs not covered by Categories 1 and 2		A	B	C	D1	D2 95% EtOH Isooctane	E

Simulant A: 10% EtOH, B: 3% Acetic acid, C: 20% EtOH, D1: 50% EtOH and D2: Vegetable oil, E: Tenax®

Since food group category 1 includes water and reconstituted milk formula, the corresponding simulants according to Annex III, table 2 from the EU Regulation 10/2011 were simulant C (for water) and simulant D1 (for reconstituted milk). The use of simulant C to simulate water was considered not suitable in this project and preference was given to migration tests performed with water as simulant for water as mentioned in the previously used Council Directive 82/711/EEC laying down the basic rules necessary for testing migration of plastic FCM.

Food group category 2 comprises the following types of food:

- Clear drinks (Simulant B and C)
- Cloudy drinks (Simulant B and D1)
- Milk and milk products (Simulant D1)
- Alcoholic beverages of an alcoholic strength between 6%vol and 20% (Simulant C)
- Alcoholic beverages of an alcoholic strength above 20% and all cream liquors
- Undenaturated ethyl alcohol (Simulant B and 95% EtOH)

Since 95% EtOH is only mentioned as a simulant for a very specific type of food (Undenaturated ethyl alcohol), it was considered not suitable as simulant for food group category 2. Consequently, the selected simulants for this category were simulant B, C and D1.

Food group category 3 contains all the foodstuffs not covered by food group categories 1 and 2. Therefore, all simulants were taken into account. Since the dossiers of the substances were submitted based on the previous plastics regulation (EU Directive 2002/72), alternative simulants could have been used to replace simulant D2 (vegetable oil) when its use was not possible for technical reasons connected with the method of analysis, as is described in 'Council Directive 82/711/EEC laying down

the basic rules necessary for testing migration of the components of plastic materials and articles intended to come into contact with foodstuffs'. The substitute simulants mentioned in this directive are isooctane and 95% EtOH. Therefore, these alternative simulants were also considered adequate for food group category 3.

Once the different simulants for each food group category were identified, migration data for the exposure calculations could be selected. This selection required to establish a structured scheme provided in Figure 2, explained in Table 7. Implementation of this decisional hierarchy approach was necessary to ensure a high level of consistency throughout the project.

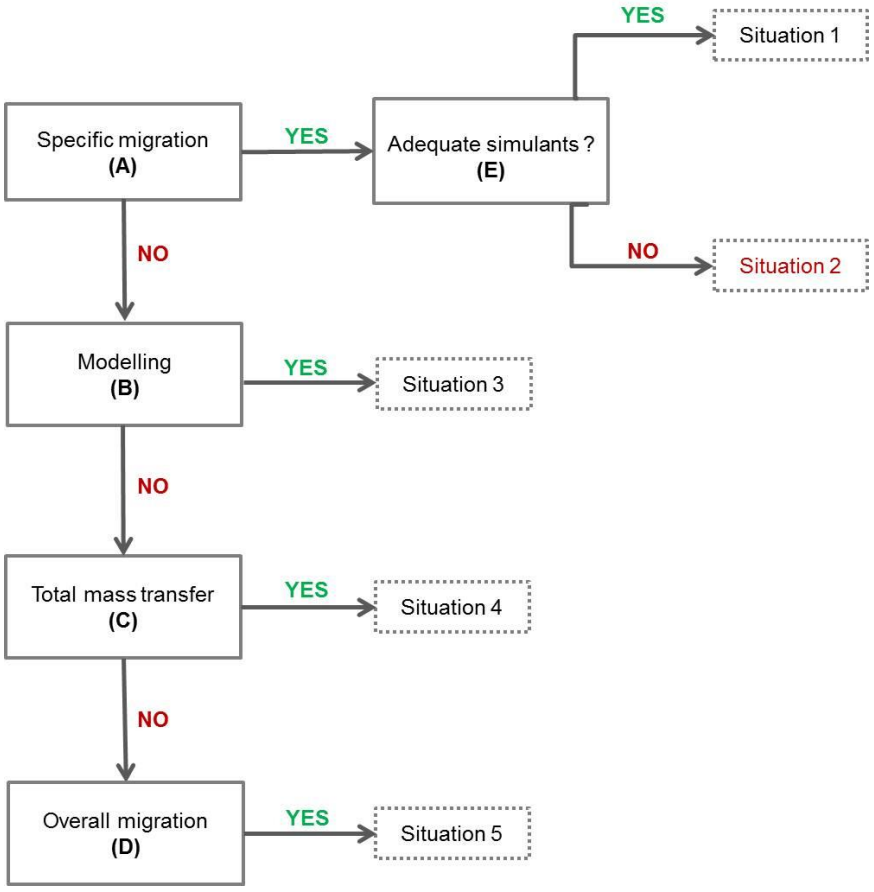

Figure 2: Decision tree for the selection of migration data according to the revised guidelines

Table 7: Description of the different situations resulting from the decision tree together with the codes used in the database to report the different types of migration data

Situation	*Path in the decision tree*	*Migration data selected for the exposure calculations*	*Code used in the column "How obtained" of the Exposure worksheet*
1	(A) (E)	Specific migration data used with adequate simulant	SM (type of simulant selected)
2	(A) (E)	Specific migration data used with a non-adequate simulant	SM_N (type of simulant selected)
3	(A) (B)	Specific migration data not available. Modelling data used.	Model
4	(A) (B) (C)	Specific migration and modelling data not available. Total mass transfer data were used.	TMT
5	(A) (B) (C) (D)	Specific migration, modelling and total mass transfer data not available. Overall migration data used.	OM

It should be noted that overall migration data were never used to calculate exposure but they were mostly considered as an inertness parameter for the FCM, giving useful information on the behaviour of the FCM. This in turn could support conclusions from specific migration testing.

In summary, data from specific migration studies performed with an adequate simulant (as described in Table 6) were preferred. When migration data obtained with more than one simulant adequate for one food group category were available, the highest migration value was retained. If no migration experiments were performed with simulants adequate for the food group category under investigation, the highest specific migration value obtained with the non-adequate simulants was selected. This particular situation was indicated by introducing "_N" after the code for the type of migration experiments. *Example:* SM_N (B) means that the selected migration data were obtained by a specific migration study with a simulant B which is not representative for the specific food group category used.

If no specific migration study was performed, modelling data were selected. For modelling, no distinction was made between 'adequate' and 'non-adequate' modelling. Modelling was considered in all cases to sufficiently cover (and even overestimate) the migration in the intended contact foods of the FCM containing the substance since the modelling data were submitted for the evaluation of the substance according to the current guidelines. When no data on specific migration nor on modelling were available, total mass transfer data were chosen over overall migration data.

It should be noted that migration data selected to calculate exposure according to the revised guidelines were considered not to underestimate the migration of the substance and the related

migrants. Indeed, the selected migration data were obtained from the evaluation of the FCM substance according to the current guidelines. In order to be useful for the evaluation, the condition of the migration experiments had to be sufficiently severe to cover the intended food contacts of the FCM substance. Overestimation of the migration, on the other hand, was possible and factors contributing to overestimation (e.g. type of migration experiments, adequacy of simulants and migration conditions) were therefore identified. Evaluation of the impact of the new migration conditions prescribed in EU Regulation 10/2011 was however outside the scope of the current project.

Finally, exposure was calculated for each substance and related migrants based on the selected migration data and the consumption values for the identified food group categories. In case the exposure had to be estimated for more than one food group category, the highest estimated exposure was selected.

3.2. Toxicological data required according to the revised guidelines

According to the revised guidelines, the amount of toxicological data required depends on the expected human exposure level, according to the principle that the higher the exposure, the greater the amount of data required. Additional data may be needed if potential structural alerts of toxicity are identified. Based on the exposure data, three different tiers, each associated with different toxicological requirements, can be distinguished (Table 8).

Table 8: Overview of the thresholds of the different tiers and the associated toxicological requirements according to the revised guidelines

Threshold values		Toxicological requirements
Tier 1	< 1.5 µg/kg bw/day	2 mutagenicity tests in vitro
Tier 2	1.5 µg/kg bw/day ≤ Exp ≤ 100 µg /kg bw/day	2 mutagenicity tests in vitro 90 day oral toxicity study ADME (if bioaccumulation or nanomaterials)
Tier 3	> 100 µg/kg bw/day	2 mutagenicity tests in vitro 90 day oral toxicity study Studies on absorption, distribution, metabolism and excretion Studies on reproduction in one species, developmental toxicity, normally in two species Studies on long-term toxicity / carcinogenicity

The toxicological requirements according to the revised guidelines are similar compared to those described in the current guidelines. While a battery of three in vitro genotoxicity tests was required according to the current guidelines, only two in vitro mutagenicity tests are required according to the revised guidelines, since the Scientific Committee of EFSA recommends, in a recent scientific opinion, to start with a basic battery of two in vitro tests for the generation and evaluation of data on

the genotoxic potential of a compound. This battery comprises a bacterial reverse gene mutation test and an in vitro micronucleus assay and covers the three genetic endpoints.

An overview of the threshold values for the toxicological requirements according to the current and the revised guidelines is presented in Table 9. In order to facilitate comparison, the threshold values according to the current guidelines were expressed as µg/kg bw/day taking into account the default assumption that a person of 60 kg may consume daily up to 1 kg of food packed in the relevant food contact material.

Table 9: Classification of the substances into tiers as established in the current and revised guidelines

Current guidelines		Revised guidelines	
Migration assessment		*Exposure assessment*	
Tier 1	< 0.05 mg/kg (Exp < 0.83 µg/kg bw/day)	**Tier 1**	< 1.5 µg/kg bw/day
Tier 2	0.05 mg/kg ≤ migr ≤ 5 mg/kg (0.83 µg/kg bw/day ≤ Exp ≤ 83 µg/kg bw/day)	**Tier 2**	1.5 µg/kg bw/day ≤ exp ≤ 100 µg/kg bw/day
Tier 3	5 mg/kg < migr ≤ 60 mg/kg (83 µg/kg bw/day < Exp ≤ 1000 µg/kg bw/day	**Tier 3**	> 100 µg/kg bw/day

For each of the 73 model substances and related migrants, the toxicological requirements according to the revised guidelines were determined based on the exposure values calculated under 3.1.

3.3. Determination of the restriction according to the revised guidelines

Based on the tier according to the revised guidelines and the understanding of the restriction according to the current guidelines, the impact of the revision of the guidelines on the restriction of the FCM substance was evaluated.

Substances covered by a migration limit (SML or GML)

Substances restricted by a migration limit according to the current guidelines will be covered by an exposure limit according to the revised guidelines. In case the toxicological data required for an FCM substance and related migrant are provided by the applicant and do not raise a concern, the upper exposure limit of the tier of the substance will be used to set an SML. The exposure limits, however, need to be translated in migration per kg of food by applying the consumption value for the food group category that contained the highest exposure value for the substance. In contrast to the current guidelines, each tier is thus not associated with one but with three SML values. The SML value to be used depends thus on the intended contact food. In Table 10, an overview of the SML values according to the revised guidelines is provided.

Table 10: Overview of the restrictions according to the revised guidelines

	Tier 1 *(1.5 µg/kg bw/day)*	***Tier 2*** *(1.5-100 µg/kg bw/day)*	***Tier 3*** *(> 100 µg/kg bw/day)*
Food group category 1 *(150 g/kg bw/day)*	0.010 mg/kg	0.67 mg/kg	6.67 mg/kg
Food group category 2 *(80 g/kg bw/day)*	0.019 mg/kg	1.25 mg/kg	12.5 mg/kg
Food group category 3 *(20 g/kg bw/day)*	0.075 mg/kg	5 mg/kg	50 mg/kg

The SML values for the revised guidelines were calculated by dividing the tier threshold by the exposure for the corresponding food group category. For example, the threshold of Tier 1 (1.5 µg/kg bw/day) divided by the consumption value for food group category 1 (150 g/kg bw/day), results in a restriction of 0.01 mg/kg. Since the upper limit of Tier 3 is not mentioned, the GML is translated from 60 mg/kg into 1 mg/kg bw/day, using the general assumption that a person of 60 kg consumes 1 kg of packed food. This value (1 mg/kg bw/day) was then used to calculate the restrictions related to Tier 3. It should be noted that the combination of Tier 2 with a highest calculated exposure from food group category 3, leads to the same restriction as in the current guidelines. Furthermore, the restriction for substances classified as Tier 1 with an highest exposure value in food group category 3 is even higher (i.e. 0.075 mg/kg) compared to the restriction according to the current guidelines (i.e. 0.05 mg/kg). Finally, the restriction obtained by combining the threshold value of Tier 3 with the consumption value for food group category 3 is very close to the 60 mg/kg restriction, according to the current guidelines

For those of the 73 model substances covered by a migration limit, the need for more toxicological and/or migration data was evaluated and, if possible, the SML value according to the revised guidelines was set.

Substances covered by a restricted use.

The impact of the revised guidelines on substances covered by a restricted use is different compared to the previous category of substances covered by a migration limit. When a substance covered by a restricted use does not change in tier, the amount of toxicological data required stays the same and consequently, the restricted use will not change. If the appointed tier of the substance does change, more toxicological and/or migration data might be required to evaluated if the substance does not raise a concern for the proposed use.

For those of the 73 model substances covered by a restricted use, the need for more toxicological and/or migration data was evaluated.

4. COMPARISON AND ANALYSIS OF THE CURRENT AND THE REVISED GUIDELINES

For each of the 73 model substances and related migrants, exposure data, toxicological requirements and restrictions according to the current and the revised guidelines were compared. The major factors causing a change in exposure, data requirements and restrictions were identified. Furthermore, the potential link between the observed changes and parameters such as the use, technological function, nature of foodstuffs in contact, etc. was investigated in order to identify indicators. Particular attention was paid to characteristics that are also included in the Union list of the EU Regulation 10/2011. This should facilitate the extrapolation of the results obtained for the 73 model substances to all substances included in the Union list.

5. EXTRAPOLATION OF THE RESULTS TO THE SUBSTANCES INCLUDED IN THE UNION LIST OF EU REGULATION 2010/11

The proposed indicators were applied to the substances listed in Annex I of the Regulation (EC) 10/2011 and the substances for which application of the revised guidelines will have an impact on the different data requirements were identified.

RESULTS AND DISCUSSION

1. DATA COLLECTION OF THE SUBSTANCES

A list of 73 model substances previously evaluated by the CEF or AFC Panel and for which Scientific Opinions and technical dossiers are available, was provided in the project call. In order to structurally summarise the relevant information present in the different Scientific Opinions of these 73 compounds, a database was developed. If necessary, the database was further completed with the information from the summary data sheets (SDS). Furthermore, other relevant information on the substances included in the EU Regulation 10/2011 for plastics, was also added to the database (e.g. present in EU Reg. 10/2011, used as additive or monomer, FRF applicable, SML and other remarks).

1.1. Substances present in the database

Different groups can be distinguished within the list of 73 model substances. An overview of the distribution of the different types of substances is given in Figure 3.

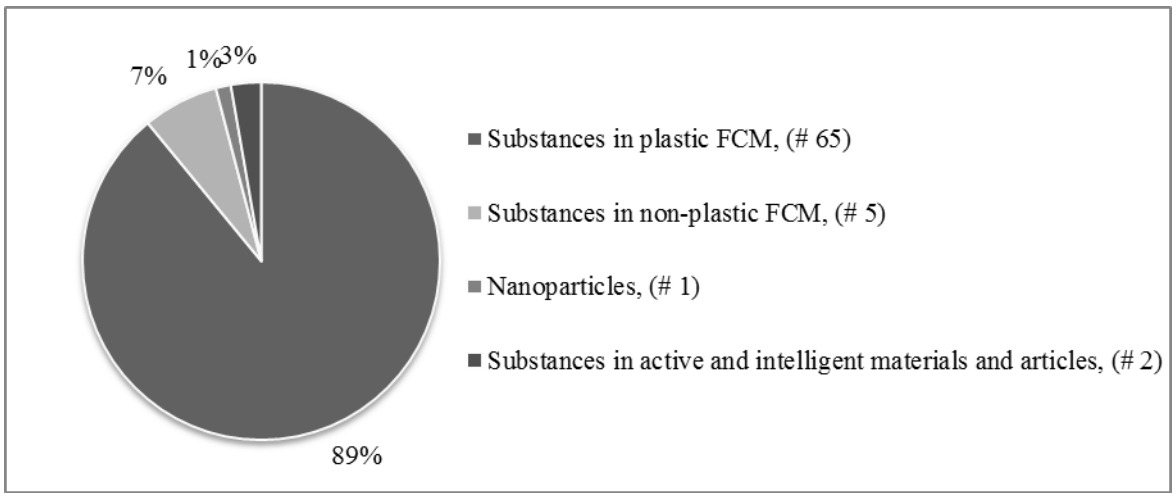

Figure 3: Overview of the different types of substances present in the list of model substances, (# 73 = 100%)

Substances used in plastic FCM (# 65)

The list includes substances already present in the Union list in Annex 1 of the specific European Regulation for plastic materials and articles intended to come into contact with food (EU Reg. 10/2011) or substances that were voted for inclusion at the end of November 2013, like 1,3-bis(isocyanatomethyl)benzene (EFSA-Q-2012-062, FCM 988) and 2-phenyl-3,3'-bis(4-hydroxyphenyl)phthalimidine (EFSA-Q-2009-834, FCM No 872). Other substances like biocides can be used on plastic FCM, but they are not included in this category since they are not present in the Union list in EU Regulation 10/2011.

Substances used in non-plastic FCM (#5)

The list also contains substances used in non-plastic food contact applications such as components of coatings [2-hydroxypropyl methacrylate (EFSA-Q-2011-1239, FCM No 995), N,N'-propane-1,3-

diylbis(N'octadecylurea) (EFSA-Q-2006-139)] or substances used in the paper making process [Tetrahydro-1,3,4,6-tetrakis(hydroxymethyl)imidazo-[4,5-d]imidazole-2,5 (1H, 3H)-dione (EFSA-Q-2006-315)].
Substances used as biocides are also present in the list [Silver Zeolite A (EFSA-Q-2009-708, FCM No 946]. Although these substances can be applied on plastic FCM, they are not authorised by the EU Regulation 10/2011 on plastic materials and articles intended to come into contact with food. The placement on the market of articles treated with biocides will only be allowed after the appropriate approval of the active substance for the relevant biocidal product type according to the EU Regulation 528/2012 concerning the making available on the market and use of biocidal products. This Regulation establishes rules and procedures for the authorization of biocidal products and approval of the active substances with which they are formulated. The biocide, Silver Zeolite A, will be evaluated in the same way as the substances authorised in EU Regulation 10/2011. Moreover, Bis(hydroxyphenyl)methane (EFSA-Q-2006-129, FCM No 965) is a precursor for BFDGE and thus already restricted by the Commission Regulation 1895/2005 on the restriction of use of certain epoxy derivatives in materials and articles intended to come into contact with food.

Nanoparticles (# 1)

One of the substances in nanoform, present on the Union List, is Titanium nitride (EFSA-Q-2011-1079, FCM No 807). When the nanoform of a substance is intended to be used in FCM, a new application should be submitted, even if the conventional form of this substance is included in the Union list. Indeed, the EU Reg. 10/2011 clearly states that authorisations which are based on the risk assessment of the conventional particle size of a substance do not cover engineered nanoparticles since the chemical and physical properties significantly differ from the particles at a larger scale, leading to different toxicological properties. Furthermore, in its guidance on nanoscience and nanotechnologies in the food and feed, the CEF Panel states that information from in-vitro genotoxicity, absorption, distribution, metabolism and excretion and repeated dose 90-day oral toxicity studies in rodents need to be provided for nanoparticles intended to be used in FCM. In contrast to the current guidelines for FCM in a non-nanoform, a reduced toxicological dataset in function of the extent of migration is not allowed for nanomaterials according to this guidance, due to the limited knowledge on the behaviour and effects of nanomaterials. Only when no migration is observed, a reduced dataset can be introduced (EFSA Scientific Committee, 2011a). Based on the migration data of the substance Titanium nitride nanoparticles, the CEF Panel however concluded that no toxicological data were required. According to the CEF Panel, the intended use would not give rise to exposure of the consumer via migration into food and that the substance would consequently not be of toxicological concern if used at up to 20 mg/kg in only PET plastics intended for contact with all types of foodstuffs under conditions of any duration of time and temperatures up to and including hot fill.

Substances in active and intelligent materials and articles (# 2)

Active and intelligent materials and articles intended to be used in contact with foodstuffs are covered by the specific European Regulation No. 450/2009. This Regulation should be applied in addition to the general requirements established in the Framework Regulation 1935/2004 (EC, 2004). In 2009, EFSA published guidelines on submission of a dossier for safety evaluation of active and intelligent substances present in active and intelligent materials and articles intended to come into contact with

food. In addition to information similar to that required by the current guidelines for substances used in FCM, more specific information on the principle and target function of the active and intelligent material or article should be provided. In the annex with the 73 model substances, two are listed that can be used in active and intelligent packaging: Sodium borohydride used in conjunction with Palladium acetate (EFSA-Q-2011-067, FCM No 981/982) and Sodium carbonate peroxyhydrate, bentonite, sodium chloride and sodium carbonate (EFSA-Q-2011-236).

1.2. Information present in the database

A database was developed containing all the relevant information from the Scientific Opinions and summary data sheets (SDS-files). Furthermore, other relevant information on the substance, included in the EU Regulation 10/2011 for plastics was also added to this database (e.g. present in EU Reg. 10/2011, used as additive or monomer, FRF applicable, SML and other remarks).

An overview of some interesting characteristics from the 73 model substances is given below.

1.2.1. Type of food contact material

As already illustrated in Figure 3, the 73 model substances are intended to be used in plastic or non-plastic FCM, as nanomaterials or in active and intelligent packaging material. This information can also be presented differently by describing the amount of applications for the substance. For example, 1,3-bis(isocyanatomethyl)benzene (EFSA-Q-2012-062, FCM No. 988) will only be used in PET, while oxidized polyethylene (EFSA-Q-2003-199, FCM No. 811) can be used in all types of plastic. The results are given in Figure 4.

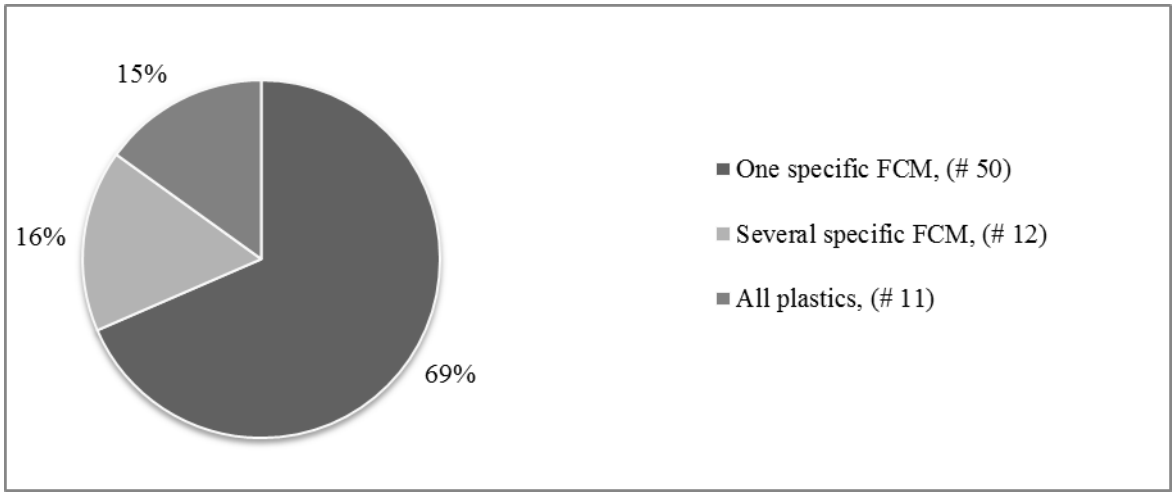

Figure 4: Overview of the intended food contact materials in which the substances (# 73) can be used.

These results show that 23 out of the 73 model substances (31%) are intended to be used in more than one type of polymer (15% in all plastics and 16% in several FCM). The remaining 50 substances (69%) are intended to be used in one particular type of food contact material like PVC, PET, PO or fluorinated polymers.

1.2.2. Technological function

Another interesting characteristic of the substance is its technological function, that sets out the function of the substance in the production process or in the finished product. In the EU Regulation 10/2011, a distinction is made between 'monomers and other starting substances' and 'additives and polymer production aid (PPA)'. The first category 'monomers and other starting substances' is described as (i) a substance undergoing any type of polymerisation process to manufacture polymers; or (ii) a natural or synthetic macromolecular substance used in the manufacture of modified macromolecules; or (iii) a substance used to modify existing natural or synthetic macromolecules. These substances will be referred to as 'monomers' in the rest of the project.

The second category includes 'additives and polymer production aids'. In the past, no clear differentiation has been made between additives that have a function in the final polymer and polymer production aids (PPA) that only exhibit a function in the manufacturing process and are not intended to be present in the final article nor have a physical or chemical in the final material. Since some substances acting as PPA were already included in the incomplete list of additives in the past, these PPA are still present in the Union list of authorised substances. If the substance is only authorised as PPA, then the use of the substance will be restricted to PPA in the specifications. In the Union list of EU Reg. 10/2011, only one substance, FCM no. 804 (poly(3-nonyl-1,1-dioxo-1-thiopropane-1,3-diyl)-block-poly(x-oleyl-7-hydroxy-1,5-diiminooctane-1,8-diyl), process mixture with x = 1 and/or 5, neutralised with dodecylbenzenesulfonic acid) with CAS No. 1010121-89-7 is restricted to be used only as PPA. Therefore, additives and PPA will be treated together in this project and they will be referred to as 'additives'.

An overview of the categories according to their technological function is provided in Figure 5.

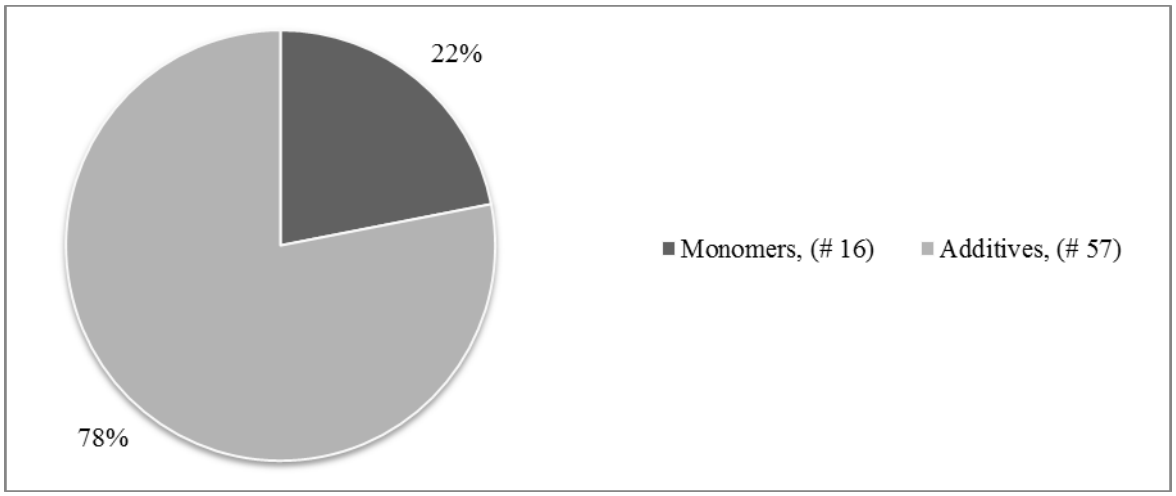

Figure 5: Overview of the technological functions of the model substances (# 73)

The results show that 16 out of the 73 model substances (22%) are used as monomer and 57 (78%) as additive. In case the substance is used as an additive, more detailed information is provided in the database on the specific use (e.g. lubricant, emulsifier, plasticizer,…).

1.2.3. Intended contact food

The type of food intended to be in contact with the finished article, is specified in the dossier, ranging from general applications like 'All foodstuffs' to very specific types of food like 'Fresh fruit'. In the current guidelines, this information was used to determine the migration test, while a larger impact of this parameter can be expected in the application of the revised guidelines, since the intended contact food will determine the food group categories used for the exposure calculations. An overview of the intended contact food is given in Figure 6. It should be noted that the intended contact foods presented in Figure 6 are based on the conclusion of the evaluation and not on the use as requested by the applicant.

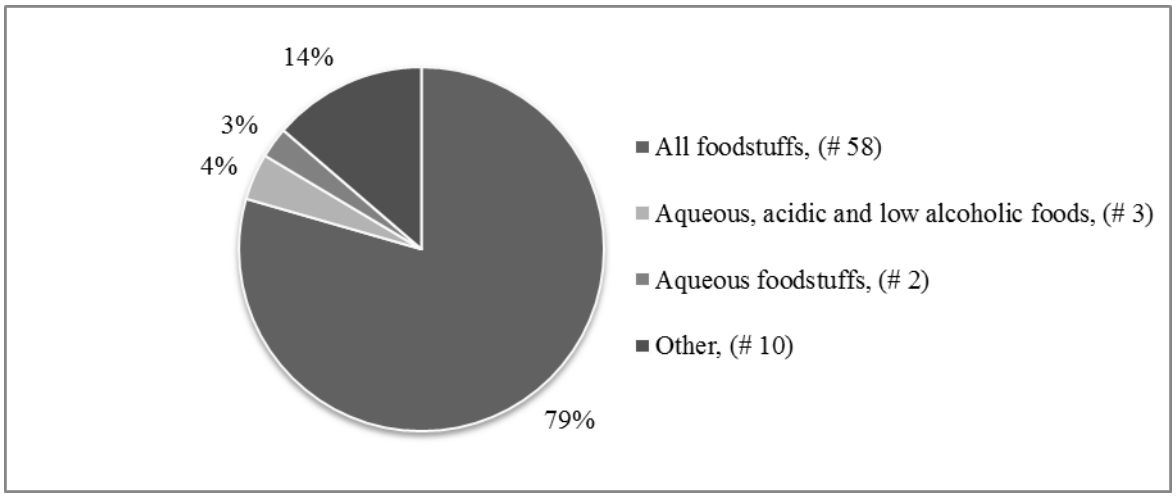

Figure 6: Overview of the intended contact food for the model substances (# 73)

Figure 6 illustrates that most of the substances can be used in contact with 'all foodstuffs', i.e. 58 out of 73 (79%), while the others are restricted to a limited number of foodstuffs like:

- Aqueous, acidic and low alcoholic food
- Aqueous, acidic and alcoholic food
- All foodstuffs packed in glass jars and bottles
- All foodstuffs, except beer and beverages
- Aqueous food
- Aqueous, acid and dairy food
- Aqueous foods, excluding acidic and alcoholic food
- All foodstuffs, excluding fatty, high alcoholic and dairy food
- Aqueous and dry foodstuffs containing no free fat at the surface
- Dry and aqueous food types
- Liquid food
- Fresh fruit

In Figure 7, the distribution between monomers and additives for each type of 'intended contact food' is provided, showing that both monomers and additives are present in each type of intended contact food. Consequently, a certain type of intended contact food cannot be correlated with only monomers or additives.

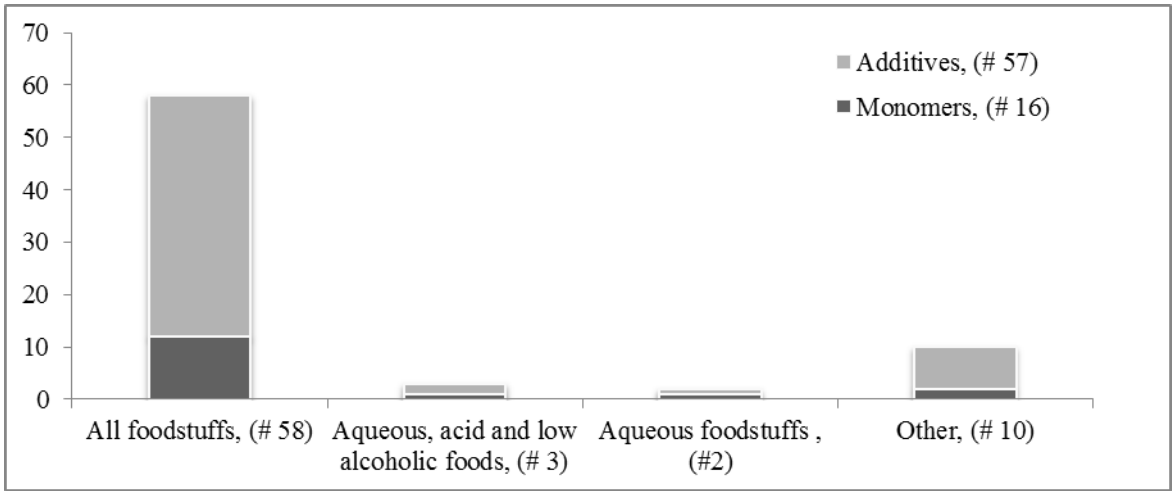

Figure 7: Overview of the intended contact food according to the technological function of the substances

1.2.4. Conclusion

A database was developed that structurally summarised all relevant information from the different data sources. The database contained, amongst others, information related to the type of food contact material, the technological function and the intended contact food. During the project, the database was first further supplemented with migration data (specific migration, overall migration, total mass transfer or modelling) and the available toxicological data, and afterwards used as a working tool.

2. INTERPRETATION OF THE RESTRICTIONS DEFINED BY THE CURRENT GUIDELINES

In the current guidelines, the restriction was derived from the toxicological data provided. The type and amount of toxicological data required was in its turn triggered by the migration data submitted by the applicant. Consequently, the interpretation of the restriction according to the current guidelines can be deduced from the migration and toxicological data provided.

2.1. Migration data

Different types of migration data can be present in the dossier of an FCM substance such as specific migration using simulants, overall migration, total mass transfer based on residual content or nominal amount and modelling using residual content or nominal amount. Migration data are not only required for the substance itself but also for its related migrants. A survey of the methodologies applied to acquire the migration data for the 73 model substances and their related migrants is given in Figure 8.

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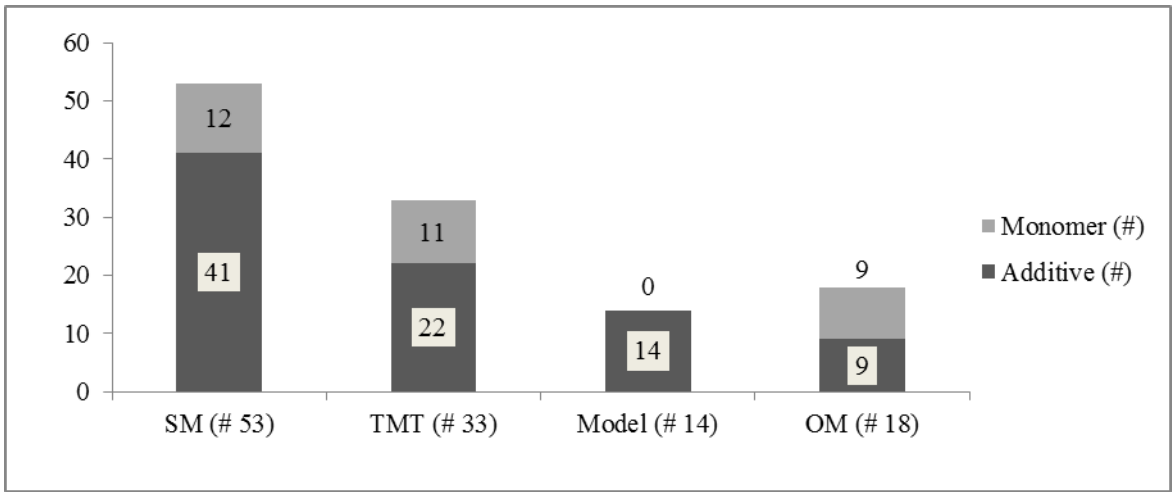

Figure 8: Overview of the methodology used to obtain migration data for the 73 model substances and their related migrants as a function of the technological function. For some substances and/or their related migrants, more than one methodology was used. SM: specific migration, TMT: total mass transfer calculation, Model: migration modelling and OM: overall migration.

It should be noted that in many dossiers different types of migration data were presented. This is further discussed in section 2.1.5.

2.1.1. Specific migration using simulants (SM)

In general, specific migration is requested to demonstrate worst case migration. The measurements for the 73 model substances and related migrants were carried out according to the specifications described in 'Council Directive 82/711/EEC laying down the basic rules necessary for testing migration of the components of plastic materials and articles intended to come into contact with foodstuffs' and in 'Council Directive 85/572/EEC laying down the list of simulants to be used for testing migration of constituents of plastic materials and articles intended to come into contact with foodstuffs'. It should be noted that migration experiments for new applications should be carried out using the food simulants and time/temperature conditions prescribed in EU Regulation 10/2011.

The following considerations should be taken into account when setting up a specific migration experiment:

- *Characteristics of the migrants in combination with the selected simulants*
  One of the most important considerations to be addressed is the solubility of the substance in the simulant. In general, the food simulant where the migrant has the highest solubility is considered to be the worst case and should be selected for further testing.
- *Test sample:*
  The test sample always represents the worst case situation. This means the highest concentration of the additive or monomer should be present in the test. Also, the thickness should represent the worst case, meaning the test sample should be selected at the highest intended layer thickness since this will have the highest migration potential. If the substance is used in different kinds of polymers, in principle, each type of polymer should be tested. However, if it is properly argued, only migration tests with the polymer representing the worst

case can be acceptable. For example, for an additive used in all types of polyolefins, tests with LDPE may be sufficient

- *Simulant:*
  The appropriate simulant should be selected, thereby covering the intended contact food. It should therefore be evaluated whether the simulant interacts with the FCM in a way that is representative for the intended application with foodstuffs. When simulant D2 (Olive oil) is replaced by a substitute simulant, the necessity of this replacement should clearly be described. Substitution of olive oil is only allowed in case of technical problems not for convenience only.
- *Time/Temperature conditions:*
  The selected conditions should cover the intended food contact applications and provide worst-case scenarios concerning time/temperature conditions.

As shown in **Figure 8**, specific migration data were used in the applications of 53 (out of 73) substances. An overview of the simulants used in these migration tests is given in Figure 9.

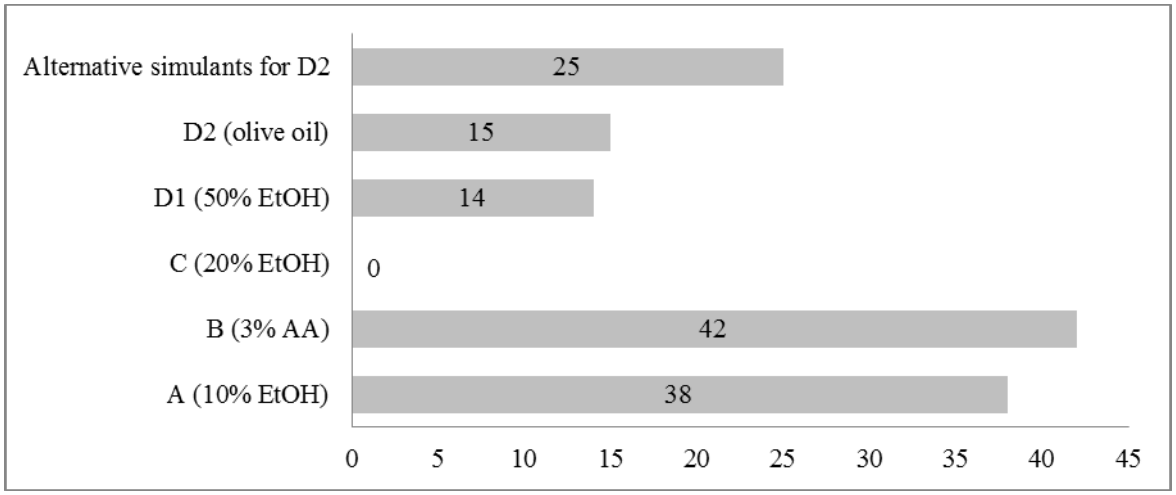

Figure 9: Overview of the simulants used for the determination of the specific migration.
Remark: 100% = 53 substances for which SM data are available.

In most applications, simulant A, B and D2 (or substitute simulants) were used for the determination of the specific migration, since it was described in Council Directive 82/711/EEC that the migration test should be performed in simulant A, B and D2 when the materials and articles were intended for contact with all types of food, as is the case for most of the 73 model substances (Figure 6).
Furthermore, it should be noted that the simulant C (20% EtOH) is never present, since this simulant did not yet exist according the previous Directive 82/711/EEC.
Interestingly, specific migration data using simulant D1 (50% EtOH) were only present for 14 substances. This is very import for the evaluation of the impact of the revised guidelines and will be explained more thoroughly further in the project (See section 4.1.1).

Although, most of the substances are covered, at least partially, by specific migration data, there are a number of exceptions where specific migration can be replaced by worst case calculation based on total mass transfer assumptions, modelling or overall migration.

2.1.2. Total mass transfer (TMT) calculations

Specific migration tests can be substituted by calculations of the maximum possible migration, thereby assuming total mass transfer of the substance from the FCM, for example when it is not possible to determine the specific migration of the additive or monomer due to e.g. instability of the substance in food simulants, or because a QM limit is more appropriate.

The data used for this calculation can originate from nominal or residual content of the substance in the FCM:

- *Nominal content (NC):*
  The nominal content of the substance is the amount of substance initially added to the polymerisation process.
- *Residual content (RC):*
  The residual content of the substance is the amount of substance that remains in the FCM after the polymerisation process. Therefore, the content of the substances in the polymer has to be determined by e.g. exhaustive extraction or dissolution of the polymer.

After determination of the nominal or the residual content of the substance in the FCM, a worst case migration calculation is carried out assuming 100% migration of the substance, i.e. total mass transfer. Due to the overestimation by this approach, if the calculation gives an acceptably low migration on first use, subsequent contacts in repeated use applications are covered too.

An advantage of the determination of the migration using total mass transfer is that the results can easily be extrapolated to any other food contact material made of the same polymer, with only one test that has to be performed.

For 32 out of the 73 model substances subject to the project, total mass transfer calculations were used. Residual or nominal contents were used to calculate total mass transfer. For one substance, total mass transfer data were based both on nominal and residual content (Figure 10).

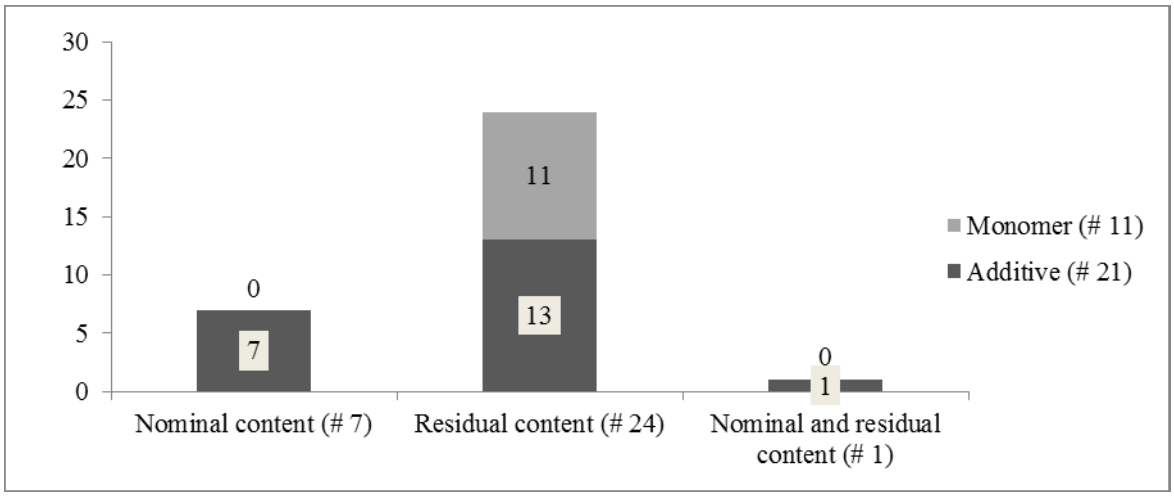

Figure 10: Number of substances with migration data obtained by TMT based on residual and/or nominal content.

Furthermore, the results in Figure 10 show that total mass transfer calculations for monomers are always based on the residual content of the monomer, since a monomer is a starting product that reacts during the polymerization process. Consequently, the residual concentration of the monomers will be much lower than the nominal concentration. For additives, both residual and nominal content are used for the calculations.

2.1.3. Migration modelling (Model)

Modelling of the migration into foods or simulants is also possible using a generally recognized diffusion model. This approach requires the same input as for the total mass transfer calculations: nominal or residual content of the substance of interest. For further guidance on migration modelling, EU Report EUR 24514 EN 2010 should be consulted.

In this project, modelling data were provided for 14 substances; all of them were additives. The repartition between nominal and residual content data used for the modelling is demonstrated in Figure 11.

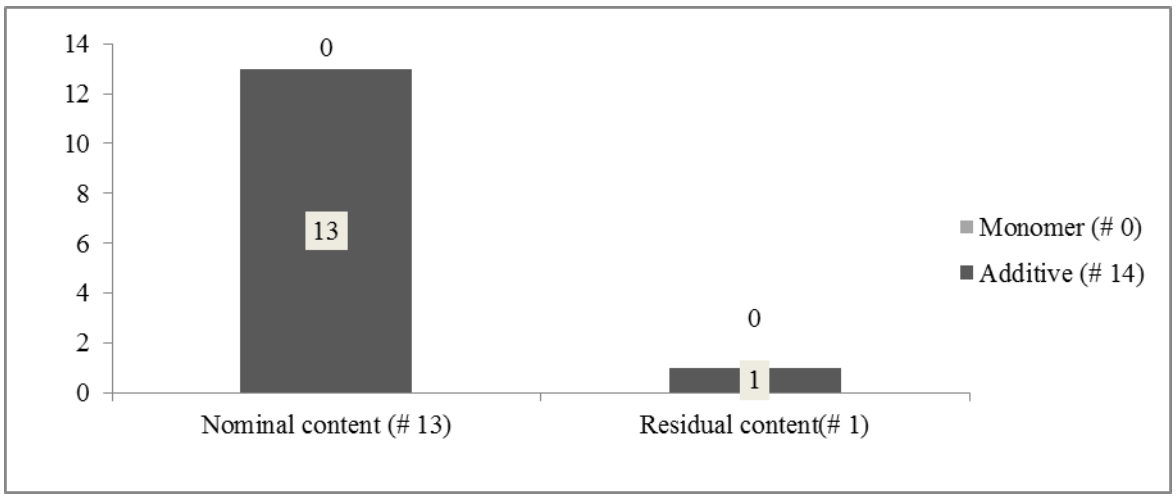

Figure 11: Number of substances with migration data obtained by Modelling based on residual or nominal content.

Figure 11 illustrates that modelling of the migration is mostly based on the nominal content. Only for one substance, the migration was modelled using the residual content. This is completely the opposite of the calculation of the migration using total mass transfer, where the input of the data was mostly coming from the residual content.

2.1.4. Overall migration (OM)

In cases where it is impossible to measure specific migration because of the properties of the substance, e.g. polymeric additives, the overall migration can be used to demonstrate worst case migration of the substance. Moreover, the CEF or AFC Panel may request overall migration data in specific cases, e.g. when larger amounts of oligomers are suspected. Overall migration is considered as an inertness parameter and will give useful information about the behaviour of the food contact material.

In 18 out of the 73 dossiers considered in the current project, overall migration data were available (**Figure 8**). However, overall migration was never used as a single technique to evaluate migration, but instead in combination with other types of migration tests. In most cases, overall migration was used to obtain an indication on the migration of the low molecular weight fraction. The obtained residue was afterwards used for the identification of the substances of the low molecular weight fraction.

2.1.5. Combination of methodologies to assess migration

For each substance and related migrants, at least one method was applied for the determination of the migration. An overview of the techniques used for each substance is given in Annex B.

For 38 out of the 73 model substances, only one type of migration data was used in the dossier of the substance, as is shown in Figure 12. Consequently, for approximately 50% of the substances (35 out of 73), more than one type of migration data was used in the application.

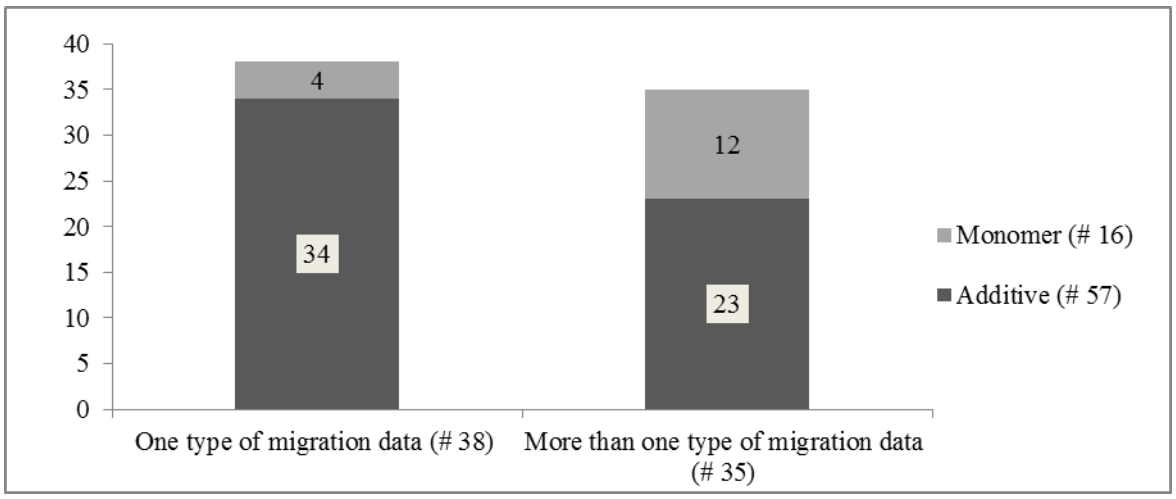

Figure 12: Overview of the number of substances for which only one or for which several methodologies were used to obtain migration data for the substance and related migrants.

Figure 12 clearly illustrates that additives are in general covered by one type of migration data, while most of the dossiers for monomers contained different types of migration data.

Substances covered by one type of migration data (# 38)

An overview of the number of dossiers which contained only one type of migration data for the substance and related migrants as a function of the methodology used, is given in Figure 13.

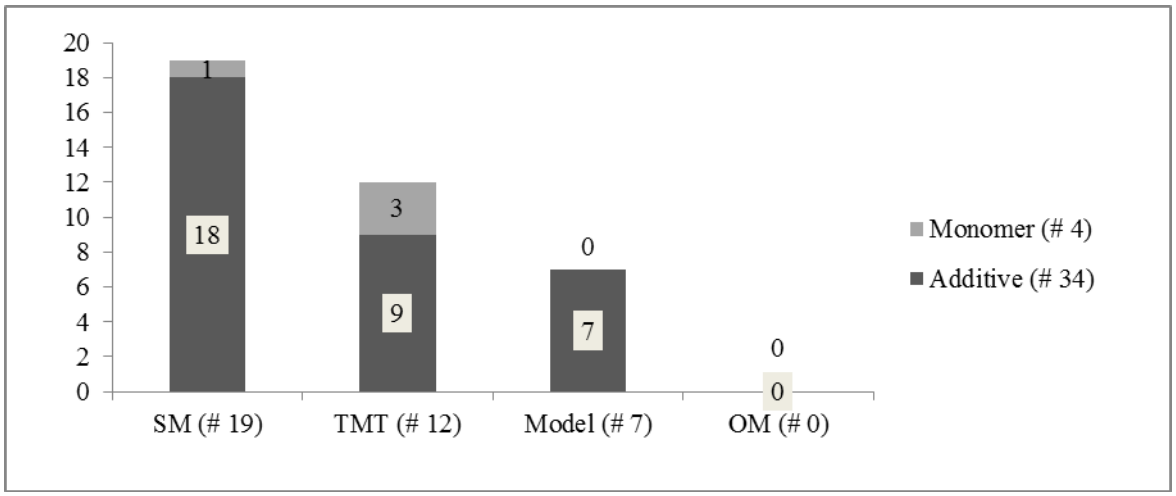

Figure 13: An overview of the number of substances which contained only one type of migration data for the substance and related migrants as a function of the methodology used (# 38).

These results show that for the substances covered by one type of migration data, specific migration was mostly used, followed by total mass transfer and modelling. As already mentioned, overall migration was never present as a single source of migration data, it was always present in combination with other types of migration data. It should also be noted that modelling was only applied for additives, and not for monomers.

Substances covered by more than one type of migration data (# 35)

In 35 out of the 73 (48%) dossiers, even more than one strategy for the determination of the migration was followed. This could have multiple goals;

- To obtain an indication on the migration of oligomers and other reaction/degradation products:
  Example: 2-Phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine (EFSA-Q-2009-834, FCM No 872)
  Specific migration is carried out for this substance. Furthermore, overall migration is executed to have an indication on the migration of the low molecular weight fraction. Afterwards, the migrants in this fraction were identified using LC-MS.
- Extension of use of the substance to all types of plastic:
  Example: Acids, fatty (C8-C22) from animal or vegetable fats and oil, esters with linear alcohols, aliphatic, monohydric, saturated, primary (C1-C22)' (EFSA-Q-2007-032, FCM No 879).
  In this case, specific migration is carried out for one type of plastic (for example PET). Afterwards, migration modelling is executed for the same plastic and other additional types of plastic (for example LDPE, PP, PS, PC, PVC). Since the same plastic is used for both specific migration and modelling, the obtained results will give an indication of the fitness for purpose of modelling. As a result, the use of the substance can be extended to all plastics.

2.1.6. Conclusion

For most of the 73 model substances and related migrants, specific migration data were provided by the applicant. Specific migration studies were often performed with simulants A, B and D2 (or its substitutes), whereas migration data for simulant D1 were only available for 14 substances. In case no specific migration data were available, total mass transfer or modelling was applied to estimate migration. While total mass transfer calculations were usually based on the residual content, data used for modelling were mostly based on the nominal content. Overall migration was never used as a single technique for the determination of the migration, but rather as an indication for the migration of the low molecular weight fraction.

2.2. Toxicological data

The toxicological information required for the evaluation was triggered by the migration values. Important to note is that toxicological requirements do not solely apply to the substances (and in case of mixtures, its constituents) themself but also to the transformation or reaction products and/or related impurities. Consequently, toxicological information on these impurities was also considered in the evaluation. In general, the core set of toxicological tests required for FCM substances and related migrants comprises genotoxicity studies, subchronic toxicity studies, studies on absorption, distribution, metabolism and excretion, studies on reproduction and developmental toxicity and studies on long-term toxicity/carcinogenicity. However, this core set of tests may be reduced depending on the migration data (Table 4).

Based on their migration results, discussed under 2.1, each of the 73 model substances was allocated to one of the three tiers. An overview of the repartition of the substances over the different tiers is shown in Figure 1.

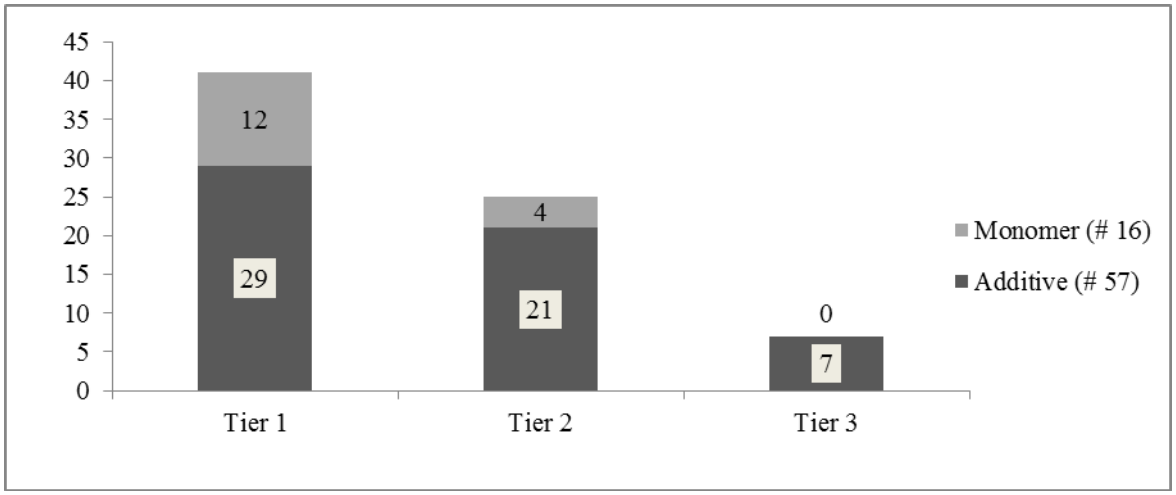

Figure 14: Allocation of the tier according to the current guidelines for the 73 model substances.

2.2.1. Toxicological data submitted for the substances allocated to Tier 3

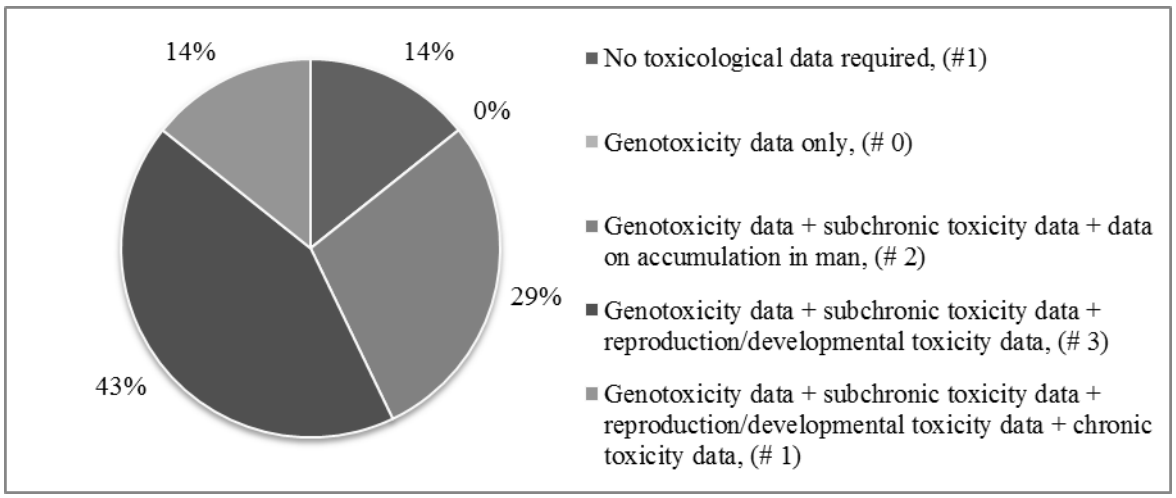

Figure 15: Type of toxicological information provided for substances classified in Tier 3 based on the migration data (# 7)

Seven out of the 73 model substances had migration values higher than 5 mg/kg and thus required the core set of toxicological tests (Figure 15). However, only for one of these seven substances, i.e. N,N-Bis(2-hydroxyethyl)dodecanamide (EFSA-Q-2009-591, FCM No 923), results of a chronic toxicity study were provided in addition to genotoxicity data, subchronic toxicity data and results from studies on absorption, distribution, metabolism and excretion. No data on reproductive or developmental toxicity of the substance were submitted by the applicant. Two potential impurities were also considered in the evaluation. No additional data were required for the thermal reaction product Monolauryl ester of N,N-Bis(2-hydroxyethyl)dodecanamdide which is expected to be hydrolysed in vivo in the parent substance and dodecanoic acid. The latter has been authorised without any restriction. However, for Diethanolamine (DELA), an impurity and thermal degradation product of the substance, genotoxicity data, results of a previous evaluation (genotoxicity data, subchronic toxicity data, data on reproductive and developmental toxicity and chronic toxicity data) were considered by the CEF Panel.

Three out of the seven substances with migration values higher than 5 mg/kg, i.e. Acids, Fatty (C8-C22), esters with pentaerythritol (EFSA-Q-2005-245, FCM No 880), Acids, Fatty (C8-C22), from animal or vegetable fats and oils, esters with branched alcohols, aliphatic, monohydric, saturated, primary (C3-C22) (EFSA-Q-2007-009, FCM No 878) and Acids, fatty (C8-C22) from animal or vegetable fats and oil, esters with linear alcohols, aliphatic, monohydric, saturated, primary (C1-C22) (EFSA-Q-2007-032, FCM No 879), were fatty acids which were expected to be efficiently cleaved in humans to their component alcohols and carboxylic acids. The absorption of esters of long chain alcohols including branched chains has reported to be poor and therefore, saturation of the involved enzymes is considered highly unlikely. Taking into account these considerations, chronic toxicity data or data on absorption, distribution, metabolism and excretion were not required for the evaluation of these three fatty acid substances. Data on genotoxity and subchronic toxicity studies were obtained from studies performed with reference compounds (and/or hydrolysis products) for each of these three substances. For two of the substances, data on developmental toxicity were also provided. In case of

the substance 'Acids, Fatty (C8-C22), from animal or vegetable fats and oils, esters with branched alcohols, aliphatic, monohydric, saturated, primary (C3-C22)', data on developmental toxicity were required as some branched chain aliphatic acids (2-propylpentanoic acid, 2-ethylhexanoic acid, 2-propylhexanoic acid) which can be formed as metabolites are teratogenic in rats and rabbits. For the substance, Acids, Fatty (C8-C22), esters with pentaerythritol (EFSA-Q-2005-245, FCM No 880), developmental toxicity data of a reference compound were available from a previous evaluation and therefore also considered by the CEF Panel.

One of the seven substances, i.e. Hydrogenated homopolymers and/or copolymers made of 1-hexene and/or 1-octene and/or 1-decene and/or 1-dodecene and/or 1-tetradecene (MW:440-12000) (EFSA-Q-2009-770, FCM No 789), had previously been evaluated for applications with lower migration values. Based on the toxicological information considered in the previous evaluation, more in particular the absence of toxicological effects in the repeated dose studies and the poor absorption of the test substance, the CEF Panel concluded that a migration up to 60 mg/kg does not raise safety concern. Consequently, no additional toxicological information was required.

For another one out of the seven substances, i.e. Acids, C2-C24, aliphatic, linear, monocarboxylic from natural oils and fats, lithium salts - EFSA-Q-2008-030, FCM No 801, no toxicological data were provided. However, this substance consisted of a mixture of authorised components, and consequently, additional toxicological information on the substance was not considered necessary.

Finally, for one out of the seven substances, i.e. Polyethylene, oxidized (EFSA-Q-2003-199, FCM No 811), genotoxicity data, subchronic toxicity data and reproductive and developmental toxicity data were provided. Data on absorption, metabolism, distribution and excretion were lacking. However, bioaccumulation in man of Polyethylene, oxidised was expected to be lower than that of the un-oxidised wax and therefore unlikely. Furthermore, no precipitation of oxidised polyethylene waxes in liver and lymph nodes was observed. In contrast, there was no clear reason to justify the absence of chronic toxicity data. Consequently, an additional safety factor was considered for the determination of the restriction (see 2.3).

2.2.2. Toxicological data submitted for the substances allocated to Tier 2

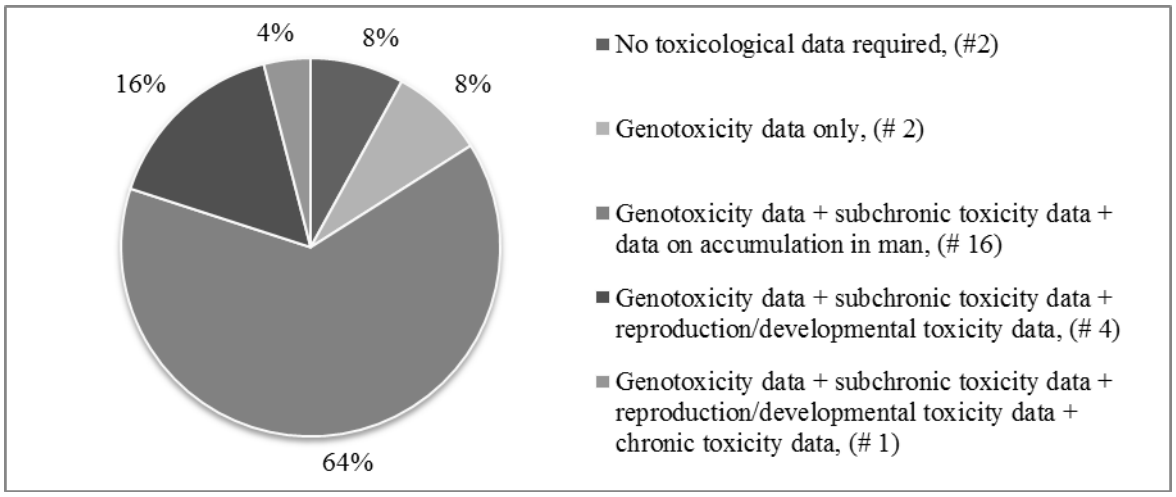

Figure 16: Type of toxicological information provided for substances classified in Tier 2 based on the migration data (# 25)

Fifteen out of the twenty five substances had migration values for the substance higher than 0.05 mg/kg but lower than or equal to 5 mg/kg. These substances thus required results of a reduced core set of toxicological tests including genotoxicity data combined with data from subchronic toxicity studies and data on the absence of a potential for accumulation in man. In case the substances could contain impurities, the required toxicological data concerning these impurities were also considered in the evaluation. For eleven out of the fifteen substances, the provided toxicological information was in accordance with the toxicological requirements. However, for four out of the fifteen substances, genotoxicity data, results of subchronic toxicity studies and data on accumulation in man were complemented with results of reproductive and/or developmental toxicity studies. In case of the substance Neopentyl glycol, mixed diesters with benzoic acid and 2-ethylhexanoic acid (EFSA-Q-2007-006, FCM No 810), results of reproductive and developmental toxicity studies with the substance were provided due to the reported embryotoxic effects of the potential impurity 2-ethylhexanoic acid. For two other substances, data on reproductive toxicity studies were considered in the evaluation as they were available in literature for one of the reference compounds of the substance (Sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salt – EFSA-Q-2005-151, FCM No 813) or for compounds structurally similar to the substance (Thiodipropionic acid, ditetradecyl ester - EFSA-Q-2010-935, FCM No 894). The fourth substance for which data on reproductive and developmental toxicity were considered in the evaluation was Phosphorous acid, mixed 2,4-bis(1,1-dimethylpropyl)phenyl and 4-(1,1-dimethylpropyl-phenyl) triesters [(RO)3P] (EFSA-Q-2010-779, FCM No 974). However, these data did not concern the substance itself but its potential impurity, 4-t-amylphenol, which had previously been evaluated.

For all fifteen substances, data to demonstrate the absence of a potential for accumulation in man were also required. Normally, a log Po/w value below 3 is considered to be sufficient evidence for the lack of accumulative potential in the mammalian body, unless special considerations give cause for concern. Four out of the 15 substances had a log Po/w value below 3. For two of these substances with a log Po/w value close to 3, i.e. Sulphosuccinic acid, mono-alkyl (C10-C16) polyethyleneglycol esters, sodium salt (EFSA-Q-2006-324, FCM No 814) and 1.3.5-tris(2,2-dimethylpropanamido)benzene

(EFSA-Q-2012-695, FCM No 784), hydrolysis of the substance was taken into account to conclude that there was no concern for accumulation. Eight out of the fifteen substances had a log Po/w value equal to or higher than 3. These values are not a proof of accumulation of the substance as a substance may not be absorbed or be metabolised to substances with no accumulation potential. For six of these substances, evidence for absence of an accumulative potential was provided. For two of the eight substances, an ADME study was performed, i.e. N,N',N''-Tris(2-methylcyclohexyl)-1,2,3-propane-tricarboxamide (EFSA-Q-2008-698, FCM No 870) and 2,4-Bis(2,4-dimethylphenyl)-6-(2-hydroxy-4-n-octyloxyphenyl)-1,3,5-triazine (EFSA-Q-2009-768, FCM No 452), whereas read-across with results of an ADME study with a structurally related substance was applied for two other substances, i.e. Phosphorous acid, mixed 2,4-bis(1,1-dimethylpropyl)phenyl and 4-(1,1-dimethylpropyl-phenyl) triesters [(RO)3P] (EFSA-Q-2010-779, FCM No 974) and Thiodipropionic acid, ditetradecyl ester (EFSA-Q-2010-935, FCM No 894). In case of the substances Bis(4-propylbenzylidene)propylsorbitol (EFSA-Q-2007-023, FCM No 808) and Sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salt (EFSA-Q-2005-151), hydrolysis was taken into account to conclude that there was no accumulative potential. For two of the subtances with a log Po/w value equal to or higher than 3, no further information was provided demonstrating the absence of a potential for accumulation in man. However, in case of the substance alpha-Alkenes(C20-C24) maleic anhydride-4-amino-2,2,6,6-tetramethylpiperidine, polymer (EFSA-Q-2006-171, FCM No 803), all migration values were below 0.05 µg/kg food except the one in 10% ethanol which was higher than 0.05 mg/kg food but lower than or equal to 5 µg/kg food. The applicant therefore provided genotoxicity data and the results of a 90 day subchronic toxicity study. Due to the instability of the substance in simulant A (10% EtOH), the restricted use of this substance was further restricted during the evaluation to 'not to be used for alcoholic foodstuffs'. As the other migration values were below 0.05 mg/kg food, no data on the potential for accumulation had to be considered. For the remaining substance with a log Po/w value equal to or higher than 3, i.e. 3,9-Bis[2-(3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propionyloxy) -1,1-dimethylethyl]-2,4,8,10-tetraoxaspiro[5,5]undecane (EFSA-Q-2009-769, FCM No 858), there was no clear reason to justify the absence of data on the potential for accumulation in man. The lack of these data was taken into account for the determination of the restriction (see Task 4). For three substances, no log Po/w values were provided. One of these three substances, i.e. Alcohols C12-C14 Secondary. Beta.-(2hydroxyethyoxy)-ethoxylated (EFSA-Q-2006-315, FCM No 802), did not raise a concern for accumulation based on its high solubility in water. For the substance Trimethylolpropane, mixed triesters and diesters with benzoic acid and 2-ethyl hexanoic acid (EFSA-Q-2007-007, FCM No 815), the possible risk of accumulation in man of the tested substance was also considered. Since the substance is intended to be used only for aqueous foods, where only the hydrophilic components of the mixture are migrating, accumulation was not considered to be a safety issue. Although not specifically stated in the evaluation, the same rationale was probably also used for the substance Neopentyl glycol, mixed diesters with benzoic acid and 2-ethylhexanoic acid (EFSA-Q-2007-006, FCM No 810).

For one substance of the twenty five substances, i.e. Sodium borohydride used in conjunction with palladium acetate (EFSA-Q-2011-067, FCM No 981), data on the two most important constituents (palladium and boron) were used for the evaluation. The migration values for boron were between 0.05 and 5 mg/kg and those of palladium below 0.05 mg/kg. Nevertheless, for both substances, genotoxicity data, subchronic toxicity data, data on reproduction/developmental toxicity and chronic

toxicity data were considered in the evaluation since these data were available from previous evaluations.

One of the twenty five substances with migration values higher than 0.05 mg/kg and below or equal to 5 mg/kg was Copper hydroxide phosphate (EFSA-Q-2010-708, FCM No 972). For this substance, however, no additional toxicological data had to be provided as the substance is readily hydrolysed in components that have been toxicologically evaluated.

In addition to these seventeen substances, there were six substances with migration values below 0.05 mg/kg food but which contained potential impurities with migration values higher than 0.05 mg/kg but lower than or equal to 5 mg/kg. For five of these substances, it was the migration of the low molecular weight fraction that exceeded 0.05 mg/kg and thus data on genotoxicity, subchronic toxicity and the absence of a potential for accumulation in man had to be provided. Three of the substances were monomers, i.e. 2,2,4,4-tetramethyl-cyclobutane-1,3-diol (TMCD) (EFSA-Q-2008-202, FCM No 881), 1,4-Cyclohexanedicarboxylic acid (CHDA) (EFSA-Q-2008-298, FCM No 806) and 2-Hydroxypropyl methacrylate (HPMA) (EFSA-Q-2011-1239, FCM No 995). For all three substances, results of genotoxicity tests with the monomer but not with the low molecular weight oligomeric fraction were submitted by the applicant. However, data on monomers are generally considered to apply also for the low molecular weight oligomeric fraction as they often have the same structural elements and functional groups and, therefore, the same toxicological profile. Within this context, subchronic toxicity data for the substances TMCD and CHDA were derived from the 90 day study with the monomer. For the substance TMCD, data on developmental toxicity of TMCD were also submitted by the applicant probably because the substance was intended to be used, amongst others, for the manufacture of baby bottles. For the substance HPMA, data on subchronic toxicity of the low molecular weight oligomeric fraction were obtained by applying read across with data from the previously evaluated structurally related oligomeric fraction with MW below 1000 Da of the polymeric additive 2,3-epoxypropyl methacrylate copolymer. All three monomers had Log Po/w values below 3 and consequently these substances did not have a potential for accumulation in man. Nevertheless, results of an ADME study were provided for TMCD. The two other substances for which the low molecular weight fraction exceeded 0.05 mg/kg food were polymers. i.e. Poly(12-hydroxystearic acid) stearate (EFSA-Q-2004-040, FCM No 875) and Poly(12-hydroxystearic acid)-polyethyleneimine copolymer (EFSA-Q-2010-1244, FCM No 812), the latter being a copolymer of the first substance. Poly(12-hydroxystearic acid) stearate is a polymer of authorised monomers, i.e. 12-hydroxystearic acid and stearic acid, which are both non-genotoxic and were classified by SCF in List 3 with no specific restriction and in List 1 with an ADI “not specified”, respectively. Consequently, no additional toxicological information was required for the low molecular weight fraction of this substance. Poly(12-hydroxystearic acid)-polyethyleneimine copolymer is a copolymer of the previously described polymer and polyethyleneimine which is predicted to be non-genotoxic. As only the migration of the PHSA low molecular weight fraction exceeded 0.05 mg/kg, no additional toxicological information was required. In addition to these seven substances, there was one substance, i.e. 3,3’,5,5’-tetrakis(tert-butyl) -2,2’-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propyl]oxy phosphonous acid (EFSA-Q-2008-678, FCM No.792), for which the migration values of the oxidation product NP-2018 exceeded 0.05 mg/kg. and consequently genotoxicity data, subchronic toxicity data and data on the absence of a potential for

accumulation in man, had to be provided for NP-2018. As the results of an ADME study indicated that the toxicity of NP-2018 was covered by tests with the mother substance, subchronic toxicity data for NP-2018 could be derived from the 90 day study with the mother substance. Genotoxicity tests were performed with NP-2018 itself.

One substance, i.e. sodium carbonate peroxyhydrate, bentonite, sodium chloride, sodium carbonate (Oxyfresh) (EFSA-Q-2011-236, FCM No 1009), had an overall migration value higher than 5 mg/kg. However, for the toxicological evaluation only data on H_2O_2 were considered relevant as this is the only substance that may be released. The migration values of H_2O_2 were higher than 0.05 mg/kg but lower than or equal than 5 mg/kg and therefore genotoxicity data and subchronic toxicity data were provided. No specific data on the absence for a potential of accumulation in man were provided. However, considering the nature of H_2O_2 there is no concern for an accumulative potential.

Finally, for one substance, i.e. N-(2,6-Diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy] -1H-benzo[de]isoquinoline-1,3(2)-dione (EFSA-Q-2007-199, FCM No. 809) with migration values higher than 0.05 mg/kg food, only genotoxicity data were provided whereas also the results of a 90 day subchronic toxicity study and data on the absence of the potential for accumulation in man were required. The absence of this information in the dossier of the substance was taken into account during the evaluation (see 2.3).

2.2.3. Toxicological data submitted for the substances allocated to Tier 1

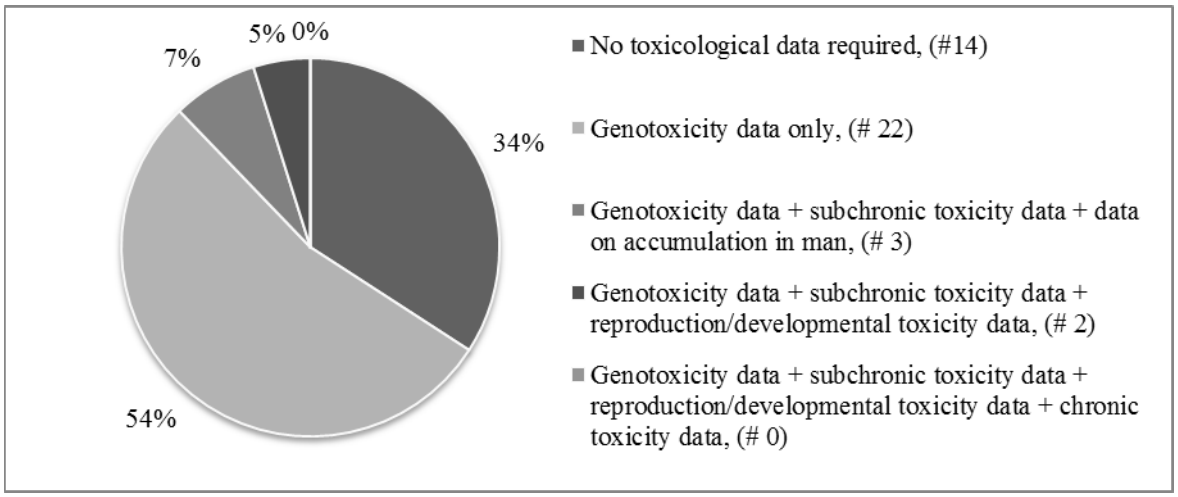

Figure 17: Type of toxicological information provided for substances classified in Tier 1 based on the migration data (# 41)

Forty-one out of the seventy-three substances had migration values lower than 0.05 mg/kg food and consequently, genotoxicity data were considered sufficient.

For twenty of the forty-one substances, the toxicological information was indeed limited to the results of genotoxicity tests. In case the substances could contain impurities, the required toxicological data concerning these impurities were also considered in the evaluation.

For five out of the forty-one substances, not only genotoxicity data but also other toxicological information was provided. Several reasons can be listed for these additional toxicological data. In some cases, the applicant improved the production process during the evaluation procedure, resulting in lower migration values. For the polyaddition product of glycidyl methacrylate with acrylic acid and/or methacrylic acid, esters with alcohols (C1-C4) aliphatic, monohydroxy, saturated (EFSA-Q-2006-203, FCM No 958) for example, genotoxicity data and the results of a 90 day subchronic toxicity study were submitted by the applicant as the migration of the oligomeric fraction was initially between 0.05 and 5 mg/kg food. However, the applicant was able to improve the production process, leading to a decrease in migration with values below 0.05 mg/kg food. Consequently, genotoxicity data on the low molecular weight oligomeric fraction of the substance (and its chlorinated form) were sufficient for the evaluation. A similar rationale can explain why for the substance Alkyl(C10-C21)sulphonic acid, esters with phenols (EFSA-Q-2009-733, FCM No 884), read-across with the results of an ADME study of a structurally related compound was applied and the results of a 90 day subchronic toxicity study with the substance were provided by the applicant. Indeed, the migration values initially exceeded the level of 0.05 mg/kg. In addition, the results of reproductive and developmental toxicity studies were provided, but the reason why these data were submitted remains unclear to us and therefore we would like to discuss this further with EFSA. In case of 3H-Perfluoro-3-[(3-methoxy-propoxy)propanoic acid], ammonium salt (EFSA-Q-2010-1216, FCM No. 896), additional data were probably provided as this substance is a perfluorocompound with a potential for accumulation in man. Two other substances, glycolic acid (EFSA-Q-2010-1090, FCM No 794) and 1,4:3,6-Dianhydrosorbitol (EFSA-Q-2011-769, FCM No. 364) had previously been evaluated, and therefore the available data were also considered in the current evaluation.

For fourteen out of the forty-one substances, no toxicological data were provided. Ten of these substances were polymers composed of authorised monomers. For polymeric additives, a distinction should be made between polymeric additives with a weight averaged molecular mass below 1000 Da and those with a molecular mass above 1000 Da as only the fraction with molecular mass below 1000 Da is regarded as toxicologically relevant. For those polymeric additives with a molecular mass above 1000 Da, a reduced set of data may be required based on the data available for the monomers involved, the size of the fraction with molecular masses below 1000 Da and the proportion of the additive in the plastic. In case migration of the low molecular weight fraction is low, genotoxicity data may be sufficient. However, by applying read-across of the polymeric substance with the authorised non-genotoxic monomers, it can be considered that the low molecular weight fraction of the polymeric substance is not genotoxic either and thus no additional genotoxicity data are required. Other substances for which no toxicological data were required include substances that have previously been evaluated (1,2-benzisothiazol-3(2H)-one 1,1 dioxide, sodium salt(saccharin) - EFSA-Q-2011-970, FCM No 902 and malic acid - EFSA-Q-2007-182, FCM No 499) or that are readily hydrolysed in components that have been toxicologically evaluated (Silver Zeolite A - EFSA-Q-2009-708, FCM No 946). Finally, one of the substances for which no toxicological data were required was a nanoparticle for which no migration was expected (Titanium nitride, nanoparticles - EFSA-Q-2011-1079, FCM No 807).

Finally, for two monomers with migration data below 0.05 mg/kg, i.e. 3-Methyl-1,5-pentanediol (EFSA-Q-2007-077, FCM No 883) and Trimethyl trimellitate (EFSA-Q-2010-838, FCM No 971), the

migration of the low molecular weight fraction exceeded 0.05 mg/kg. Consequently, data on genotoxicity, subchronic toxicity and the absence of a potential for accumulation in man had to be provided. However, no subchronic toxicity data were provided as the applicant indicated that the migration of the low molecular weight oligomeric fraction would probably be lower than 0.05 mg/kg. Genotoxicity data were considered sufficient by the CEF Panel, but the absence of the subchronic toxicity data was taken into consideration when the restriction of these substances was set (see 2.3).

2.2.4. Conclusion

Most substances and there related migrants were allocated to Tier 1, followed by Tier 2. Only seven out of the 73 model substances, all additives, were classified as Tier 3. Only for one substance classified in Tier 3, chronic toxicity data were available. However, for all but one of the other substances, i.e. Polyethylene, oxidized (EFSA-Q-2003-199, FCM No 811), the lack of the chronic toxicity data could be justified.

For most of the substances classified in Tier 1 and Tier 2, the toxicological data provided were in accordance with the toxicological requirements. In case more or less data were available, the rationale behind this deviation was clarified. However, for two substances, i.e. N-(2,6-Diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-1H-benzo[de]isoquinoline-1, 3(2)-dione (EFSA-Q-2007-199, FCM No. 809) and 3,9-Bis[2-(3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propionyloxy)-1,1-dimethylethyl]-2,4,8,10-tetraoxaspiro[5,5]undecane (EFSA-Q-2009-769, FCM No 858), the toxicological data submitted by the applicant were considered insufficient.

For 17 out of the 73 model substances, no toxicological data were required. Most of these substances were polymeric additives, classified in Tier 1. For these polymeric substances, no toxicological data were required as read-across could be applied between the low molecular weight fraction of these polymers and the authorised non-genotoxic monomers. Other substances for which no toxicological data were required included substances that had previously been evaluated or that readily hydrolyse in components that have been toxicologically evaluated, and substances for which no migration is expected.

2.3. Interpretation of the restriction

In general, two groups of substances could be distinguished based on the type of restriction: substances covered by a specific or generic migration limit and substances covered by a restricted use. An overview of the restrictions of the seventy-three substances is provided in Figure 18.

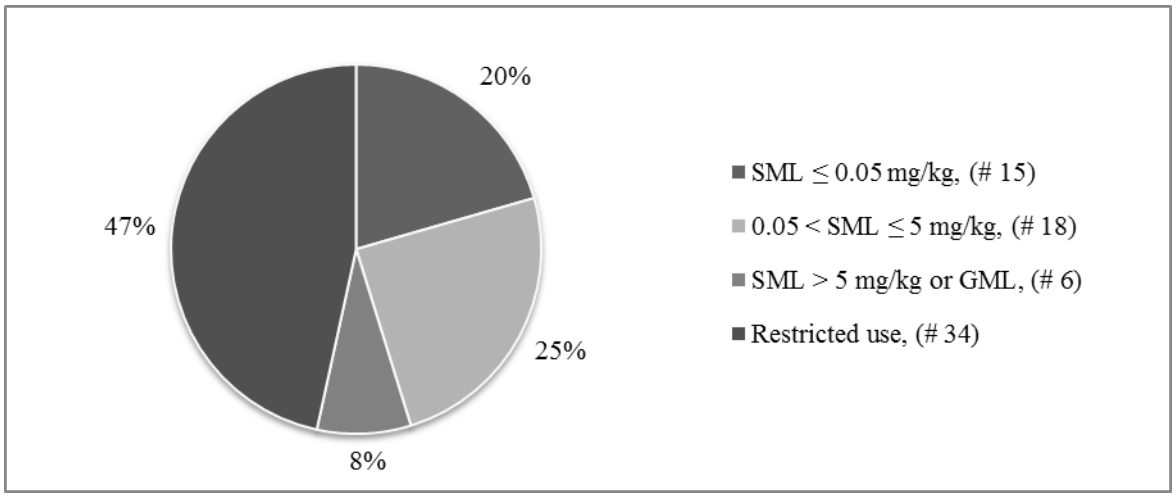

Figure 18: Overview of the restrictions of the substances according to the current guidelines (# 73)

Thirty-nine out of the 73 model substances (43%) were restricted by a migration limit. Substances with a migration limit can be divided in those covered by a specific migration limit (SML) and those covered by the generic migration limit (GML). Based on the value of the SML, these substances can be further subdivided in three categories: (i) substances with an SML lower than or equal to 0.05 mg/kg (15 out of 73 or 20%) (ii) substances with an SML higher than 0.05 and lower than or equal to 5 mg/kg (18 out of 73 or 25%) and (iii) substances with an SML higher than 5 mg/kg (1 out of 73 or 1%). Five of the 73 model substances were not covered by an SML but only needed to be compliant with the GML of 60 mg/kg (according to EU Reg. 10/2011). These substances were also included in the group of substances with an SML higher than 5 mg/kg. For thirty-four of the 73 model substances (47%), no migration limit was set but instead the use of these substances was restricted. Different types of restrictions can be distinguished:

- Restrictions excluding certain types of food
  Example: alpha-Alkenes(C20-C24) maleic anhydride-4-amino-2,2,6,6-tetramethylpiperidine, polymer (EFSA-Q-2006-171, FCM No 803)
  This substance is not authorised to be used for articles in contact with fatty foods for which simulant D is laid down and for articles in contact with alcoholic foods.
- Restrictions on the concentration used
  Example: Malic acid (EFSA-Q-2007-182, FCM No 499)
  In case of use as a monomer, this substance can only be used as a co-monomer in aliphatic polyesters up to max level of 1% on a molar basis.
- Restrictions on the type of plastic
  Example: N-(2,6-Diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-1H-benzo[de]isoquinoline-1,3(2H)-dione (EFSA-Q-2007-199, FCM No 809)
  The use of this substance is only authorised for PET.

For some substances, the CEF/ACF Panel has set both an SML and a restricted use. For example, 3-Methyl-1,5-pentanediol (EFSA-Q-2007-077, FCM No 815) has an SML of 0.05 mg/kg and, in addition, the use of this substance is restricted to materials in contact with food at a surface to mass

ratio of 0.5 dm²/kg. Figure 19 demonstrates the distribution of the number of substances covered by an SML with and without an additional restricted use in function of the category of SML.

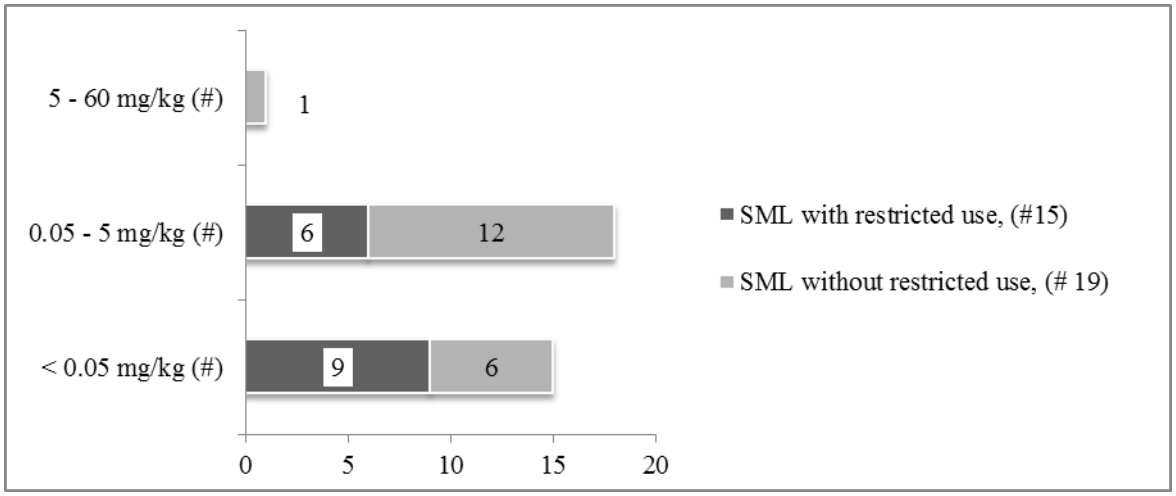

Figure 19: Distribution of the number of substances covered by a specific migration limit (SML) (#34) with and without an additional restriction regarding the use in function of the category of SML

Figure 19 illustrates that the two categories 'substances with an SML lower than or equal to 0.05 mg/kg' and 'substances with an SML higher than 0.05 and lower than or equal to 5', both contained comparable numbers of substances with and without additional restricted use. Most of these restrictions are related to the exclusion of certain types of food like fatty food or alcoholic foods. Other restrictions were related to surface to volume ratio or the prohibition of a repeatable use. This is in contrast to the substances only covered by a restricted use, where the restrictions were mostly based on the type of polymer used for the evaluation of the substance. The one substance in the category of the highest SML (5-60 mg/kg) did not have an additional restricted use.

Figure 20 and Figure 21 illustrate the distribution of the substances covered by restricted use (#34) as a function of the intended use and the technological function, respectively.

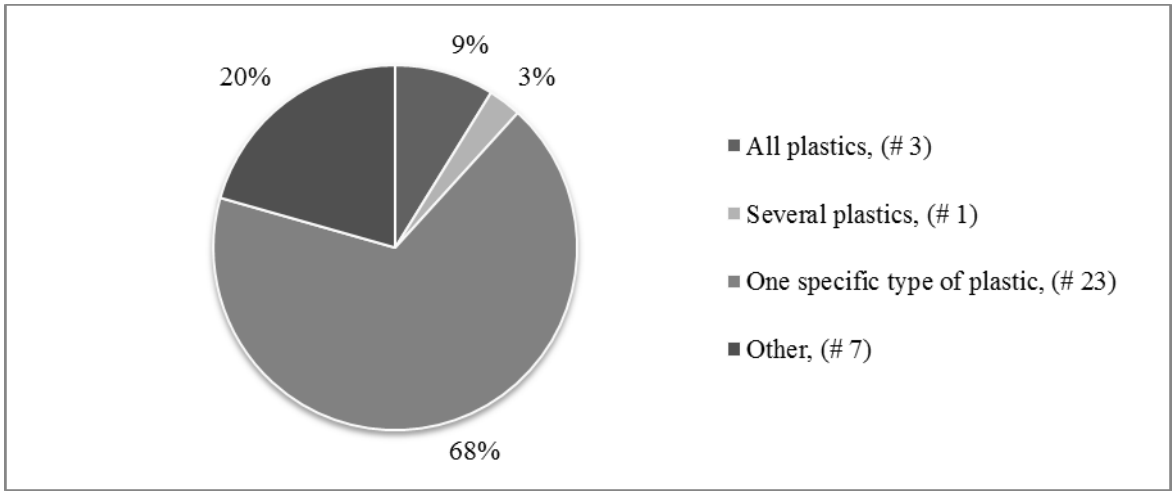

Figure 20: Repartition of the substances with restricted use (# 34) according to the intended use of the substances

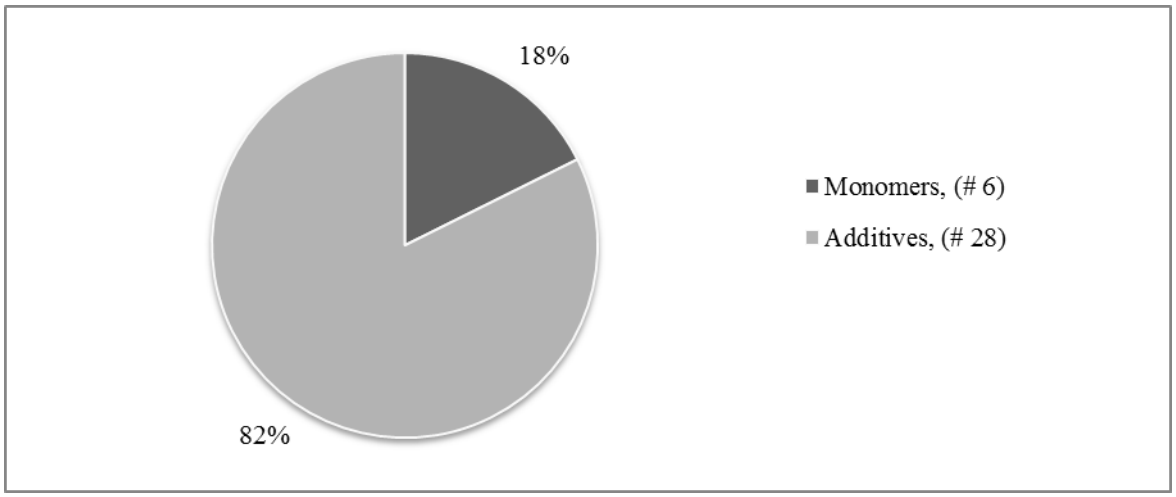

Figure 21: Repartition of the substances with restricted use (# 34) according to technological function

2.3.1. Substances covered by a migration limit

Substances covered by SML ≤ 0.05 mg/kg

Fifteen out of the 73 model substances had a specific migration limit of 0.05 mg/kg.
Twelve of these substances were classified in Tier 1 based on their migration data, and thus only genotoxicity data had to be provided. For ten of the substances, the toxicological information submitted by the applicant was indeed limited to the results of genotoxicity tests. No genotoxic effects were reported for any of these substances, and consequently all ten substances received a specific migration limit of 0.05 mg/kg. For Silver Zeolite A (EFSA-Q-2009-708, FCM No. 946) no toxicological data were provided by the applicant. Based on previous evaluations of silver, it was however considered that setting a restriction of 0.05 mg/kg would limit intake of silver to less than 13% of the human NOAEL (under the assumption that each day a kg of food is consumed containing silver at the restriction limit). Consequently, the CEF Panel concluded there would be no toxicological concern for the substance with a restriction of 0.05 mg/kg. For the substance Alkyl(C10-C21) sulphonic acid, esters with phenols (EFSA-Q-2009-733, FCM No. 884), data on subchronic toxicity and the results of an ADME study were provided supplementary to the results of genotoxicity tests, although the migration value was below 0.05 mg/kg. Some of these data were obtained from a previous evaluation whereas other data were derived from newly performed studies. The reason why these additional data were available, is unclear to us as the SML was also set at 0.05 mg/kg and therefore we would like to discuss this further with EFSA.

Two of the substances (i.e. N-(2,6-Diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy] -1H-benzo[de]isoquinoline-1,3(2)-dione (EFSA-Q-2007-199, FCM No. 809) and 3,9-Bis [2-(3-(3-tert-butyl-4-hydroxy-5-methylphenyl)(propionyloxy)-1,1-dimethylethyl]-2,4,8,10-tetraoxaspir o[5,5]undecane) (EFSA-Q-2009-769, FCM No. 858) had migration values between 0.05 and 5 mg/kg and required more detailed toxicological data than only genotoxicity data. In case of N-(2,6-Diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-1H-benzo[de]isoquinoline-1,3(2

H)-dione, only results of genotoxicity tests were provided. Consequently, the specific migration limit was set at 0.05 mg/kg. For 3,9-Bis[2-(3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propionyloxy) -1,1-dimethylethyl]-2,4,8,10-tetraoxaspiro[5,5]undecane, results of a 90d study were available. However, a relatively low NOAEL value (i.e. 8 mg/kg bw/day) was obtained in this study. Moreover, the lack of data demonstrating the absence of a potential for accumulation of this highly lipophilic substance, probably explains why the SML was set at 0.05 mg/kg.

In addition to these fourteen substances, there was one substance, i.e. 1,3-bis(isocyanatomethyl) benzene (EFSA-Q-2012-062, FCM No 988) for which the fixed SML of 0.05 mg/kg did not apply to the substance itself but to its hydrolysis product 1,3-benzenedimethanamine. This is related to the immediate and complete hydrolysis of the substance in water and gastric fluid simulant with formation of 1,3-benzenedimethanamine. The migration value of the hydrolysis product was below 0.05 mg/kg and therefore only genotoxicity data had to be provided. As the substance was non-genotoxic, the SML for the hydrolysis product was set at 0.05 mg/kg.

Seven of the substances with an SML of 0.05 mg/kg were monomers and 8 were additives. In addition to an SML, eight substances –both monomers and additives – received a restricted use.

Substances covered by 0.05 mg/kg < SML ≤ 5 mg/kg

Eighteen substances received an SML higher than 0.05 mg/kg but lower than or equal to 5 mg/kg. Fourteen of these substances were classified in Tier 2 based on migration data and thus genotoxicity data, results of a 90 day subchronic toxicity study and data on the absence of the potential for accumulation in man had to be provided. For thirteen of these substances, the toxicological information provided allowed to set the SML value at 5 mg/kg. The substance phosphorous acid, mixed 2,4-bis(1,1-dimethylpropyl)phenyl and 4-(1,1-dimethylpropyl-phenyl) triesters [(RO)3P] (EFSA-Q-2010-779, FCM No.974) received a supplementary SML (i.e. 0.05 mg/kg) for the hydrolysis product 2,4-di-t-amylphenol which may also be present as an impurity. For one of the twelve substances, i.e. sulphosuccinic acid, mono-alkyl (C10-C16) polyethyleneglycol esters, sodium salt (EFSA-Q-2006-324, FCM No. 814), the SML was however not set at 5 mg/kg but at 2 mg/kg as this SML had previously been fixed for its hydrolysis product, polyethyleneglycol (EO = 1-50) ethers of linear and branched C8 - C22 alcohols.

One out of 18 substances, i.e. N,N-Bis(2-hydroxyethyl)dodecanamide (EFSA-Q-2009-591, FCM No. 923), had migration values above 5 mg/kg and thus required the core set of toxicological data. In addition to genotoxicity data, results of a 90 day subchronic toxicity study and ADME data, the results of a dermal chronic toxicity/oncogenicity study were provided. In female mice, there was some evidence of carcinogenicity based on a not dose-related increased incidence of hepatocellular adenomas and carcinomas. This was attributed to the presence of 5% of diethanolamine (DELA) in the sample tested which may induce an oncogenic effect through a non-genotoxic mode of action. Consequently, the substance received an SML of 5 mg/kg with an additional SML (i.e. 0.3 mg/kg) for the potential impurity, DELA.

Two of the 18 substances had migration values below 0.05 mg/kg and were thus expected to have an SML of 0.05 mg/kg instead of 5 mg/kg. Both substances however contained impurities, oxidation

products or low molecular weight fractions for which the migration values exceeded 0.05 mg/kg. For 2,2,4,4-tetramethyl- cyclobutane-1,3-diol (TMCD) (EFSA-Q-2008-202, FCM No. 881), the migration of the oligomeric fraction was estimated to be between 0.05 mg/kg and 5 mg/kg. The applicant therefore provided not only genotoxicity data, but also the results of the subchronic 90 day study and data on the absence of a potential for accumulation in man for TMCD. The data obtained for the monomer are considered to apply also for the oligomeric fraction as they often have the same structural elements and functional groups and, therefore, the same toxicological profile. Based on the NOAEL value obtained in the 90 day study, the TDI of TMCD was estimated to be high enough to set an SML of 5 mg/kg for the substance. The CEF Panel noted however that Good Manufacturing Practices would keep migration in all cases well below 0.05 mg/kg. For the other substance 3,3',5,5'-tetrakis(tert-butyl)-2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propyl]oxy phosphonous acid (EFSA-Q-2008-678, FCM No.792), a subchronic 90 day study and an ADME study were performed to investigate the potential toxicity of the oxidation product NP-2018, which had migration values between 0.05 and 5 mg/kg. Results of the ADME study indicated that the toxicity of NP-2018 was indeed covered by the 90 day study with the substance. Based on the NOAEL value obtained in the 90 day study, the TDI of the substance was estimated to be high enough to set an SML of 5 mg/kg for the substance. This SML however applies not only to the substance but to the sum of phosphite and phosphate form of the substance and the hydrolysis products.

One out of 18 substances, i.e. 1,4:3,6-Dianhydrosorbitol (EFSA-Q-2011-769, FCM No. 364), had previously been evaluated by the ACF Panel in 2007 for use in PEIT. Based on the set of toxicological data provided for the evaluation by the AFC Panel, an SML of 5 mg/kg was set. As the specific migration of the substance from polyester samples manufactured with the maximum use level of the substance was below the SML of 5 mg/kg, the CEF Panel concluded that the substance 1,4:3,6-dianhydrosorbitol does not raise a safety concern for the consumer. Another substance, poly(12-hydroxystearic acid) stearate (EFSA-Q-2004-040, FCM No. 875), received an SML of 5 mg/kg based on read-across with a structurally related substance (9,10-dihydroxystearic acid oligomers). This substance can thus not be used to evaluate the impact of the revision of the guidelines on the restriction, as the restriction depends not on the toxicological data of the substance itself but on the data of a structurally related compound.

Three of the substances with an SML of 5 mg/kg were monomers and 14 were additives. The substance with an SML of 2 mg/kg was also an additive. In addition to an SML, six substances –both monomers and additives – received a restricted use.

Substances covered by SML > 5 mg/kg or GML

Only one out of the 73 model substances had an SML higher than 5 mg/kg i.e. 60 mg/kg which corresponds to the GML.

For three substances, no SML or restricted use was defined. Nevertheless, these substances need to be compliant with the generic migration limit which is also 60 mg/kg. All four substances had migration values above 5 mg/kg and thus required the core set of toxicological data for their evaluation. However, for none of these substances, the complete core set of toxicological tests – including a

chronic toxicity/oncogenicity study was provided. In case of Oxidized polyethylene (EFSA-Q-2003-199, FCM No 811), the TDI was calculated by applying an extra safety factor of five in order to correct for both the absence of subchronic toxicity data for the low molecular weight fraction and the absence of chronic toxicity data. Based on a NOAEL value of 500 mg/kg bw/day, this resulted in a TDI of 1 mg/kg which corresponds to an SML of 60 mg/kg. The other three substances - Acids, Fatty (C8-C22), esters with pentaerythritol (EFSA-Q-2005-245, FCM No 880), Acids, Fatty (C8-C22), from animal or vegetable fats and oils, esters with branched alcohols, aliphatic, monohydric, saturated, primary (C3-C22) (EFSA-Q-2007-009, FCM No 878) and Acids, fatty (C8-C22) from animal or vegetable fats and oil, esters with linear alcohols, aliphatic,monohydric, saturated, primary (C1-C22) (EFSA-Q-2007-032, FCM No 879) – are fatty acids which were expected to be efficiently cleaved in humans to their component alcohols and carboxylic acids. Consequently, the results of genotoxicity and subchronic 90 day toxicity test were considered sufficient to set no restriction, and the substances thus only needed to be compliant with the generic migration limit i.e. 60 mg/kg. For the substance 'Acids, Fatty (C8-C22), from animal or vegetable fats and oils, esters with branched alcohols, aliphatic, monohydric, saturated, primary (C3-C22)', data on developmental toxicity were also provided as some branched chain aliphatic acids (2-propylpentanoic acid, 2-ethylhexanoic acid, 2-propylhexanoic acid) which can be formed as metabolites are teratogenic in rats and rabbits. However, as no effects were observed in the developmental toxicity study with a model compound, the presence of branched chain aliphatic acids was considered of no concern and the generic migration limit was considered sufficient for this substance.

Two out of the 73 model substances were mixtures of authorised substances restricted by an SML i.e. acids, C2-C24, aliphatic, linear, monocarboxylic from natural oils and fats, lithium salts (EFSA-Q-2008-030, FCM No 801) and copper hydroxide phosphate (EFSA-Q-2010-708, FCM No 972). Substances that are mixtures of authorised substances are automatically authorised and consequently, they need to be compliant both with the generic migration limit and with the SML values of the various components. For the substance 'Acids, C2-C24, aliphatic, linear, monocarboxylic from natural oils and fats, lithium salts', both components had indeed been authorised. The substance acids, C2-C24, aliphatic, linear, monocarboxylic, from natural oils and fats is listed without any SML, but nevertheless needs to be compliant with the generic migration limit. Lithium salts are listed with a group SML of 0.6 mg/kg (expressed as lithium). Similarly, the components of copper hydroxide phosphate, i.e. phosphoric acid and several copper salts, are included in the positive list of the Directive 10/2011 without restriction and with a restriction of 5 mg copper/kg respectively.

The substance with an SML of 60 mg/kg and those that needed to be compliant with the GML were all additives.

2.3.2. Substances covered by a restricted use

Substances covered by a restricted use: Toxicological data corresponds to appointed tier

Thirty-four out of the 73 model substances did not receive a migration limit, but instead a restricted use. These substances were evaluated by the AFC/CEF Panel for a specific type of plastic or for only

one type of use. In case the applicant intends to use the substance for another use, a new evaluation should be performed.

For twenty-one of the substances with a restricted use, the evaluation was based on the type and the amount of toxicological data triggered by the migration values. Sixteen substances had migration values below 0.05 mg/kg, and consequently, only the genotoxic potential had to be investigated. Some of the substances also contained potential impurities with migration values below 0.05 mg/kg food. These impurities were also considered in the evaluations. In case the substance and the potential impurities were non-genotoxic, the proposed use was considered to not raise any toxicological concern, and consequently the substance was approved with a restricted use. For nine of the substances with migration values below 0.05 mg/kg genotoxicity data were provided. As these substances and the potential impurities were non-genotoxic, the AFC/CEF Panel concluded that for the proposed use of the substance, there was no toxicological concern. For three out of the sixteen substances, no toxicological data were provided by the applicant. Furthermore, the oligomers and starting products did not contain a structural alert for genotoxicity. Based on these data, the CEF Panel concluded that there was no toxicological concern associated with the proposed use. For titanium nitride, nanoparticle, migration could not be detected and therefore the CEF Panel concluded that the proposed use of the substance did not raise a toxicological concern. The substance malic acid (EFSA-Q-2007-182, FCM No 499) did also not require additional toxicological information for its evaluation as (i) a low level of malic acid is used in copolymer; (ii)- malic acid has previously been evaluated by JECFA and SCF and was considered to cause no safety concern and (iii) absence of oligomers with MW <1000 Da containing malic acid units. Consequently, the substance was considered of no toxicological concern and received a restricted use. For the substance 1,2-benzisothiazol-3(2H)-one 1,1 dioxide, sodium salt (EFSA-Q-2011-970, FCM No 902) which had migration values below 0.05 mg/kg, also no additional toxicological data was required as the substance had been evaluated by SCF (1995) and concluded that an ADI (sodium saccharin) of 0-5 mg/kg bw could be set. For two other substances, i.e. glycolic acid (EFSA-Q-2010-1090, FCM No. 794) and 3H-Perfluoro-3-[(3-methoxy-propoxy) propanoic acid], ammonium salt (EFSA-Q-2010-1216, FCM No. 896), more toxicological data were provided. Glycolic acid had previously been evaluated, and therefore the available data were also considered in the current evaluation. In case of 3H-Perfluoro-3-[(3-methoxy-propoxy)propanoic acid], ammonium salt, more data were probably provided as this substance is a perfluorocompound with a potential for accumulation in man. For two other substances, i.e. trimethyl trimellitate (EFSA-Q-2010-838, FCM No. 971) and 2-Hydroxypropyl methacrylate (HPMA) (EFSA-Q-2011-1239, FCM No. 995), the migration values were below 0.05 mg/kg, whereas that of the oligomeric fraction was between 0.05 and 5 mg/kg. However, the oligomeric fraction and reaction products of these monomers were considered not of toxicological concern as (i) the substances did not contain a structural alert for genotoxicity; (ii) hydrolysis products are expected to be covered by in vivo experiments with mother compound and (ii) the migration of the LMWF below 1000 Da was low. Consequently, genotoxicity data on the substance was considered sufficient to conclude that for the proposed use, there was no toxicological concern.

Three substances had migration values between 0.05 and 5 mg/kg, i.e. Tetrahydro-1,3,4,6-tetrakis (hydroxymethyl)imidazo-[4,5-d]imidazol-2,5(1H,3H)-dion (EFSA-Q-2006-315), Sodium borohydride used in conjunction with palladium acetate (EFSA-Q-2011-067, FCM 981/982) and Sodium carbonate peroxyhydrate, bentonite, sodium chloride, sodium carbonate (Oxyfresh) (EFSA-Q-2011-236, FCM

No 1009). These three substances thus required genotoxicity data, the results of a 90 day subschronic toxicity study and data on the absence of a potential for accumulation in man for the substance. For all three substances, the results of the toxicological studies did not raise a toxicological concern. Consequently, the substances were allowed with a restricted use. One substance, i.e. alpha-Alkenes(C20-C24) maleic anhydride-4-amino-2,2,6,6- tetramethylpiperidine, polymer (EFSA-Q-2006-171, FCM No 803) had migration values between 0.05 and 5 mg/kg when simulant A (10% EtOH) was used and therefore genotoxicity data and the results of a 90 day subchronic toxicity study were provided by the applicant. However, due to the instability of the substance in simulant A (10% EtOH), the CEF Panel restricted the use of the substance further to 'not to be used for alcholic foodstuffs'. For the other simulants, all migration values were below 0.05 mg/kg and since the substance was non-genotoxic, the other proposed uses were considered to be of no toxicological concern.

There was one substance, i.e. 'hydrogenated homopolymers and/or copolymers made of 1-hexene and/or 1-octene and/or 1-decene and/or 1-dodecene and/or 1-tetradecene (MW : 440-12000)' (EFSA-Q-2009-00770, FCM No 789) which had migration values that exceeded 5 mg/kg food. This substance had however previously been evaluated for applications with lower migration. Based on the absence of toxicological effects in repeated dose studies and the poor absorption of the test substance, the CEF Panel concluded that a migration up to 60 mg/kg food does not raise safety concern. Consequently, the substance was approved with a restricted use.

Substances covered by a restricted use: Substance made of authorised monomers

Thirteen of the substances covered by a restricted use were substances composed of authorised monomers. For these substances, the authorised monomers that may be present as impurities have to comply with their restriction. Furthermore, toxicological data need to be provided for the low molecular weight oligomeric fraction and potential impurities. The type and amount of toxicological information again depends on the migration.

The migration values of the low molecular weight oligomeric fraction of twelve substances were below 0.05 mg/kg and thus only genotoxicity data were required for their evaluation. However, by applying read-across of the polymeric substance with the authorised non-genotoxic monomers, it can be considered that the low molecular weight fraction of the polymeric substance is not genotoxic either and thus no additional genotoxicity data had to be provided for these substances. For one of the twelve substances, i.e. (methyl methacrylate, butyl acrylate, styrene, glycidyl methacrylate) copolymer (EFSA-Q-2009-806, FCM No 857), limited genotoxicity data were provided for two potential impurities, i.e. dibutyl ether and 2,2-dimethylpropanoic acid which both had migration values below 0.05 mg/kg. As the impurities were also non-genotoxic, the substance was considered of no toxicological concern at the proposed use. For another substance, i.e. polyaddition product of glycidyl methacrylate with acrylic acid and/or methacrylic acid, esters with alcohols (C1-C4) aliphatic, monohydroxy, saturated (EFSA-Q-2006-203, FCM No 958), genotoxicity data and the results of a 90 day subchronic toxicity study were submitted by the applicant. Initially, this toxicological information was required as the migration of the oligomeric fraction was between 0.05 and 5 mg/kg. However, the applicant was able to improve the production process, leading to a decrease in migration with values below 0.05 mg/kg. Consequently, genotoxicity data on the low molecular weight oligomeric fraction of the substance (and its chlorinated form) were sufficient for the evaluation.

For one substance, i.e. Poly(12-hydroxystearic acid)-polyethyleneimine copolymer (extension of application (EFSA-Q-2010-1244, FCM No 812), the migration value of the PHSA low molecular weight oligomeric fraction exceeded 0.05 mg/kg but stayed below 5 mg/kg. However, as PHSA had previously been authorised with an SML of 5 mg/kg, read-across of the low molecular weight oligomeric fraction with the authorised monomer could be applied. Consequently, the substance was considered to be of no toxicological concern at the proposed use.

All thirteen substances were additives.

2.3.3. Conclusion

Two groups of substances could be distinguished: substances covered by a migration limit and substances covered by a restricted use. Some substances were covered both by a migration limit and a restricted use. Substances covered by a migration limit could be divided into substances covered by the generic migration limit and substances covered by a specific migration limit. Based on the value of the SML, the latter group could be further subdivided in three categories: (i) substances with an SML lower than or equal to 0.05 mg/kg (i) substances with an SML higher than 0.05 and lower than or equal to 5 mg/kg and (iii) substances with an SML between 5 and 60 mg/kg. Substances with a generic migration limit were discussed together with those covered by an SML between 5 and 60 mg/kg. Most of the substances had an SML higher than 0.05 and lower than or equal to 5 mg/kg. Different types of restrictions could be distinguished for substances covered by a restricted use: (i) restrictions excluding certain types of food, (ii) restrictions on the concentration used and (iii) restrictions on the type of plastic. For substances only covered by a restricted use, restrictions were mostly based on the type of plastic, whereas for substances covered both by a migration limit and a restricted use, restrictions were mostly related to the intended contact food. Many of the substances covered by a restricted use were polymeric additives composed of authorised monomers. For all 73 model substances, the rationale behind the restriction could be clarified.

3. DETERMINATION OF THE RESTRICTIONS ACCORDING TO THE REVISED GUIDELINES

In the revised guidelines, the restriction is also derived from the toxicological data provided. The type and amount of toxicological data required, however, depends on the exposure and not solely on migration of the FCM substance and related migrants. Consequently, the determination of the restriction according to the revised guidelines required to calculate exposure and to assess the toxicological requirements based on these exposure values.

3.1. Exposure calculations according to the revised guidelines

Exposure values according to the revised guidelines were calculated by combining the predicted level of the FCM substance in food, obtained from migration data, with the consumption data for each food group category covered by the intended uses of the FCM.

The intended contact food as mentioned in the conclusion of the AFC/CEF Panel (and which might differ from the intended use requested by applicants), was translated into the different food group categories. An overview of the intended contact foods and their corresponding food group category or categories is provided in Table 11.

Table 11: Overview of the different foodstuffs intended to be in contact with the substance and the corresponding food group category (Cat.1, Cat. 2, Cat. 3) according to the revised guidelines

Intended contact food	Cat. 1	Cat. 2	Cat. 3
All foodstuffs (# 58)	X	X	X
Aqueous, acidic and low alcoholic foods (# 3)	X	X	X
Aqueous, acidic and alcoholic foodstuffs (# 1)	X	X	X
All foodstuffs packed in glass jars and bottles (# 1)	X	X	X
All foodstuffs, except beer and beverages (# 1)	X		X
Aqueous foodstuffs (# 2)	X	X	X
Aqueous foodstuffs, acidic and dairy foodstuffs (# 1)	X	X	X
Aqueous foodstuffs, excluding acidic and alcoholic foods (# 1)	X	X	X
All foodstuffs, excluding fatty foods, high alcoholic and dairy products (# 1)	X	X	X
Aqueous and dry foodstuffs containing no free fat at the surface (# 1)	X	X	X
Dry and aqueous food types (# 1)	X	X	X
Liquid food (# 1)	X	X	X
Fresh fruits (# 1)			X

Only for one substance, i.e. Sodium carbonate peroxyhydrate, bentonite, sodium chloride, sodium carbonate (oxyfresh) (EFSA-Q-2011-236, FCM No 1009), the intended contact food (fresh fruits) could be translated into one food group category (i.e. category 3). For most of the substances, i.e. 71 out of the 73 model substances, the intended contact foods could only be covered by a combination of all 3 different food group categories. In addition, there was one substance, i.e. Polyaddition product of glycidyl methacrylate with acrylic acid and/or methacrylic acid, esters with alcohols (C1-C4) aliphatic, monohydroxy, saturated (EFSA-Q-2006-203, FCM No 958) for which the intended contact food (all foodstuffs, except beer and beverages) was covered by two food group categories (i.e. category 1 and category 3).

Second, migration data relevant for the different food group categories were selected according to the methodology presented under 3.1. In case no specific migration data were available, i.e. for 20 out of the 73 model substances, the same migration data as those selected for the current guidelines were used. However, for the 53 out of the 73 model substances for which specific migration studies were performed, the adequacy of the simulants needed to be assessed for the different required food group categories by using Table 6 (Figure 22). For 11 out of the 53 substances, adequate simulants could be identified for different required food group categories, both for the substances and their related migrants. However, for 38 out of the 53 substances, not all simulants required by the different food group categories were used in the migration experiments, both for the substances and their related migrants. Furthermore, there were four substances, i.e. 2,2,4,4-tetramethylcyclobutane-1,3-diol

(TMCD) (EFSA-Q-2008-202, FCM No 881), N,N-Bis(2-hydroxyethyl)dodecanamide (EFSA-Q-2009-591, FCM No 923), 1,10-decanediamine (EFSA-Q-2009-674, FCM No 863) and 2-Phenyl-3,3-bis(4-hydroxyphenyl) phthalimidine (EFSA-Q-2009-834, FCM No 872), for which data with an adequate simulant were available for the substance but not for all its related migrants or vice versa. In the absence of migration tests with adequate simulants, the highest migration data obtained with an non-adequate simulant were retained to calculate exposure. For most substances and related migrants, an adequate food simulant was lacking for food group category one, i.e. simulant D1 or water.

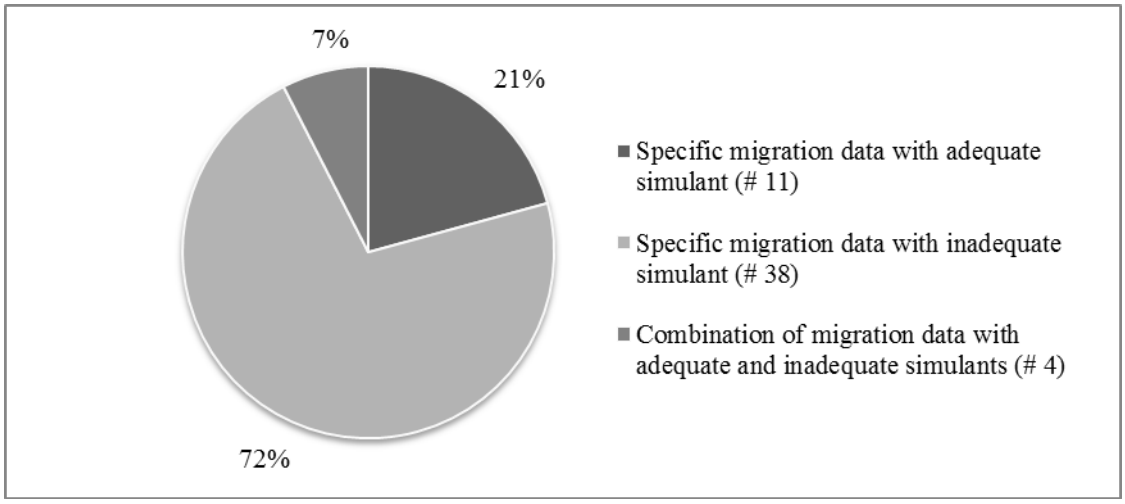

Figure 22: Overview of the number of substances (# 53) with specific migration data for which adequate and non-adequate simulants were used, or a combination of both

Third, exposure data were obtained by combining the consumption value corresponding to the food group category with the selected migration data. For 71 out of the 73 model substances, three exposure values had to be calculated corresponding to the three different food group categories. Only one exposure value corresponding to category 3 was required for Sodium carbonate peroxyhydrate, bentonite, sodium chloride, sodium carbonate (oxyfresh), whereas for Polyaddition product of glycidyl methacrylate with acrylic acid and/or methacrylic acid, esters with alcohols (C1-C4) aliphatic, monohydroxy, saturated, both the exposure values for category 1 and 3 were needed.

Finally, for each substance and related migrants, the highest value was selected out of the different calculated exposure values (Figure 23).

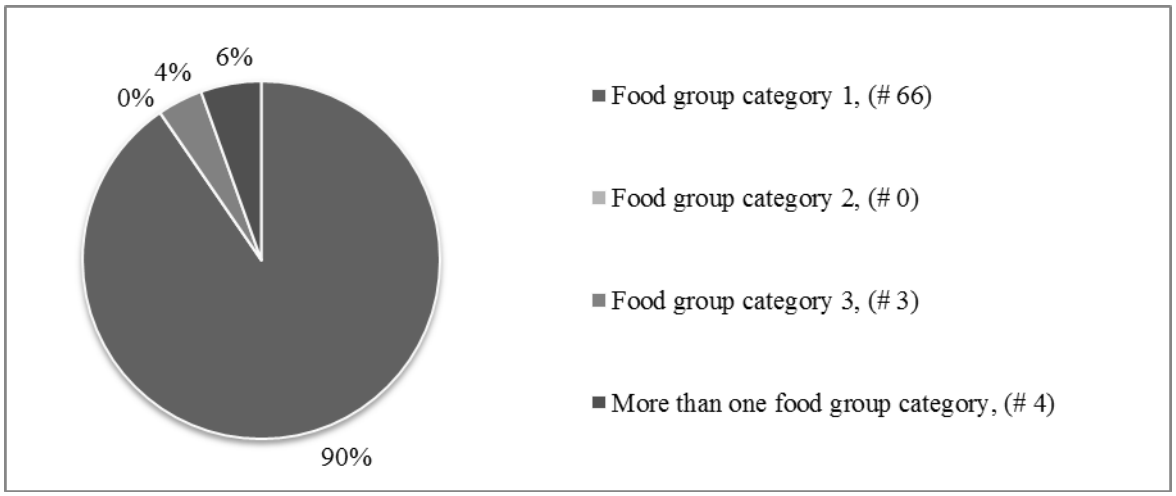

Figure 23: Distribution of the 73 model substances according to the food group category for which the highest exposure value was found

For sixty-six out of the 73 model substances, the highest exposure values of the substance and related migrants were found in food group category 1. These 66 substances included all 16 monomers. Two main reasons can be listed why food group category 1 contained in many cases the highest exposure values. First, food group category 1 is associated with the highest consumption value i.e. 150 g/kg bw/ day. Second, for many substances, migration data obtained with the correct simulant (i.e. water or simulant D1) were not available for food group category 1. Consequently, the highest migration values obtained with an non-adequate simulant were used. These values may substantially overestimate migration, in particular in case an oil or other fatty food simulant was used.

For three out of the 73 model substances, i.e. Sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salt (EFSA-Q-2005-151, FCM No 813), Sulphosuccinic acid, mono-alkyl (C10-C16) polyethyleneglycol esters, sodium salt (EFSA-Q-2006-324, FCM No 814) and Sodium carbonate peroxyhydrate, bentonite, sodium chloride, sodium carbonate (Oxyfresh) (EFSA-Q-2011-236, FCM 1009), the highest exposure value was present in food group category 3. For the latter substance, this is not surprising as exposure was only calculated for food group category 3. For the other two substances, both esters of sulphosuccinic acid, migration data obtained with an adequate simulant (i.e. simulant D1) were used to calculate the exposure value for food group categories 1 and 2. In contrast, exposure for food group category 3 was based on migration data obtained with 100% ethanol. Although not an official substitute simulant for simulant D2 (i.e. olive oil), the use of 100% ethanol was justified by the applicant based on analytical and technical considerations. As the migration value in 100% ethanol was considerably higher than the value in simulant D1, the highest exposure value was obtained in food group category 3. It is important to note that not all substances for which migration studies have been performed with simulant D1, the highest exposure value will be in food group category 3. For example, the substance 3,3',5,5'-tetrakis(tert-butyl)-2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propyl]oxyphosphonous acid (EFSA-Q-2008-678, FCM No 792) has migration data obtained with different simulants, including simulant D1, but nevertheless, the highest calculated exposure value was found in food group category 3.

Finally, for four substances, i.e. 2,2,4,4-tetramethylcyclobutane-1,3-diol (TMCD) (EFSA-Q-2008-202, FCM No 881), 3,9-Bis[2-(3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propionyloxy)-1,1-dimethyl ethyl]-2,4,8,10-tetraoxaspiro[5,5]undecane (EFSA-Q-2009-769, FCM No 858), Thiodipropionic acid, ditetradecyl ester (EFSA-Q-2010-935, FCM No 894) and Sodium borohydride used in conjunction with palladium acetate (EFSA-Q-2011-067, FCM No 981/982), the highest exposure values for the substance and the related migrants were found in two different food group categories. In case of TMCD, the highest exposure value of the substance was found in food group category 1, whereas that of the oligomeric fraction this value was present in food group category 2. This difference can be explained by the fact that for the substance no adequate simulant was used for food group category 1, whereas for the oligomeric fraction, migration data with simulant D1 were available. For the substance 3,9-Bis[2-(3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propionyloxy)-1,1-dimethylethyl]-2,4,8,10-tetra oxaspiro[5,5]undecane migration experiments were performed with the same simulants for the substance and the oxidation products. For both the substance and the oxidation products, the highest migration was observed in the simulant iso-octane. However, the difference between the migration values in isooctane (determinant for food group category 3) and simulant D1 (determinant for food group category 1) was much more pronounced for the substance than for the oxidation products. Consequently, the highest exposure value was found in food group category 3 for the substance and in food group category 1 for the oxidation products. The substance Thiodipropionic acid, ditetradecyl ester had the highest migration value in food group category 1, whereas for the related migrants; the highest migration values were found in two different food group categories, i.e. 1 and 3. The substance and related migrants all had migration values lower than LOD when simulant D1 was used. However, for one of the oxidation products (TPM+1O), the limit of detection in simulant D1 (determinant for food group catergory 1) was more than double as high as the LOD for the substance and the other oxidation product. In contrast, migration values in iso-octane (determinant for food group category 3) were of the same magnitude, explaining why different food group categories contained the highest exposure value. For Sodium borohydride used in conjunction with palladium acetate, data on boron and palladium were considered in the evaluation. Boron showed a different migration pattern than palladium and consequently it is not surprising that the highest exposure values were found in different food group categories, i.e. 1 (Palladium) and 2 (Boron).

3.1.1. Conclusion

For most of the substances, the intended contact foods could only be covered by a combination of all three food group categories. Only for two substances, one (food group category 1) or two (food group category 1 and 3) food group categories were sufficient to cover the intended contact foods, i.e. fresh fruit and all foodstuffs excluding beer and beverages, respectively. In most cases, specific migration data were used to calculate exposure. However, an adequate simulant for all requested food group categories was only available for a minority of FCM substances and related migrants, what might impact the interpretation of results and the impact of the revised guidelines on already evaluated substances. The highest exposure value of most of the FCM substances was found in food group category 1.

3.2. Toxicological data required according to the revised guidelines

3.2.1. Toxicological requirements according to the revised guidelines

The toxicological information required for the evaluation was triggered by the exposure values. Like for the current guidelines, the toxicological requirements do not solely apply to the substances (and in case of mixtures, its constituents) themself but also to the transformation or reaction products and/or related impurities. Consequently, the toxicological requirements for the related migrants also needed to be determined. In general, the core set of toxicological tests required for FCM substances and their related migrants comprises the same studies as in the current guidelines. This core set of tests may be reduced depending on the exposure data. An overview of the threshold values of the different tiers and the associated toxicological requirements is provided in Table 8.

Based on the exposure results calculated under 2.1, each of the 73 model substances was assigned to one of the three tiers. As toxicological requirements also applied to the related migrants, the highest tier accorded to the substance or one of the related migrants was considered as the tier for the FCM substance. An overview of the repartition of the substances over the different tiers is shown in **Figure 24**.

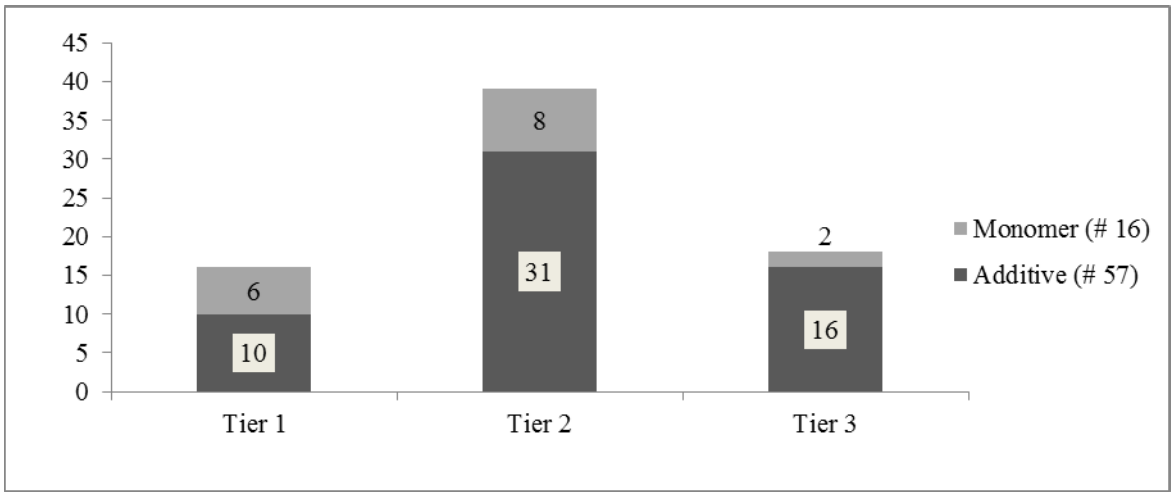

Figure 24: Allocation of the tier according to the revised guidelines for the 73 model substances.

3.2.2. Comparison of the toxicological requirements according to the current and the revised guidelines

In a next step, the toxicological tiers assigned to the 73 model substances according to the current and the revised guidelines were compared. Figure 25 illustrates that the revision of the guidelines had an impact on the tier of 36 out of the 73 model substances. For each of these 36 substances, a change in tier was observed for the substance and/or for one or more of its related migrants. Consequently, the toxicological requirements for the substance and/or the related migrants according to the revised guidelines were changed compared to the current guidelines.

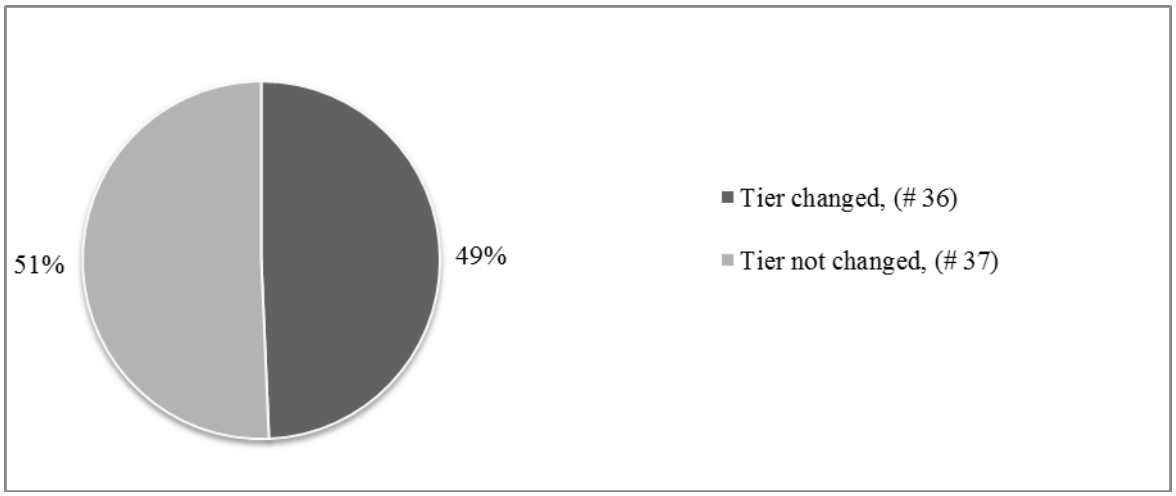

Figure 25: Overview of the impact of the revision of the guidelines on the tier of the substances (# 73)

Interestingly, 8 out of the 16 substances used as a monomer were allocated to a different tier according to the revised guidelines. In the group of additives, a change in tier was observed for 28 out of the 57 substances (Figure 26).

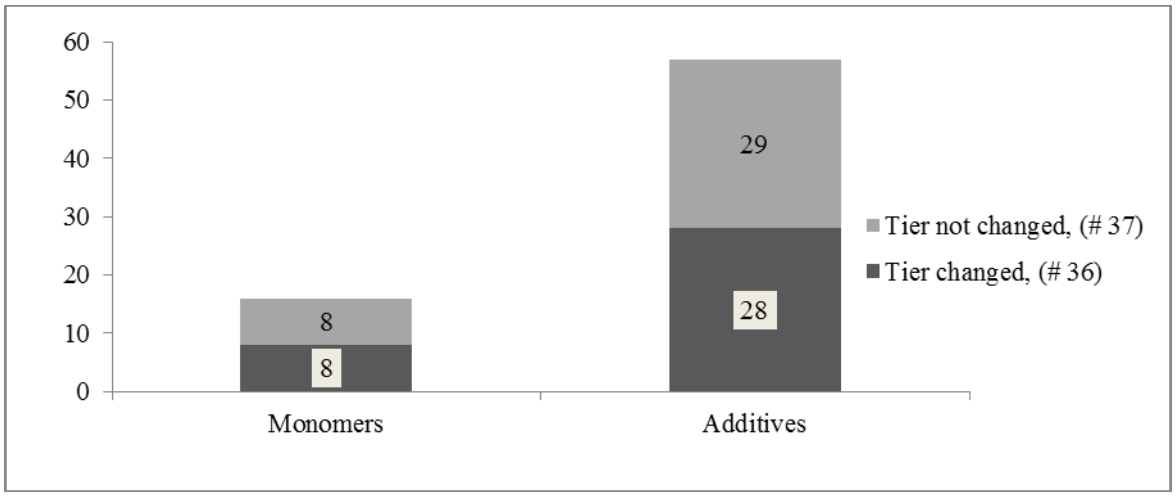

Figure 26: Impact of revision of the guidelines on the tier classification for monomers and for additives

The three tiers are associated with different toxicological requirements and thus, the nature of the shifts in tier had to be identified (e.g from Tier 1 to Tier 2, from Tier 2 to Tier 3,…) (Figure 27). For some substances, more than one shift in tier was observed as also the related migrants could require a different amount of toxicological data according to the revised guidelines. For 25 out of the 36 substances, the substance and/or one or more of its related migrants shifted from Tier 1 to Tier 2. Nineteen of these substances were additives and 6 substances were monomers. For 9 substances, a shift from Tier 2 to Tier 3 was observed for the substance and/or one or more of its related migrants. Two of these substances were monomer; the remaining seven substances were additives. Finally, both a shift from Tier 1 to Tier 2 and a shift from Tier 2 to Tier 3 was observed for two substances and their

related migrants. Both were additives. For none of the 36 substances, the shift occurred from Tier 1 to Tier 3.

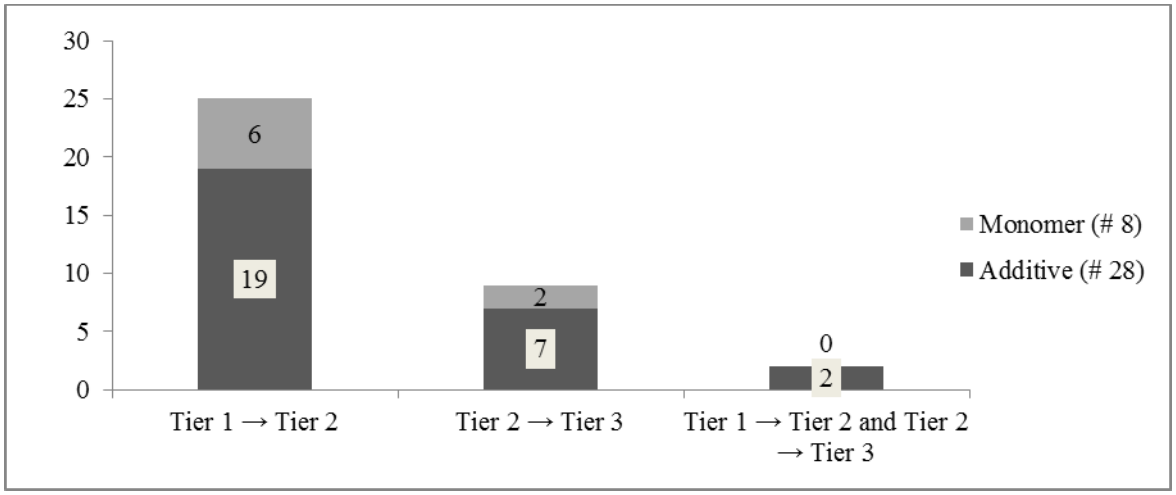

Figure 27: Overview of the nature of the observed changes in tiers according to the revised guidelines for both monomers and additives (# 36)

3.2.3. Discussion of the observed differences in toxicological requirements

Type of migration data used to calculate exposure

As discussed previously, the amount and type of toxicological data required according to the revised guidelines is no longer based on migration data but instead on exposure estimates. Exposure values were obtained by combining the consumption value of a food group category with migration data relevant for this food group. In case the intended food contact could only be covered by multiple food group categories, exposure values were calculated for all these food group categories and the highest value was selected. The type of migration data used to calculate exposure had thus an important impact on the tier. As discussed in the methodology section, migration data selected to calculate exposure according to the revised guidelines were considered not to underestimate the migration of a substance and related migrants. In contrast, overestimation of migration often occurs and needed to be taken into account. Several factors may contribute to the overestimation of migration including the type of migration experiments, the adequacy of the simulants and the migrations conditions. In Figure 28, the number of substances and related migrants with a change in tier is expressed as a function of the methodology used to obtain the migration data. In case modelling (9 out of 37) or total mass transfer (8 out of 37) were used to evaluate migration, the exposure can have been overestimated. Indeed, these data are not indicative for specific migration and should rather be considered as 'worst case' data. According to the current guidelines, their migration was in most cases below 50 µg/kg, leading to a Tier 1 classification, while the revised guidelines classify them as Tier 2 due to the exposure-based calculation.

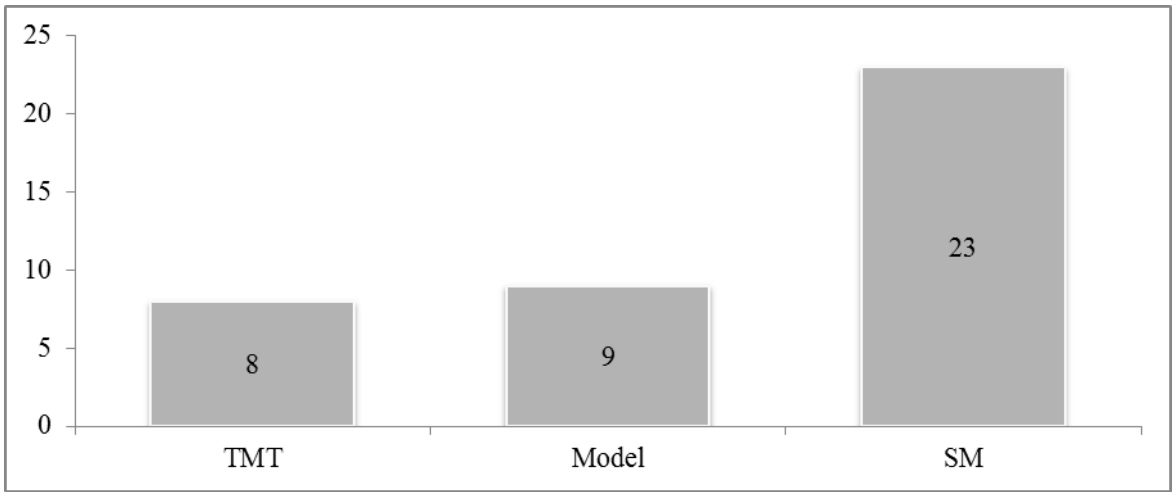

Figure 28: The number of FCM substances and related migrants with a change in tier as a function of the methodology used to obtain the migration data (# 37). TMT: total mass transfer, Model: modelling and SM: specific migration.

For the majority of the substances and related migrants that changed in tier, the selected migration data were obtained through specific migration (23 out of 37). However, for 19 of the 23 substances for which specific migration data were used, an adequate simulant was lacking for one or more of the food group categories covering the intended contact food. Hence, in these cases the use of a non-suited food simulant might have led to an over estimation of the migration potential, which, in its turn, might have caused the classification in a higher tier according to the revised guidelines. Finally, for some FCM substances and related migrants (covered by adequate migration data), migration conditions might have been too severe, thereby overestimating the migration. The impact of migration conditions on overestimation of migration is further discussed under 3.3.

Use of the limit of detection

For 19 of the substances and related migrants that changed in tier, the LOD value was used to estimate migration. According to the current guidelines, an LOD lower than 50 µg/kg was sufficient for the substance to be classified as Tier 1. However, this is no longer valid for the revised guidelines, where the LOD should be lower than 10 µg/kg. Consequently, substances and related migrants with an LOD between 10 and 50 µg/kg were classified as Tier 1 according to the current guidelines, but as Tier 2 according to the revised guidelines. For these substances and related migrants, the revision of the guidelines thus triggered new toxicological requirements, while it is not even sure that migration will exceed 10 µg/kg. In these cases, the applicant could be asked to confirm that the amount of substance or/and related migrants that migrates will not be equal to or higher than 10 µg/kg.

3.2.4. Conclusion

According to the revised guidelines, most substances and their related migrants were allocated to Tier 2, followed by Tier 3. Only sixteen substances were classified as Tier 1, including 10 additives and 6 monomers. Forty-nine % of the 73 FCM model substances changed in tier when the revised guidelines were applied. For these substances, a change in tier was observed for the substance and/or one or more of its related migrants. Interestingly, both for monomers and

additives, about half of the substances was allocated to a different tier according to the revised guidelines.

Most of the substances and/or the related migrants, shifted from Tier 1 to Tier 2. No shift from Tier 1 to Tier 3 was observed. For many substances that shifted in tier, exposure might have been calculated with migration data that significantly overestimated migration. Factors contributing to overestimation of migration include the type of migration experiments, the adequacy of the simulants, the migration conditions and the use of an LOD to calculate exposure.

3.3. Determination of the restrictions according to the revised guidelines

For the 73 model substances, the impact of the revision of the guidelines on the restrictions was evaluated as a function of the types of restriction. Furthermore, the need for more toxicological and/or migration data was discussed. Substances that are covered both by a migration limit and a restricted use, were not discussed separately, but included in the categories of the substances covered by a migration limit.

3.3.1. Substances for which an ADI not needs to be established or for which a previously established ADI or equivalent value is considered acceptable

Until May 2003, the Scientific Committee on Food (SCF) evaluated the applications for authorization of a substance to be used in plastic materials and articles. Substances were classified into one of the ten SCF-lists based on the availability of data regarding the daily intake of the substance. After 2003, the SCF was replaced by the AFC Panel on food additives, flavourings, processing aids and materials in contact with food of the European Food Safety Authority (EFSA), which endorsed the FCM guidelines, including the classification into SCF-lists. In 2008, the Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel) was set and continued to use the SCF-list annotation. The ten SCF-lists are defined in the Note for Guidance. For substances classified in SCF-list 0 and SCF-list 1, an ADI did not need to be established or the previously established ADI or equivalent value was considered appropriate, respectively:

- List 0:
  Substances, e.g. foods, which may be used in the production of plastic materials and articles, e.g. food ingredients and certain substances known from the intermediate metabolism in man and for which an ADI does not need to be established for this purpose. In principle, no restriction needs to be determined for these substances.
- List 1:
  Substances, e.g. food additives, for which an ADI (= Acceptable Daily Intake), a t-ADI (= Temporary ADI), a MTDI (= Maximum Tolerable Daily Intake), a PMTDI (= Provisional Maximum Tolerable Daily Intake), a PTWI (= Provisional Tolerable Weekly Intake) or the classification "acceptable" has been established by this Committee or by JECFA.

Consequently, no additional toxicological data were required for the evaluation according to the current guidelines for substances classified in SCF-lists 0 and 1. Revision of the guidelines will not trigger the demand for more toxicological data. Furthermore, restrictions according to the revised

guidelines will not change compared to the current guidelines for substances classified in SCF-list 0, as for these substances no restriction needed to be determined. For substances classified in SCF-list 1, the highest calculate exposure should be compared to the ADI in order to evaluate if the exposure to the substance related to its use in FCM is considered acceptable.

Two out of the 73 model substances were allocated to SCF-list 1, i.e. Malic acid (EFSA-Q-2007-182, FCM No. 499) and Saccharin (EFSA-Q-2011-970, FCM No. 902). Both substances were classified in Tier 1 according to the current guidelines. Only for Malic acid, a change in tier was observed when the revised guidelines were applied, i.e. from Tier 1 to Tier 2. However, as for Malic acid, an ADI 'non specified' had been set (indicating that the substance has very low toxicity and no safe upper-limit of intake is established, or deemed necessary), the restricted use as defined according to the current guidelines was not affected by the revision of the guidelines.

3.3.2. Substances covered by a migration limit

In the revised guidelines, the limits of the toxicological tiers are no longer migration values, but instead exposure values. Translation of these exposure limits into migration limits expressed as mg/kg food results in 9 migration limits, three for each food group category (Table 10). The migration limits according to the revised guidelines range from 0.01 mg/kg (Tier 1 in combination with food group category 1) to 50 mg/kg (Tier 3 in combination with food group category 3). Consequently, the restriction of almost all substances covered by a migration limit changes when the revised guidelines are applied, regardless a change in tier. Only for substances classified as Tier 2 with a highest exposure value found in food group category 3, the SML value is not altered.

For one out of the 39 FCM model substances covered by a migration limit, i.e. sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salt (EFSA-Q-2005-151, FCM No. 813), the migration limit did indeed not change when the revised guidelines were applied. This FCM substance was classified in Tier 2 according to the current guidelines and received an SML of 5 mg/kg based on the toxicological data provided. When applying the revised guidelines, the highest exposure value was calculated for food group category 3, due to the high migration in 100% EtOH compared to that in simulant D1 (lower than LOD), used for the calculations for food group category 1. As the substance remained classified in Tier 2 according to the revised guidelines and the highest exposure value was found in food group category 3, the migration limit was also fixed at 5 mg/kg. This was the only example of a substance covered by a migration limit, for which the revision of the guidelines had no impact on the restriction.

In general, the 39 FCM model substances covered by a migration limit can be divided into two categories based on the presence or absence of a change in tier. For the substances without a change in tier, the restriction changed when the revised guidelines were applied, although no additional toxicological data were required. For the substances with a change in tier, the restriction changed not only because exposure limits were used to calculate the migration limit, but also because the exposure values of the substance and related migrants triggered more toxicological data. However, in some cases, the migration data used to calculate exposure according to the revised guidelines might have overestimated the migration. In order to evaluate if the revision of the guidelines indeed required more toxicological data for the substance and related migrants to set the restriction, overestimation of migration needed to be evaluated. As discussed under 3.2.3, several factors can contribute to

overestimation of migration including the type of migration experiments (e.g. total mass transfer calculations, modelling, specific migration with a non-adequate simulant), the migration conditions or the use of a too high LOD to calculate exposure. For substances and related migrants with an overestimated migration, more adequate migration data could first be requested. In case the results of the new migration experiments confirm the change in tier, more toxicological data are needed to set the restriction.

Substances covered by SML ≤ 0.05 mg/kg

An overview of the substances covered by a specific migration limit lower than 0.05 mg/kg is given in Table 12.

Table 12: Summary of the impact of the revised guidelines on the substances covered by an SML ≤ 0.05 mg/kg.

	Substance	Tier change?	Possible overestimation of the migration?	Restriction (mg/kg)
Monomers	2,3,6-Trimethylphenol *EFSA-Q-2006-144, FCM No. 882*	No		0.01 mg/kg (Cat 1, Tier 1)
	3-Methyl-1,5-pentanediol *EFSA-Q-2007-077, FCM No.883*	Yes	Yes, SM_N	To be determined (non-adequate migration)
	1,10-decanediamine *EFSA-Q-2009-674, FCM No. 863*	Yes	No, SM (D1)	To be determined (more tox data required)
	alpha-dimethyl-3-(4'-hydroxy-3'-methoxyphenyl)propylsilyloxy, omega-3-dimethyl-3-(4'-hydroxy-3'-methoxyphenyl)propylsilyl polydimethylsiloxane *EFSA-Q-2009-821, FCM No. 874*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)
	2-Phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine *EFSA-Q-2009-834, FCM No.872*	No		0.01 mg/kg (Cat 1, Tier 1)
	N-(2-Aminoethyl) ethanolamine (AEEA) *EFSA-Q-2011-968, FCM No.262*	No		0.01 mg/kg (Cat 1, Tier 1)
	1,3-bis(isocyanatomethyl) benzene *EFSA-Q-2012-062, FCM No. 988*	No		0.01 mg/kg (Cat 1, Tier 1)
Additives	N,N''-propane-1,3-diylbis(N'-octadecyl)urea *EFSA-Q-2006-139, FCM No. 965*	No		0.01 mg/kg (Cat 1, Tier 1)
	N-(2,6-Diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-1H-benzo[de]isoquinoline-1,3(2H)-dione *EFSA-Q-2007-199, FCM No.809*	No		0.01 mg/kg (Cat 1, Tier 1)
	Silver Zeolite A (Silver zinc sodium ammonium alumino silicate) *EFSA-Q-2009-708, FCM No. 946*	Yes	Yes, SM_N	No change in restriction
	Alkyl(C10-C21)sulphonic acid, esters with phenols *EFSA-Q-2009-733, FCM No. 884*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)

	3,9-Bis[2-(3-(3-tert-butyl-4-hydroxy-5-methyl phenyl)propionyloxy)-1,1-dimethylethyl]-2,4, 8,10-tetraoxaspiro[5,5]undecane *EFSA-Q-2009-769, FCM No 858*	No		0.01 mg/kg (Cat 1, Tier 1)
	Trimethylolpropane, mixed triester and diesters with n-octanoic and n-decanoic acid *EFSA-Q-2010-045, FCM No. 924*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)
	Bis(2,6-diisopropylphenyl)carbodiimide (CDI) *EFSA-Q-2010-813, FCM No. 438*	Yes	Yes, TMT, SM_N ≤ LOD	To be determined (non-adequate migration)
	Benzenepropanoic acid, 3,-bis(1,1-dimethylethyl)-4-hydroxy-, C13-15 branched and linear alkyl esters (Anox 1315) *EFSA-Q-2010-934, FCM No. 895*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)

As illustrated in Table 12, fifteen substances are present in this category. Seven of them did not change in tier, while eight of these substances did change in tier.

Substances without change in tier

Seven out of the 15 substances (3 additives and 4 monomers) did not change in tier after application of the revised guidelines. Five of the substances were already classified in Tier 1 according to the current guidelines and remained in Tier 1 when the revised guidelines were applied. No additional toxicological data were thus required to set the restriction according to the revised guidelines. The new restrictions of these substances could range from 0.01 mg/kg to 0.075 mg/kg depending on the food group category responsible for the highest exposure calculation. However, for all five substances, the first food group category was responsible for the highest exposure and therefore the new restriction for these substances was set at 0.01 mg/kg.

Two out of the seven substances with an SML ≤ 0.05 mg/kg were classified as Tier 2 according to the current guidelines, but the toxicological data provided did not allow to set a migration limit higher than 0.05 mg/kg. Both substances remained classified as Tier 2 according to the revised guidelines. For the additive N-(2,6-Diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-1H-benzo[de] isoquinoline-1,3(2H)-dione (EFSA-Q-2007-199, FCM No. 809), classification in Tier 2 according to the current guidelines was due to the high specific migration value in simulant D1 (50% EtOH). Since only genotoxicity data were provided, a restriction of 0.05 mg/kg was set. Application of the revised guidelines for this FCM substance, changed the migration limit to 0.01 mg/kg (Cat 1, Tier 1) but had no effect on the toxicological requirements. For the other substance, 3,9-Bis[2-(3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propionyloxy)-1,1-dimethylethyl]-2,4,8,10-tetra oxaspiro[5,5]undecane (EFSA-Q-2009-769, FCM No. 858), classification as Tier 2 was triggered by the high migration value obtained in iso-octane. The latter is considered to be an adequate simulant for food group category 3. Although the results of a 90d oral study were provided, leading to a NOAEL of 8 mg/kg bw/day, the restriction was set at 0.05 mg/kg due to the absence of data on the potential bioaccumulation. However, since the migration in the simulant D1 (50% EtOH) was lower than 50 µ/kg, the CEF Panel stated during the evaluation that the petitioner should take precautions to reduce

the migration by a factor of 3, which would result in a migration lower than 50 µg/kg in iso-octane. When this is taken into account for the exposure calculations, the highest exposure value for the substance is found in food group category 1 (in contrast to the previous calculations using the elevated value for iso-octane, leading to a high exposure calculations for food group category 3), resulting in a restriction of 0.01 mg/kg.

Substances with change in tier

Eight of the substances restricted with an SML ≤ 0.05 mg/kg, were classified as Tier 1 according to the current guidelines and changed to Tier 2 after application of the revised guidelines.

The restriction of Silver Zeolite (EFSA-Q-2009-708, FCM No. 946), as already discussed above (3.3), was not derived from the migration data, but based on other considerations. Consequently, the impact of the revised guidelines on the restriction of this substance cannot be evaluated.

For the other substances, the first food group category was responsible for the highest exposure calculations. Exposure calculations were however performed with specific migration data obtained with a non-adequate simulant for six out of the seven substances. In order to evaluate if more toxicological data are indeed required to set the restriction according to the revised guidelines for these substances, more adequate migration data could first be requested from the applicant. If the results of new migration experiments confirm the change in tier, more toxicological data are needed. Furthermore, for 5 out of the 7 substances, an LOD was used for the exposure calculations. While an LOD lower than 50 µg/kg was sufficient for the substance to be classified as Tier 1 in the current guidelines, this is no longer valid for the revised guidelines, where the LOD should be lower than 10 µg/kg. When a change in tier was triggered by the use of a too high LOD, more migration data could be demanded from the petitioner to demonstrate that the migration of the substance and related migrants is below 10 µg/kg.

The additive 1,10-decanediamine (EFSA-Q-2009-674, FCM No. 863) was the only FCM substance covered by an SML ≤ 0.05 mg/kg for which the exposure value for food group category 1 could be calculated with migration data for simulant D1. Migration of the substance in simulant D1 was clearly detected. The change in tier could thus not be explained by overestimation of migration due to the type of migration experiments or the use of a too high LOD. For this substance, migration conditions should be analysed in order to evaluate if more toxicological data are needed or not to set the restriction. It should also be noted that this substance is not only restricted by an SML = 0.05 mg/kg, but the use is also restricted to 'Only to be used as a co-monomer for manufacturing polyamide articles for repeated uses in contact with aqueous, acidic and dairy foodstuffs at room temperature or for short term contact up to 150°C'.

Substances covered by 0.05 mg/kg < SML ≤ 5 mg/kg

As already mentioned above, eighteen substances are covered by a migration limit higher than 0.05 mg and lower or equal to 5 mg/kg (Table 13).

Table 13: Summary of the impact of the revised guidelines on the substances covered by an SML between 0.05 and 5 mg/kg.

	Substance	Tier change ?	Possible overestimation of the migration?	Restriction (mg/kg)
Monomers	2,2,4,4-tetramethylcyclobutane-1,3-diol (TMCD) *EFSA-Q-2008-202, FCM No. 881*	No		0.67 mg/kg (Cat 1, Tier 2)
	1,4-Cyclohexanedicarboxylic acid (CHDA) *EFSA-Q-2008-298, FCM No 806*	Yes	Yes, SM_N	To be determined (non-adequate migration)
	1,4:3,6-Dianhydrosorbitol *EFSA-Q-2011-769, FCM No. 364*	Yes	Yes, SM_N ≤ LOD	To be determined (Previous evaluation)
Additives	Poly(12-hydroxystearic acid)stearate *FCM No. 811, EFSA-Q-2004-040*	No		To be determined (Read-across)
	Sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salt *EFSA-Q-2005-151, FCM No 813*	No		5 mg/kg (Cat 3, Tier 2)
	Alcohols C12-C14 Secondary. Beta.-(2hydroxyethyoxy)-ethoxylated *EFSA-Q-2006-183, FCM No. 802*	No		0.67 mg/kg (Cat 1, Tier 2)
	Sulphosuccinic acid, mono-alkyl (C10-C16) polyethyleneglycol esters, sodium salt *EFSA-Q-2006-324, FCM No. 814*	No		To be determined (Read-across)
	Neopentyl glycol, mixed diesters with benzoic acid and 2-ethylhexanoic acid *EFSA-Q-2007-006, FCM No 810*	Yes	Yes, SM_N	To be determined (non-adequate migration)
	Trimethylolpropane, mixed triesters and diesters with benzoic acid and 2-ethyl hexanoic acid *EFSA-Q-2007-007, FCM No. 815*	No		0.67 mg/kg (Cat 1, Tier 2)
	Bis(4-propylbenzylidene)propylsorbitol *EFSA-Q-2007-023, FCM No. 808*	Yes	Yes, TMT, SM_N	To be determined (non-adequate migration)
	3,3',5,5'-tetrakis(tert-butyl)-2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propyl]oxyphosphonous acid *EFSA-Q-2008-678, FCM No. 792*	Yes	No	To be determined (more tox data required)
	N,N',N''-Tris(2-methylcyclohexyl)-1,2,3-propane-tricarboxamide *EFSA-Q-2008-698, FCM No. 870*	Yes	No	To be determined (more tox data required)
	N,N-Bis(2-hydroxyethyl)dodecanamide *EFSA-Q-2009-591, FCM No. 923*	No		0.67 mg/kg (Cat 1, Tier 2)
	2,4-diamino-6-hydroxypyrimidin *EFSA-Q-2009-681, FCM No. 864*	No		0.67 mg/kg (Cat 1, Tier 2)
	2,4-Bis(2,4-dimethylphenyl)-6-(2-hydroxy-4-n-octyloxyphenyl)-1,3,5-triazine *EFSA-Q-2009-768, FCM No. 452*	Yes	Yes, SM_N	To be determined (non-adequate migration)

	Phosphorous acid, mixed 2,4-bis(1,1-dimethylpropyl)phenyl and 4-(1,1-dimethylpropyl-phenyl) triesters [(RO)3P] *EFSA-Q-2010-779, FCM No. 974*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)
	Thiodipropionic acid, ditetradecyl ester *EFSA-Q-2010-935, FCM No. 894*	Yes	No	To be determined (Read-across)
	1,3,5-tris(2,2-dimethylpropanamido)benzene *EFSA-Q-2012-695, FCM No. 784*	No		0.67 mg/kg (Cat 1, Tier 2)

The restriction of four of these substances are derived from read-across with a structurally similar substance or from a previous evaluation as already discussed more thoroughly in paragraph 3.3. Consequently, the impact of the revised guidelines on the restriction for these substances cannot be evaluated since these previous evaluations or the evaluations used for the read-across are not at our disposal.

Substances without change in tier

Seven of these substances (6 additives and 1 monomer) did not change in tier after application of the revised guidelines. Most of the substances were already classified in Tier 2 according to the current guidelines and remained in Tier 2 when the revised guidelines were applied. No additional toxicological data were thus required to set the restriction according to the revised guidelines. The new restrictions of these substances could range from 0.67 mg/kg to 5 mg/kg depending on the food group category responsible for the highest exposure calculation. For all but one substance, the first food group category delivered the highest exposure and therefore the new restriction for these substances was set at 0.67 mg/kg. Only for the additive sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salt (EFSA-Q-2005-151, FCM No. 813), the restriction remained unchanged since the third food group category delivered the highest exposure.

One substance, N,N-Bis(2-hydroxyethyl)dodecanamide, (EFSA-Q-2009-591, FCM No. 923) was classified as Tier 3 based on the migration data and required thus the core set of toxicological data. In addition to genotoxicity data, results of a 90 day subchronic toxicity study and ADME data, the results of a dermal chronic toxicity/oncogenicity study were provided. As described above, the migration limit was set at 5 mg/kg based on the results of the toxicological studies. After applying the revised guidelines, the substance remained in Tier 3. The restriction according to the revised guidelines was set by replacing the migration limit of 5 mg/kg by the migration limit corresponding to the combination of Tier 2 and food group category 1, i.e. 0.67 mg/kg. Consequently, the applicant should take precautions to ensure that the migration is kept below 0.67 mg/kg, while the specific migration data in the dossier varies from 10 mg/kg for simulant B (3% Acetic acid) to 16 mg/kg for simulant D2 (olive oil). It should further be discussed if the proposed restriction is feasible.

Substances with change in tier

Seven of the substances (1 monomer and 6 additives) restricted with a 0.05 mg/kg < SML ≤ 5 mg/kg, were classified as Tier 2 according to the current guidelines and changed to Tier 3 after the application of the revised guidelines.

As for the substances covered by a migration limit lower or equal to 0.05 mg/kg, exposure of most of the substances that changed in tier was calculated with specific migration data obtained with a non-adequate simulant and/or by using the LOD value. Only for two out of the seven substances that changed in tier, i.e. the additive N,N',N''-Tris (2-methylcyclohexyl)-1,2,3-propane-tricarboxamide (EFSA-Q-2008-698, FCM No. 870) and the additive 3,3',5,5'-tetrakis(tert-butyl)-2,2'-dihydroxy biphenyl, cyclic ester with [3-(3-tert-butyl-4- hydroxy-5-methylphenyl)propyl]oxyphosphonous acid (EFSA-Q-2008-678, FCM No. 792), specific migration data with the adequate simulant for food group category 1 were provided. Furthermore, migration in simulant D1 was clearly detected for both substances. Consequently, overestimation of migration due to the type of migration experiments or the use of the LOD was not applicable. Nevertheless, the migration conditions used might have been too severe compared to the intended use for food group category 1. Migration conditions should thus first be evaluated. In case no overestimation of migration is assumed, more toxicological data are required for these substances to set the restriction according to the revised guidelines.

Substances covered by a specific migration limit > 5 mg/kg or GML

All substances covered by a specific migration limit higher than 5 mg/kg were classified as Tier 3 according to the current guidelines and remained in Tier 3 when the revised guidelines were applied. Consequently, no additional toxicological data were required to set the restriction according to the revised guidelines. The new restrictions of these substances could range from 6.67 mg/kg to 50 mg/kg depending on the food group category responsible for the highest exposure calculation. An overview of the substances is given in Table 14.

Table 14: Summary of the impact of the revised guidelines on the substances covered by an SML higher than 5 mg/kg or GML

	Substance	Tier change ?	Possible overestimation of the migration?	Restriction (mg/kg)
Monomers	/			
Additives	Polyethylene, oxidized *EFSA-Q-2003-199, FCM No. 811*	No		6.67 mg/kg (Cat 1, Tier 3)
	Acids, Fatty (C8-C22), esters with pentaerythritol *EFSA-Q-2005-245, FCM No. 880*	No		6.67 mg/kg (Cat 1, Tier 3)
	Acids, Fatty (C8-C22), from animal or vegetable fats and oils, esters with branched alcohols, aliphatic, monohydric, saturated, primary (C3-C22) *EFSA-Q-2007-009, FCM No. 878*	No		6.67 mg/kg (Cat 1, Tier 3)

	Acids, fatty (C8-C22) from animal or vegetable fats and oil, esters with linear alcohols, aliphatic,monohydric, saturated, primary (C1-C22) *EFSA-Q-2007-032, FCM No. 879*	No		6.67 mg/kg (Cat 1, Tier 3)
	Acids, C2-C24, aliphatic, linear, monocarboxylic from natural oils and fats, lithium salts *EFSA-Q-2008-030, FCM No. 801*	No		6.67 mg/kg (Cat 1, Tier 3)
	Copper hydroxide phosphate *EFSA-Q-2010-708, FCM No. 972*	No		6.67 mg/kg (Cat 1, Tier 3)

For the six substances covered by a specific migration limit > 5 mg/kg or GML, all additives, the highest exposure value was found in the first food group category, leading to a restriction of 6.67 mg/kg. It should however be noted that for none of these substance, simulant D1 was used to obtain specific migration data.

In conclusion, the application of the revised guidelines had no impact on the toxicological data requirements for substances covered by a migration limit higher than 5 mg/kg.

3.3.3. Substances covered by a restricted use

Substances evaluated by the AFC/CEF Panel for a specific type of plastic or for only one type of use, are mostly covered by a 'restricted use' and not by a migration limit. Since the toxicological data required for these substances also depend on the migration data, the impact of the revised guidelines on the restricted use of the substances can be evaluated similarly to the discussion described above for the substances covered by a migration limit.

In analogy with the substances covered by a migration limit, substances covered by a restricted use can be divided into two categories based on the absence or presence of a change in tier. For the substances without a change in tier, no additional toxicological data are required, and the restriction will - in contrast to the substances covered by a migration limit - not change. On the other hand, if the appointed tier of the substance changes, more toxicological data may be required to evaluate if the restricted use can be maintained according to the revised guidelines.

Substances covered by a restricted use: Toxicological data corresponds to appointed tier

For twenty-one of the FCM substances covered by a restricted use, the results of toxicological studies triggered by the migration data were evaluated. In case sufficient toxicological data were provided and did not raise any concern, a restricted use was accorded to the substance instead of a migration limit. Two out of the 21 substances covered by a restricted used were allocated to SCF-list and discussed under 3.3.1. An overview of the remaining 19 substances is given in Table 15.

Table 15: Summary of the impact of the revised guidelines on the substances covered by a restricted use, where the toxicological data provided corresponds to the appointed tier.

	Substance	Tier change?	Possible overestimation of the migration?	Restriction (mg/kg)
Monomers	Bis(hydroxyphenyl)methane *EFSA-Q-2006-129, FCM No. 965*	No		No influence on the restricted use
	Trimethyl trimellitate *EFSA-Q-2010-838, FCM No. 971*	No		No influence on the restricted use
	(perfluorobutyl)ethylene (PFBE) *EFSA-Q-2010-1039, FCM No. 973*	No		No influence on the restricted use
	Glycolic acid *EFSA-Q-2010-1090, FCM No. 794*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)
	2-Hydroxypropyl methacrylate (HPMA) *EFSA-Q-2011-1239, FCM No. 995*	Yes	Yes, TMT	To be determined (non-adequate migration)
Additives	alpha-Alkenes(C20-C24) maleic anhydride-4-amino-2,2,6,6-tetramethylpiperidine, polymer *EFSA-Q-2006-171, FCM No .803*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)
	Tetrahydro-1,3,4,6-tetrakis(hydroxymethyl)imidazo-[4,5-d]imidazol-2,5(1H,3H)-dione *EFSA-Q-2006-315, FCM No.-*	Yes	Yes, TMT	To be determined (non-adequate migration)
	Titanium dioxide, coated with the copolymer of n-octyltrichlorosilane and [aminotris(methylenephosphonic acid), penta sodium salt)] *EFSA-Q-2007-019, FCM No. 805*	No		No influence on the restricted use
	Perfluoro acetic acid, a-substituted with the copolymer of perfluoro-1,2-propylene glycol and perfluoro-1,1-ethylene glycol, terminated with chlorohexafluoropropyloxy groups *EFSA-Q-2007-068, FCM No .854*	No		No influence on the restricted use
	Perfluoro[2-(n-propoxy)propanoic acid] *EFSA-Q-2008-683, FCM No. 861*	No		No influence on the restricted use
	Perfluoro[2-(poly(n-propoxy))propanoic acid] *EFSA-Q-2008-686, FCM No. 860*	Yes	Yes, TMT	To be determined (non-adequate migration)
	Hydrogenated homopolymers and/or copolymers made of 1-hexene and/or 1-octene and/or 1-decene and/or 1-dodecene and/or 1-tetradecene *EFSA-Q-2009-770, FCM No. 789*	No		No influence on the restricted use
	Titanium dioxide, reacted with octyltriethoxysilane *EFSA-Q-2009-917, FCM No. 873*	No		No influence on the restricted use
	Perfluoro[(2-ethyloxy-ethoxy)acetic acid], ammonium salt *EFSA-Q-2010-860, FCM No. 926*	No		No influence on the restricted use

	3H-Perfluoro-3-[(3-methoxy-propoxy) propanoic acid], ammonium salt *EFSA-Q-2010-1216, FCM No. 896*	Yes	Yes, TMT	To be determined (non-adequate migration)
	Sodium borohydride used in conjunction with palladium acetate *EFSA-Q-2011-067, FCM No. 981, 982*	No		No influence on the restricted use
	Sodium carbonate peroxyhydrate, bentonite, sodium chloride, sodium carbonate (Oxyfresh) *EFSA-Q-2011-236, FCM No. 1009*	No		No influence on the restricted use
	2H-Perfluoro-[(5,8,11,14-tetramethyl)-tetraeth yleneglycol ethyl propyl ether] (TFEE5) *EFSA-Q-2011-966, FCM No. 903*	No		No influence on the restricted use
	Titanium nitride, nanoparticles *EFSA-Q-2011-1079, FCM No. 807*	No		No influence on the restricted use

Substances without change in tier

For 13 substances, the tier did not change when the revised guidelines were applied, and consequently, the restricted use remained.

Only one out of the 13 substances was used as monomer. This substance is not present in the positive list of the EU Regulation 10/2011 as the monomer is used as precursor of BFDGE and thus restricted by the Commission Regulation 1895/2005 'only to be used to the manufacture of coatings applied in large volume containers for repeated use at ambient temperature'.

For most substances, the type of migration experiments used could have overestimated the migration. However, overestimation of migration did not pose a problem as no change in tier was observed.

Substances with change in tier

For substances that changed in tier, more toxicological data were needed to set the restriction according to the revised guidelines. However, as discussed for substances that changed in tier covered by a migration limit, the migration data used to calculate exposure according to the revised guidelines might have overestimated the migration. Consequently, factors contributing to overestimation of migration including the type of migration experiments (e.g. total mass transfer calculations, modelling, specific migration with a non-adequate simulant), the migration conditions or the use of a too high LOD to calculate exposure, should first be identified. In case migration has indeed been overestimated, more adequate migration data could be requested to the applicant. When the results of the new migration experiments confirm the change in tier, more toxicological data are needed to set the restriction.

Table 15 demonstrates that a change in tier occurred for 2 monomers and 4 additives. For all these substance, the first food group category was responsible for the highest exposure. Moreover, for none of these substances, specific migration data with a suitable simulant (D1 in the case of food group category 1) were present. Most of the migration data used were obtained by total mass transfer assumptions, while the migration data used for substances covered by a migration limit were mostly obtained from specific migration data. Only for the substances alpha-Alkenes(C20-C24) maleic

anhydride-4-amino-2,2,6,6-tetramethylpiperidine, polymer (EFSA-Q-2006-171, FCM No. 803) and Glycolic acid (EFSA-Q-2010-1090, FCM No. 794), specific migration with a non-adequate simulant and/or too high LODs were used for the exposure calculations for the first food group category.

As a result, more adequate migration data and/or toxicological data (according to the new appointed tier) might be demanded to the applicant in order to either confirm the tier by providing adequate migration data or to confirm that a higher tier classification is justified based on the results of the supplementary toxicological tests. Afterwards, the impact on the restricted use must be evaluated.

Substances covered by a restricted use: Substance made of authorised monomers

According to the EU Regulation 10/2011, polymeric substances are authorised as additive if they are capable of functioning as the main structural component of the final materials or articles. The substances in this category were all additives synthesized from authorised monomers. Consequently, these monomers have to be compliant with their proper restrictions and/or specifications. Furthermore, the migration of the low molecular weight fraction of these polymeric substances also needs to be evaluated. An overview of the substances classified in this category is given in Table 16.

Table 16: Summary of the impact of the revised guidelines on the substances covered by an SML higher than 5 mg/kg or GML

	Substance	**Tier change ?**	**Possible overestimation of the migration?**	**Restriction (mg/kg)**
Monomers	/			
Additives	Polyaddition product of glycidyl methacrylate with acrylic acid and/or methacrylic acid, esters with alcohols (C1-C4) aliphatic, monohydroxy, saturated *EFSA-Q-2006-203, FCM No. 958*	Yes	Yes, SM ≤ LOD	To be determined (non-adequate migration)
	(Butyl acrylate, methyl methacrylate) copolymer, crosslinked with allyl methacrylate *EFSA-Q-2007-025, FCM No. 866*	Yes	Yes, M	To be determined (non-adequate migration)
	(Methyl methacrylate, butyl acrylate, styrene) copolymer *EFSA-Q-2007-028, FCM No. 869*	Yes	Yes, M	To be determined (non-adequate migration)
	(Butyl methacrylate, ethyl acrylate, methyl methacrylate) copolymer (BMA/EA/MMA copolymer) *EFSA-Q-2007-030, FCM No. 867*	Yes	Yes, M	To be determined (non-adequate migration)
	Cyclic oligomers of (butylene terephthalate) *EFSA-Q-2007-096, FCM No. 885*	Yes	Yes, SM_N	To be determined (non-adequate migration)

	(Butadiene – styrene – methyl methacrylate – butyl acrylate) copolymer *EFSA-Q-2009-805, FCM No .856*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)
	(methyl methacrylate, butyl acrylate, styrene, glycidyl methacrylate) copolymer copolymer *EFSA-Q-2009-806, FCM No. 857*	Yes	Yes, TMT, SM_N ≤ LOD	To be determined (non-adequate migration)
	Butadiene, styrene, methyl methacrylate) copolymer *EFSA-Q-2009-807, FCM No. 855*	Yes	Yes, SM_N ≤ LOD	To be determined (non-adequate migration)
	Poly(12-hydroxystearic acid)-polyethyleneimine copolymer (extension of application) *EFSA-Q-2010-1244, FCM No. 812*	Yes	Yes, M	To be determined (non-adequate migration)
	(polyethylene terephthalate, hydroxylated polybutadiene, pyromellitic anhydride) copolymer *EFSA-Q-2010-1461, FCM No. 979*	Yes	Yes, M, SM_N ≤ LOD	To be determined (non-adequate migration)
	(Butyl acrylate, butyl methacrylate, methyl methacrylate) copolymer (BA-BMA-MMA) *EFSA-Q-2011-937, FCM No. 865*	Yes	Yes, M	To be determined (non-adequate migration)
	(ethyl acrylate, methyl methacrylate) copolymer (EA-MMA) *EFSA-Q-2011-938, FCM No. 868*	Yes	Yes, M	To be determined (non-adequate migration)
	1,4-Benzenedicarboxylic acid dimethyl ester, polymer with 1,4-butanediol, cyclized, polymers with glycidyl methacrylate, hydroxyl-terminated polybutadiene, methyl methacrylate and styrene *EFSA-Q-2011-967, FCM No. 1004, 1005*	Yes	Yes, M	To be determined (non-adequate migration)

It should be noted that no monomers are present in this category. Furthermore, the appointed tier has changed for all these substances after the application of the revised guidelines. Consequently, the toxicological data required have also changed. If more toxicological data are needed for one of the authorised monomers, this could not be evaluated since the evaluation of the monomers are not included in the dossier of the polymeric substance. By evaluating, the type of migration data provided, it can be concluded that all these migration data might overestimate the migration since they are based on modelling, Total mass transfer calculations and specific migration data with a non-adequate simulant. Only for the substance, Polyaddition product of glycidyl methacrylate with acrylic acid and/or methacrylic acid, esters with alcohols (C1-C4) aliphatic, monohydroxy, saturated (EFSA-Q-2006-203, FCM No. 958), adequate simulant was present for food group category 1, but a too high LOD was used for the calculations, so the migration can still be overestimated

3.3.4. Conclusion

For substances for which an ADI does not need to be established or for which a previously established ADI or equivalent value was considered acceptable, revision of the guidelines had no effect on the toxicological requirements.

Most of the substances covered by a migration limit received a different restriction according to the revised guidelines, regardless a change in tier. For substances without a change in tier, no additional toxicological data were required to set the new restriction. The value of the new restriction depended of the food group category containing the highest exposure value. For all substances covered by an SML ≤ 0.05 mg/kg without a change in tier, the new SML was set at 0.01 mg/kg as the highest exposure value was in all cases found in food group category 1. For most of the substances covered by an SML between or equal to 0.05 mg/kg and 5 mg/kg, the highest exposure value was also found in food group category 1 and consequently, the new SML value was set at 0.67 mg/kg. Only for one substance, the SML remained at 5 mg/kg since for this substance, the third food group category delivered the highest exposure value. Finally, none of the substances covered by a migration limit > 5 mg/kg, changed in tier and consequently, the new migration limit could just be set by identifying the food group category containing the highest exposure value. For all substances in this category, an SML of 6.67 mg/kg was set as category 1 was responsible for the highest exposure. For substances with a change in tier, additional toxicological data were required to set the restriction. However, exposure calculations were often performed with data overestimating migration. For this reason, the migration data were first further studied. In many cases, overestimation could indeed be expected. Only for the substance 3,3',5,5'-tetrakis(tert-butyl)- 2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5- methylphenyl)propyl] oxyphosphonous acid (EFSA-Q-2008-678, FCM No. 792), migration data were expected to be adequate.

For substances covered by a restricted use without a change in tier, no additional toxicological data were required and the restriction did not change. In contrast, for substances with a change in tier, additional toxicological data were required to evaluate if the restricted use could be maintained according to the revised guidelines. However, as for the substances covered by a migration limit, exposure calculations were often performed with data overestimating migration. For this reason, the migration data were first further studied. As for substances covered by a migration limit, overestimation could indeed be expected in many cases.

4. EVALUATION OF THE IMPACT OF THE REVISED GUIDELINES

Application of the revised guidelines had an impact on the toxicological requirements and the restrictions of many of the 73 model substances. For most substances that changed in tier, exposure calculations were however performed with data overestimating migration. When specific migration data with simulants adequate for the corresponding food group categories were provided and the substance and/or related migrants still changed in tier, the migration conditions had to be further evaluated. In case the experimental conditions were considered not to overestimate migration, it was concluded that more toxicological data are required.

In this section, some reflections on the impact of the revised guidelines are discussed, followed by a proposal for indicators to identify substances for which the application of the revised guidelines could potentially result in different data requirements or restrictions. Two types of indicators can be distinguished. The first category of indicators are those that are clearly derived based on the evaluation of the 73 model substances. These indicators can easily be applied to the substances of the Union list

included in EU Regulation 10/2011. The second category comprises the indicators based on assumptions regarding the migration data and should be applied to the Union list with a certain degree of uncertainty.

4.1. Reflections on the impact of the revised guidelines

4.1.1. Impact of the migration data on the changes in restriction and/or data requirement

Under 3.3, it was thoroughly discussed that in most cases, the migration data used for the exposure calculations might overestimate the real migration, e.g. migration data obtained by total mass transfer, modelling or specific migration data with non-adequate simulants. The use of overestimated migration data could have triggered a change in tier and subsequently a change in restriction, which would not have occurred when appropriate migration data (e.g. specific migration with an adequate simulant) were used.

Evaluation of the impact of the revised guidelines for the substances covered by adequate migration data

Only for fifteen out of the 73 model substances, adequate simulants were used to determine the specific migration of the substance and/or its related migrants (Figure 22). For fourteen of these substances, migration data obtained with simulant D1 were provided which allowed to calculate exposure for food group category 1 with adequate migration data. For the other substance, i.e. sodium carbonate peroxyhydrate, bentonite, sodium chloride, sodium carbonate (EFSA-Q-2011-236, FCM No. 1009), exposure only had to be calculated for food group category 3 based on the intended contact food (i.e. fresh fruit). Consequently, migration data obtained with simulant B were considered adequate for exposure calculations and no migration data with simulant D1 were required. Since migration was not overestimated, the fifteen substances covered by adequate migration data were considered most relevant to evaluate the impact of the revised guidelines on the data requirements and/or corresponding restrictions.

An overview of the substances with adequate specific migration data is given in Table 17.

Table 17: Overview of the substances for which migration data were obtained by specific migration studies with adequate simulants. The food group categories responsible for the highest exposure values, the occurrence of a change in tier and the possible reasons for overestimation of the migration were also included.

	Substance	**Food group category?**	**Tier change?**	**Possible overestimation of the migration?**
Monomers	2,2,4,4-tetramethylcyclobutane-1,3-diol (TMCD) *EFSA-Q-2008-202, FCM No. 881*	Cat 3	No	
	1,10-decanediamine *EFSA-Q-2009-674, FCM No. 863*	Cat 1	Yes	Migration conditions too severe
	2-Phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine *EFSA-Q-2009-834, FCM No. 872*	Cat 1	No	

Additives	Sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salt *EFSA-Q-2005-151, FCM No.813*	Cat 3	No	
	Alcohols C12-C14 Secondary. Beta.-(2hydroxyethyoxy)-ethoxylated *EFSA-Q-2006-183, FCM No. 802*	Cat 1	No	
	Polyaddition product of glycidyl methacrylate with acrylic acid and/or methacrylic acid, esters with alcohols (C1-C4) aliphatic, monohydroxy, saturated *EFSA-Q-2006-203, FCM No. 958*	Cat 1	Yes	Yes, SM ≤ LOD
	Sulphosuccinic acid, mono-alkyl (C10-C16) polyethyleneglycol esters, sodium salt *EFSA-Q-2006-324, FCM No. 814*	Cat 3	No	
	N-(2,6-Diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-1H-benzo[de]isoquinoline-1,3(2H)-dione *EFSA-Q-2007-199, FCM No.809*	Cat 1	No	
	3,3',5,5'-tetrakis(tert-butyl)-2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propyl]oxyphosphonous acid *EFSA-Q-2008-678, FCM No. 792*	Cat 1	Yes	More toxicological data required
	N,N',N''-Tris(2-methylcyclohexyl)-1,2,3-propane-tricarboxamide *EFSA-Q-2008-698, FCM No. 870*	Cat 1	Yes	Migration conditions too severe
	N,N-Bis(2-hydroxyethyl)dodecanamide *EFSA-Q-2009-591, FCM No. 923*	Cat 1	No	
	3,9-Bis[2-(3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propionyloxy)-1,1-dimethylethyl]-2,4,8,10-tetraoxaspiro[5,5]undecane *EFSA-Q-2009-769, FCM No 858*	Cat 3	No	
	Thiodipropionic acid, ditetradecyl ester *EFSA-Q-2010-935, FCM No. 894*	Cat 3	Yes	Yes, SM ≤ LOD
	Sodium borohydride used in conjunction with palladium acetate *EFSA-Q-2011-067, FCM No. 981, 982*	Cat 1	No	
	Sodium carbonate peroxyhydrate, bentonite, sodium chloride, sodium carbonate (Oxyfresh) *EFSA-Q-2011-236, FCM No. 1009*	Cat 3	No	

This table illustrates that substances with adequate migration data more frequently had the highest exposure value in food group category 3 (6 out of 15) compared to all 73 model substances (6 out of 73), for many of which no adequate migration data were provided (Figure 23).

Moreover, only five of the fifteen substances with adequate migration data changed in tier, corresponding to 33%, while more than 50% of all 73 model substances changed in tier (Figure 25). Migration could still have been overestimated for these five substances, although specific migration experiments with adequate simulants were performed. First, migration could have been overestimated when an LOD value was used to calculate exposure. For two substances, i.e. Polyaddition product of

glycidyl methacrylate with acrylic acid and/or methacrylic acid, esters with alcohols (C1-C4) aliphatic, monohydroxy, saturated (EFSA-Q-2006-203, FCM No. 958) and Thiodipropionic acid, ditetradecyl ester (EFSA-Q-2010-935, FCM No. 894), an LOD higher than 10 µg/kg was indeed used. Second, the conditions of the migration experiments could have been too severe, thereby overestimating the migration of a substance and related migrants. For all three remaining substances, the highest exposure value was found in food group category 1. Consequently, the migration conditions should have covered the intended contact foods corresponding to food group category 1, i.e. water and other liquids such as milk formula consumed by babies and infants up to 12 months old. The appropriate migration conditions for these contact foods can be derived from the EU Regulation 10/2011. For bottled water, the appropriate migration conditions could be 10 days at 40°C, while the appropriate migration conditions for milk formula are more difficult to decide. If the intended application is a baby bottle, than the migration conditions should be 2 hours at 70°C, but if the intended use is a packaging for milk formula, than the conditions could be 10 days (or less) at 40°C. Based on this information, the migration conditions for two out of the three remaining substances can certainly be considered as too severe. Indeed, migration of the substance N,N',N''-Tris(2-methylcyclohexyl)-1,2,3-propane-tricarboxamide (EFSA-Q-2008-698, FCM No. 870) was evaluated for 30 minutes at 121°C followed by 10 days at 40°C. For the substance 1,10-decanediamine (EFSA-Q-2009-674, FCM No. 863), 4 hours at reflux was used, which will also largely overestimate migration. No significant overestimation of migration was expected for the other substance, as migration was studied for 10 days at 40°C for simulant D1.

These data indicate that when migration data are obtained by specific migration studies with adequate simulants under appropriate migration conditions, the toxicological data requirements for most substances do not change. Only for one of the 15 substances with appropriate migration data, more toxicological data may be required, i.e the additive 3,3',5,5'-tetrakis(tert-butyl)-2,2'-dihydroxy biphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5-methylphenyl)propyl] oxyphosphonous acid (EFSA-Q-2008-678, FCM No. 792). This substance was classified as Tier 2 according to the current guidelines but changed to Tier 3 after applying the revised guidelines. Based on the results of the 90d subchronic toxicity study provided by the applicant, a NOAEL of 100 mg/kg bw/day was set. Although no chronic toxicity data or results of reproductive and developmental toxicity were available for this FCM substance, the NOAEL value based on the results of the subchronic toxicity study can be used to provide an indication if changing the restriction according to the revised guidelines would trigger a toxicological concern. When applying an extra safety factor of 5 to correct for the lack of chronic toxicity data and data on reproductive and developmental toxicity in addition to the safety factor of 100 to correct for inter- and intraspecies variability, a TDI of 0.2 mg/kg bw/day can be assumed which corresponds to an hypothetical SML of 12 mg/kg. The SML value according to the revised guidelines was set at 6.67 mg/kg as food group category 1 contained the highest exposure value (Table 10). This SML value is clearly below 12 mg/kg and consequently, no toxicological concern is expected when the restriction is changed according to the revised guidelines. Furthermore, the difference between the SML according to the current guidelines and the revised guidelines is very limited, i.e. 5 mg/kg and 6.67 mg/kg respectively.

4.1.2. Impact of the translation of the intended contact food in food group categories

In the revised guidelines, the toxicological data required are determined by the highest calculated exposure value of the three food group categories. Consequently, when a substance is destined to be used in FCM for food group category 3, this should also be defined in the restricted use. For some substances, combination of the migration data with consumption values of food group category 1 or 2 may indeed result in different toxicological requirements compared to those triggered by food group category 3. This is illustrated by the following hypothetical example:

In case the intended use of an FCM substance is limited to dry food, exposure only needs to be calculated for food group category 3. Under the hypothetical assumption that the specific migration of this substance is 1 mg/kg, an exposure of 20 µg/kg bw/day can be calculated for food group category 3, which triggers the toxicological requirements associated with Tier 2. When the limitation 'only to be used in materials used for food group category 3' is not included, the substance might also be used for a material in contact with foods covered by food group category 1. However, the calculated exposure for food group category 1 would be 150 µg/kg bw/day, thus requiring the toxicological information associated with a Tier 3 classification. The toxicological data provided in the initial application of the FCM substance for use for dry food would be insufficient.

In the current project, the situation described above never occurred. However, for future evaluations of substances covered by a restricted use, the intended contact food should be considered when setting the restriction.

4.1.3. Conclusion

Two factors that have an important impact on the outcome of the application of the revised guidelines include the migration data used to calculate exposure and the intended contact food of the FCM substance. For most substances with adequate migration data (obtained from specific migration experiments with adequate simulants and under appropriate migration conditions), no change in toxicological requirements was observed when the revised guidelines were applied. The intended contact food on the other hand determines the food group categories for exposure calculations, and so indirectly the restriction of the substance. Consequently, for future evaluations of substances covered by a restricted use, the intended contact food should be considered when setting the restriction.

4.2. Proposal for reliable indicators to identify substances for which the application of the revised guidelines will change the data requirements and/or restrictions

4.2.1. Indicators to identify substances for which the application of the revised guidelines will not require additional toxicological data

As already discussed in section 4.1.1, substances with adequate specific migration data obtained under appropriate conditions were considered most relevant to define indicators to identify substances for which the application of the revised guidelines will change the data requirements and/or restrictions. However, the number of substances with adequate specific migration data obtained under appropriate

migration conditions for which more toxicological data were required was limited to one out of 15. This substance, i.e. 3,3',5,5'-tetrakis(tert-butyl)- 2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5- methylphenyl)propyl] oxyphosphonous acid (EFSA-Q-2008-678, FCM No. 792), is an additive only to be used in polypropylene, intended to be in contact with all foodstuffs. Based on the characteristics of one substance, indicators for substances that will require more toxicological data when the revised guidelines are applied could not be defined. In contrast, the results of the evaluation of the 73 model substances allowed to propose some indicators for substances for which application of the revised guidelines will not affect the toxicological data requirements.

Substances classified in SCF-List '0' or '1'
As described under 3.3.1, the toxicological requirements of substances for which an ADI does not need to be established or for which a previously established ADI or equivalent value is considered acceptable (classified in SCF-list '0' and '1'), are not influenced by the revised guidelines. Therefore, 'classification in SCF-list 0 or 1' can be used as an indicator.

Substances SML = Not detected
In the Union list of the EU Regulation 10/2011, some substances are covered by a specific migration limit stating that the substance may not be detected with an LOD of 10 µg/kg. The migration limit of these substances will not be influenced by the revised guidelines since they will remain 'not detected'.

Substances covered by SML > 5 mg/kg or GML
All substances covered by an SML higher than 5 mg/kg or the GML are classified as Tier 3 according to the current guidelines. These substances remain in Tier 3 when the exposure based approach as described in the revised guidelines is used. Consequently, the toxicological requirements for the substances covered by a migration limit higher than 5 mg/kg do not change after the application of the revised guidelines.

4.2.2. Indicators to identify substances for which application of the revised guidelines will require more adequate migration data

Most of the changes in toxicological requirements for a substance and/or related migrants were due to the lack of adequate migration data (see 3.2). Indeed, specific migration data obtained with adequate simulants were only available for 3 out of the 36 FCM substances that changed in tier. For the remaining 33 substances, migration might have been significantly overestimated due to the methodology applied (modelling or total mass transfer), the adequacy of the simulants used or the use of the LOD to calculate exposure. In order to correctly evaluate the impact of the revised guidelines on the toxicological requirements and restrictions of these substances, more adequate migration data are needed for these substances. However, one of these substances, i.e. Malic acid (EFSA-Q-2007-182, FCM No. 499), was included in SCF-list '0' (see also section 86) and the change in tier was considered of no toxicological concern based on its ADI 'non specified'. For the remaining 32 substances, an attempt was made to define indicators to identify substances for which the application of the revised guidelines will require more adequate migration data.

Since the indicators were later used to extrapolate the results of the 73 model substances to all substances present in the Union list of EU Regulation 10/2011, the information that could be used to

define an indicator was limited. Potential indicators that were evaluated included the technological function, the type of restriction, restricted use covering material types, intended contact food or other conditions of use.

Technological function

The EU Regulation 10/2011 describes whether the FCM substance can be used as additive or polymer production aid or as monomer or other starting substance. Consequently, the technological function of the substance was considered to be a good candidate indicator and the potential relationship between the technological function of the substance and the need for more adequate migration data was investigated (Figure 29).

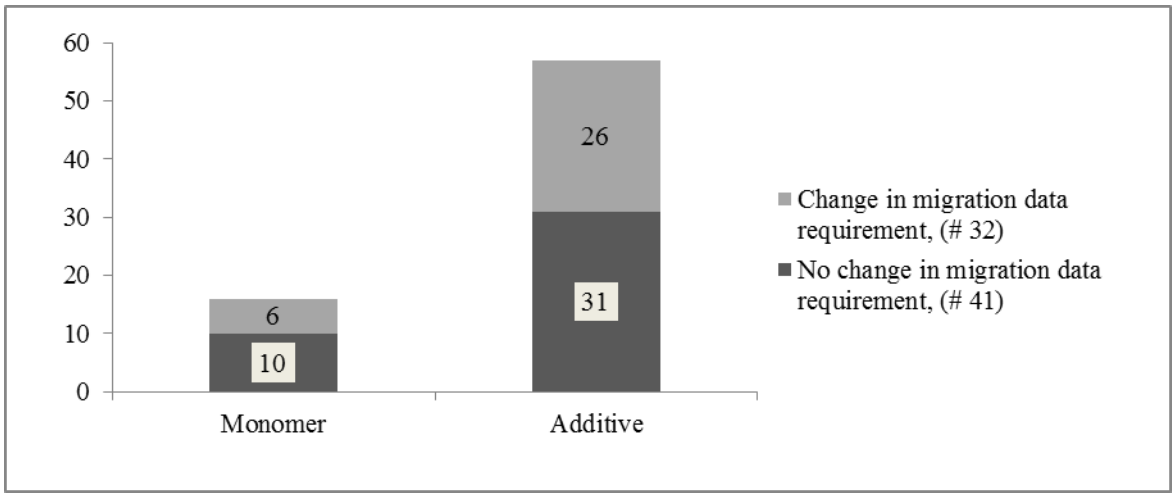

Figure 29: Overview of the number of substances for which the application of the revised guidelines did or did not require more adequate migration data as a function of the technological function.

Figure 29 illustrates that there was no clear relation between the technological function and the need for more adequate migration data, since 6 monomers (out of 16) and 26 (out of 57), required more migration data.

For those of the 73 model substances used as additives, more detailed information on the technological function was provided, e.g. use as plasticizer, stabilizer… An overview of additives according to the different subcategories and the impact of the revised guidelines on the data requirements is given in Figure 30. Only the subcategories containing more than 1 substance were included in Figure 30. Other subcategories like antistatic agent, clarifying agent, processing agent,… were only represented by 1 of the 73 model substances. Furthermore, some substances were covered by more than one subcategory, e.g. Acids, fatty (C8-C22) from animal or vegetable fats and oils, esters with linear alcohols, aliphatic, monohydric, saturated primary (C1-C22) (EFSA-Q-2007-032, FCM No. 879) which can be used as release agents, plasticizer and lubricant. Consequently, the total number of additives presented in Figure 30 is 50 instead of 57.

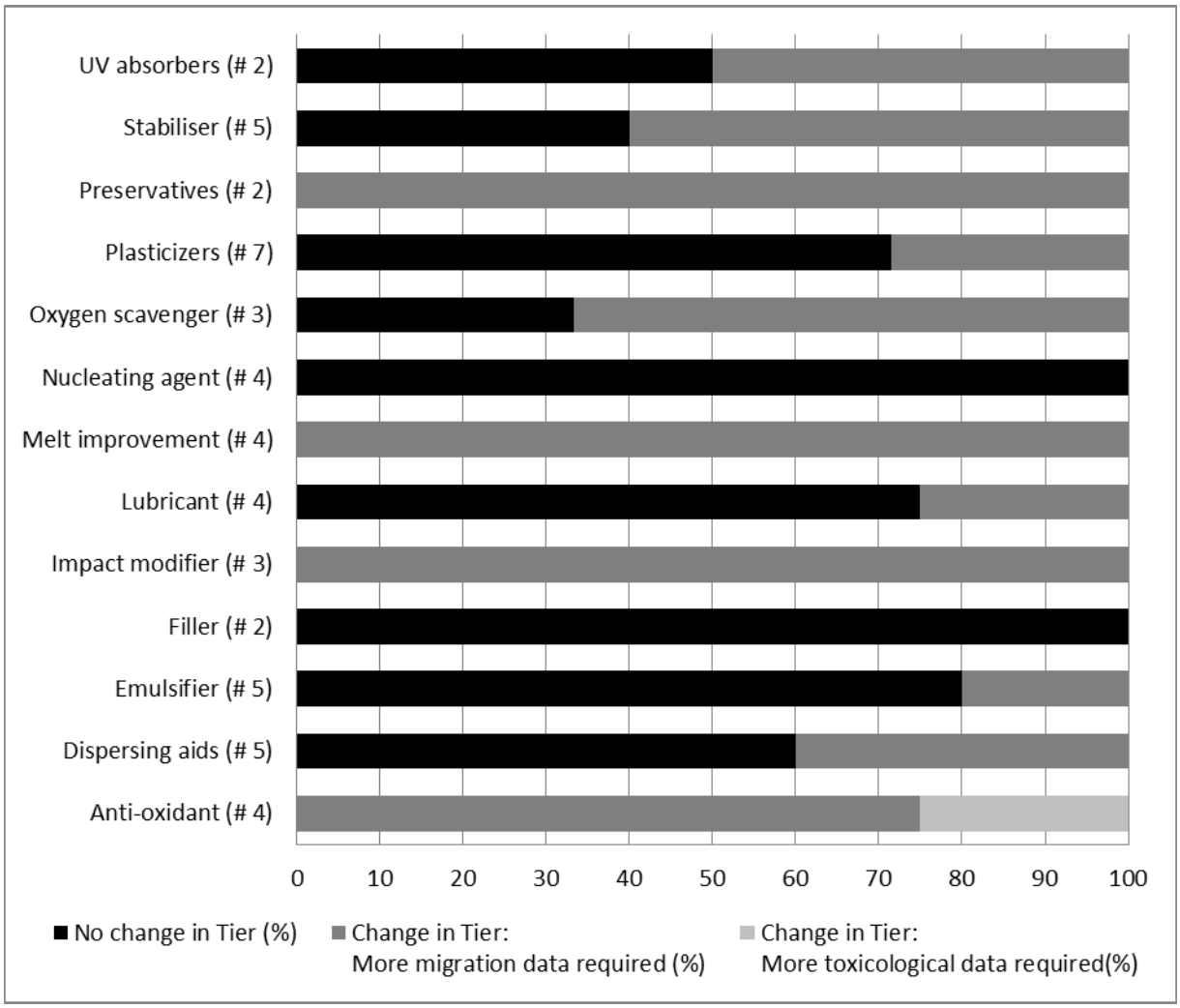

Figure 30: Overview of the impact of the revised guidelines on the data requirements for the different subcategories of additives (based on the detailed technological function).

Analysis of the data presented in Figure 30 reveals that the application of the revised guidelines changed the data requirements of all additives used as nucleating agents or fillers, whereas the data requirements of all additives used as preservatives, melt improvement or impact modifier remained unaltered. For all the other subcategories, no clear association could be established between the specific technological function of the additive and the need for more adequate migration data. These data indicate that the specific technological function of a substance can only be used as an indicator for the following subcategories of additives:

- Nucleating agents,
- Fillers,
- Preservatives,
- Melt improvement,
- Impact modifier

These indicators should however be applied with caution as they were defined based on a limited number of additives.

Nature of the foodstuffs in contact

Another potential indicator to identify substances for which the application of the revised guidelines will require more adequate migration data included the nature of the intended contact food (Figure 31).

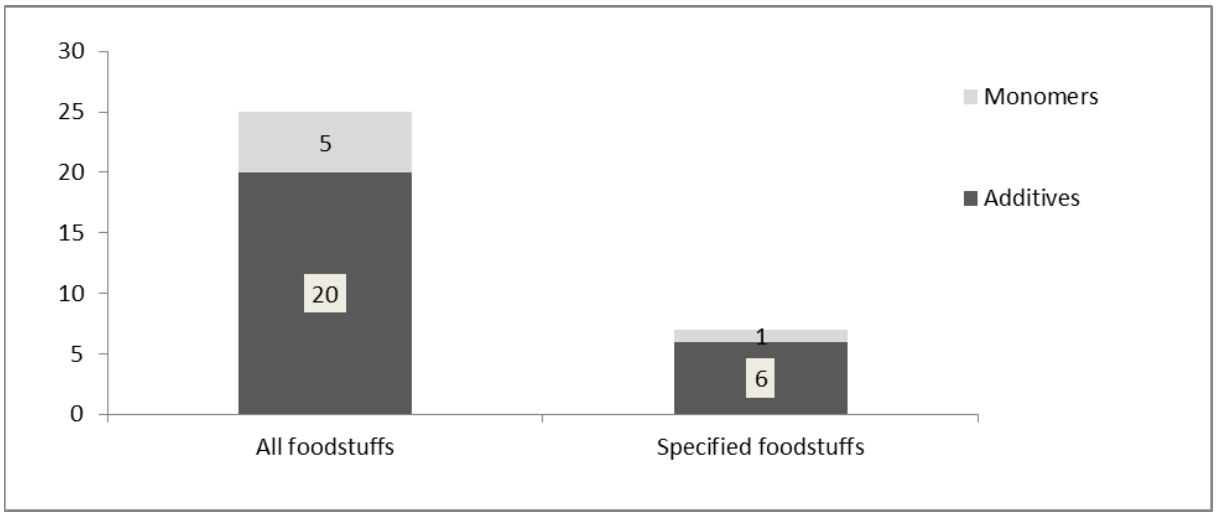

Figure 31: Overview of the number of monomers and additives requiring more adequate migration data as a function of the intended contact food.

Figure 31 illustrates that 25 FCM substances (20 additives and 5 monomers) for which more adequate migration data were required according to the revised guidelines, were intended to be used in contact with 'all foodstuffs'. When the intended contact food was more specified, adequate migration data were still requested for 7 substances (1 monomer and 6 additives). Consequently, the combination of intended contact food with the technological function of the substance cannot be used as an indicator to identify the substances for which more adequate migration data will be required according to the revised guidelines.

Use of the substances

The use of the substance was also considered as a candidate indicator. An overview of the FCM substances requiring more adequate migration data as a function of the use of the substance is given in Figure 32.

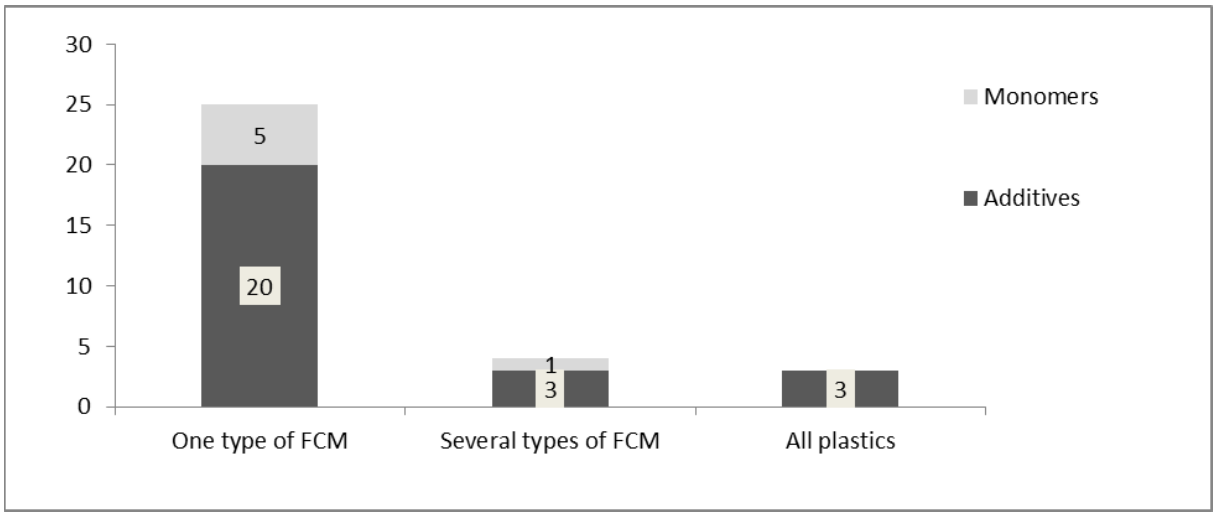

Figure 32: Overview of the number of monomers and additives requiring more adequate migration data as a function of the use of the substance.

The data presented in Figure 32 indicate that 25 of the FCM substances requiring more adequate migration data (20 additives and 5 monomers) were used in only one type of FCM. In contrast, the number of additives intended to be used in all types of plastic for which more toxicological data were needed was limited to 3.

For those of the 73 model substances used in one type of FCM, more detailed information on the type of FCM was provided, e.g. PO, PET, PVC, PA,…. For the type of FCM, for which more than one substance was present in the database, its potential as indicator was evaluated. The results are given in Figure 33.

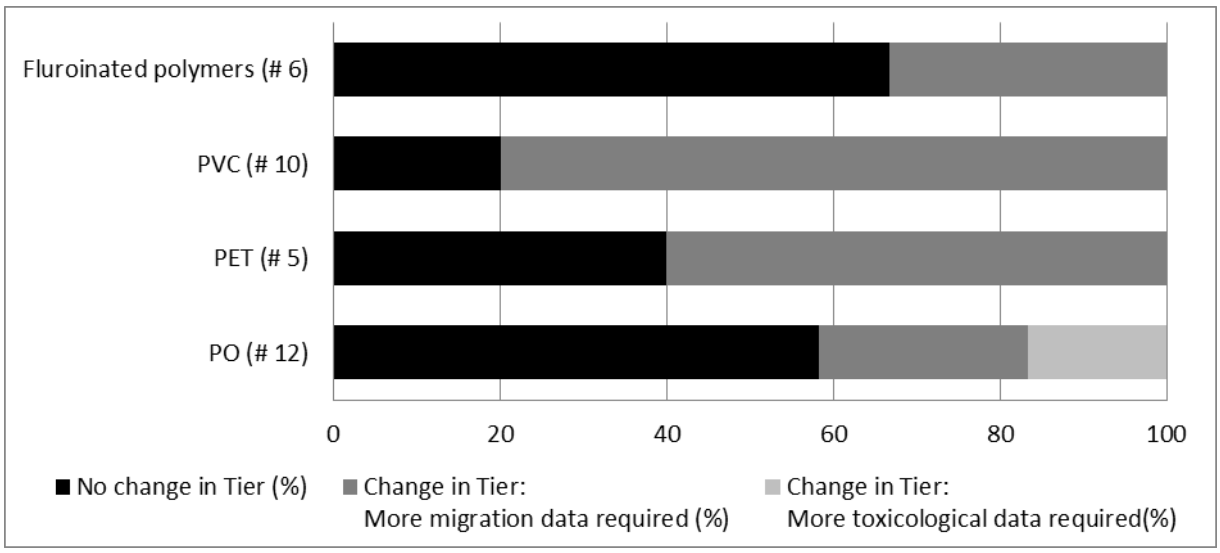

Figure 33: Overview of the impact of the revised guidelines on the data requirements for the different single types of FCM covered by more than one substance (# 33).

From this Figure, it can be seen that the detailed information on the type of FCM, for the substances intended to be used in only one type of FCM, cannot be used as an indicator to predict the impact of the application of the revised guidelines on the data requirements.

Type of restriction

Another potential indicator was the type of restriction according to the current guidelines. An overview of the need for more adequate migration data as a function of the type of restriction is given in Figure 34.

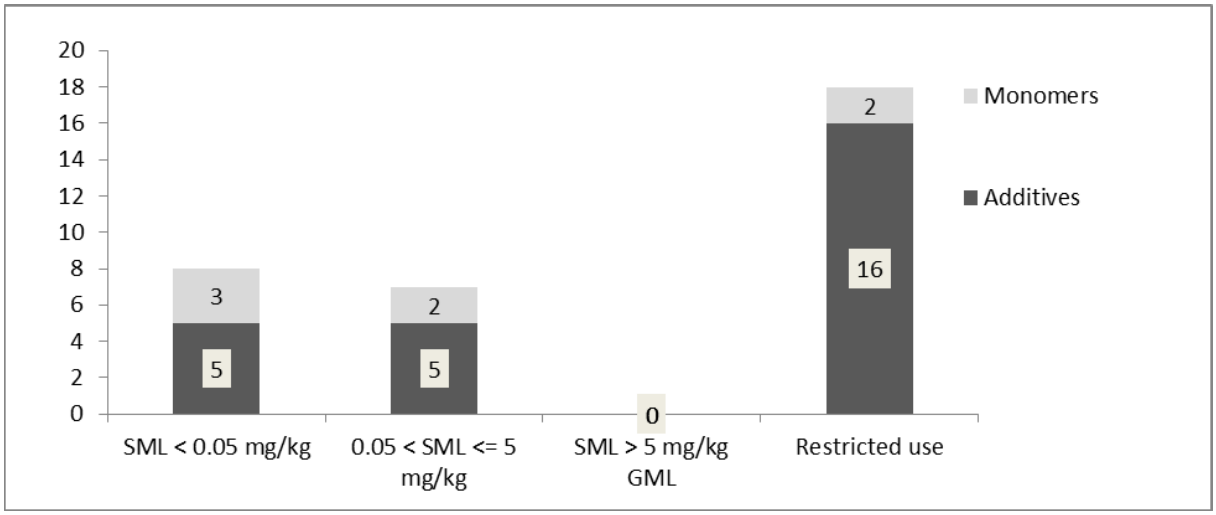

Figure 34: Overview of the number of monomers and additives requiring more adequate migration data as a function of the type of restriction.

Figure 34 confirms that substances covered by an SML > 5 mg/kg or a GML according to the current guidelines did not require more adequate migration data when the revised guidelines were applied (see also 4.2.1.). For the other types of restriction, no clear correlation could be found between the need for more adequate migration data and the combination of the technological function and the type of restriction of the substance.

4.2.3. Conclusion

Reliable indicators to identify substances for which the application of the revised guidelines will require additional toxicological data could not be defined as only one substance with adequate migration data changed in tier. In contrast, reliable indicators to identify substances for which the application of the revised guidelines will not require additional toxicological data could be set. These indicators include (i) substances for which an ADI did not need to be established or for which a previously established ADI or equivalent value was considered acceptable, (ii) substances with SML = Not detected and (iii) substances covered by SML > 5 mg/kg or GML. For the substances not covered by adequate migration data, an attempt was made to set indicators based on some straightforward characteristics of the FCM substances. However, no clear indicators could be defined to identify substances for which application of the revised guidelines will trigger the need for more adequate migration data.

4.3. Proposal for indecisive indicators to identify substances for which the application of the revised guidelines will change the data requirements and/or restrictions

No reliable indicators to identify substances for which the application of the revised guidelines will change the data requirements and/or restrictions, could be defined based on the most straightforward characteristics of the FCM substances. For this reason, indicators containing a certain degree of uncertainty ('indecisive') were proposed to further identify substances for which the application of the revised will not require more adequate migration data.

4.3.1. Indecisive indicators based on the use of the limit of detection to estimate migration

As discussed under section 3.2.3, for some of the FCM substances, the LOD value was used to calculate the exposure according to the revised guidelines. In case the LOD was too high compared to the threshold values of the toxicological tiers according to the revised guidelines, the FCM substance may have changed in tier thereby triggering the need for more toxicological data or more adequate migration data. According to the current guidelines, FCM substances and related migrants were classified as Tier 1 in case migration was below 50 µg/kg. Consequently, substances and related migrants were allocated to tier 1 in case (i) the substance was not detected by a method with an LOD below 50 µg/kg, or (ii) modelling or total mass transfer calculations demonstrated that the migration was expected to be below 50 µg/kg, without giving the exact migration (the migration was expressed as 'lower than a certain value'). When the revised guidelines are applied, however, the LOD should not be higher than 10 µg/kg in order to obtain a Tier 1 classification for food group category 1.

For 21 out of the 32 substances requiring more adequate migration data, an LOD or migration data derived from modelling or total mass transfer calculations (with a result 'lower than') was used for the exposure calculations. Migration data of most of these substances were obtained by specific migration studies with non-adequate simulants and expressed as a function of an LOD that was too high. For one substance, i.e. Bis(2,6-diisopropylphenyl)carbodiimide (EFSA-Q-2010-813, FCM No. 971), the migration data were derived from total mass transfer calculations, thus resulting in a migration expressed as '< 48 µg/kg'. For six other substances covered by modelling data, similar values were obtained. For example, modelling of the migration of the copolymer of methyl methacrylate, butyl acrylate and styrene (EFSA-Q-2007-028, FCM No. 869) resulted in a value of 30 µg/kg.

For these 21 substances, it is unclear whether migration will actually trigger a change in toxicological requirements as migration values are only indicated to be lower than a particular value. In order to confirm that the amount of substance and/or related migrants that migrate will not result in exposure values that exceed the threshold values of the revised guidelines, the applicant could be asked to submit more adequate migration data. However, when accepting a certain level of uncertainty, it can be assumed that migration of all substances and related migrants will be low enough to ensure no change in tier. Based on this assumption, the number or substances requiring more adequate migration data can be reduced from 32 to 11.

As discussed under 4.2.2, migration data used to calculate exposure of these 11 substances might have been significantly overestimated due to the use of non-adequate simulants in the specific migration, total mass transfer calculations or migration modelling. In case the change in toxicological requirements was triggered by an exposure value close to the lower threshold value of the tier of the revised guidelines, it can be assumed that the substance will not change in tier when adequate migration data are used. Substances for which the change in tier was triggered by an exposure value close to the lower threshold of the tier include:

- 3-Methyl-1,5-pentanediol (EFSA-Q-2007-077, FCM No. 883):
  The exposure calculation results in a value of 2.3 µg/kg bw/day for food group category 1 which is very close to the threshold of 1.5 µg/kg bw/day
- Silver Zeolite A (EFSA-Q-2009-708, FCM No. 946):
  The exposure calculation results in a value of 6 µg/kg bw/day for food group category 1 which is still in the lower bound of Tier 2 according to the revised guidelines.
- Poly(12-hydroxystearic acid)-polyethyleneimine copolymer (EFSA-Q-2010-1244, FCM No. 1244):
  The change in Tier is triggered by the oligomeric fraction with an exposure calculation of 111 µg/kg bw/day which is very close to the upper limit of Tier 2.

Based on this assumption, the number of substances requiring more adequate migration data can be further reduced to 8.

After applying the two assumptions, the adequateness of the candidate indicators proposed under 4.2.2 to identify substances for which application of the revised guidelines will require more adequate migration data was re-evaluated.

Technological function

Figure 35 illustrates that, even when a certain degree of uncertainty is taken into account due to the assumptions regarding the too high LOD and the exposure values close to the threshold, the technological function can still not be used as an indicator to identify substances for which the application of the revised guidelines will require more adequate migration data. Indeed, more adequate migration data were required for 2 out of the 16 monomers and 6 out of the 57 additives.

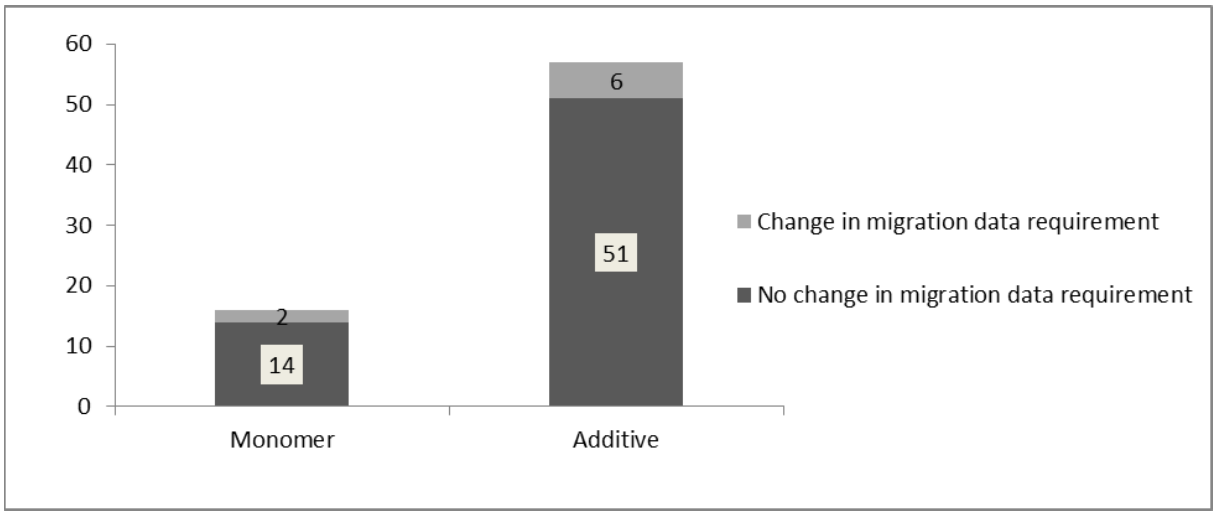

Figure 35: Overview of the number of substances for which the application of the revised guidelines did or did not require more adequate migration data, taking into account the assumptions related to a too high limit of detection and exposure values close to the thresholds, as a function of the technological function.

The specific technological function of the additives was also re-evaluated as indicator to identify substances that will require more adequate migration data according to the revised guidelines (Figure 36).

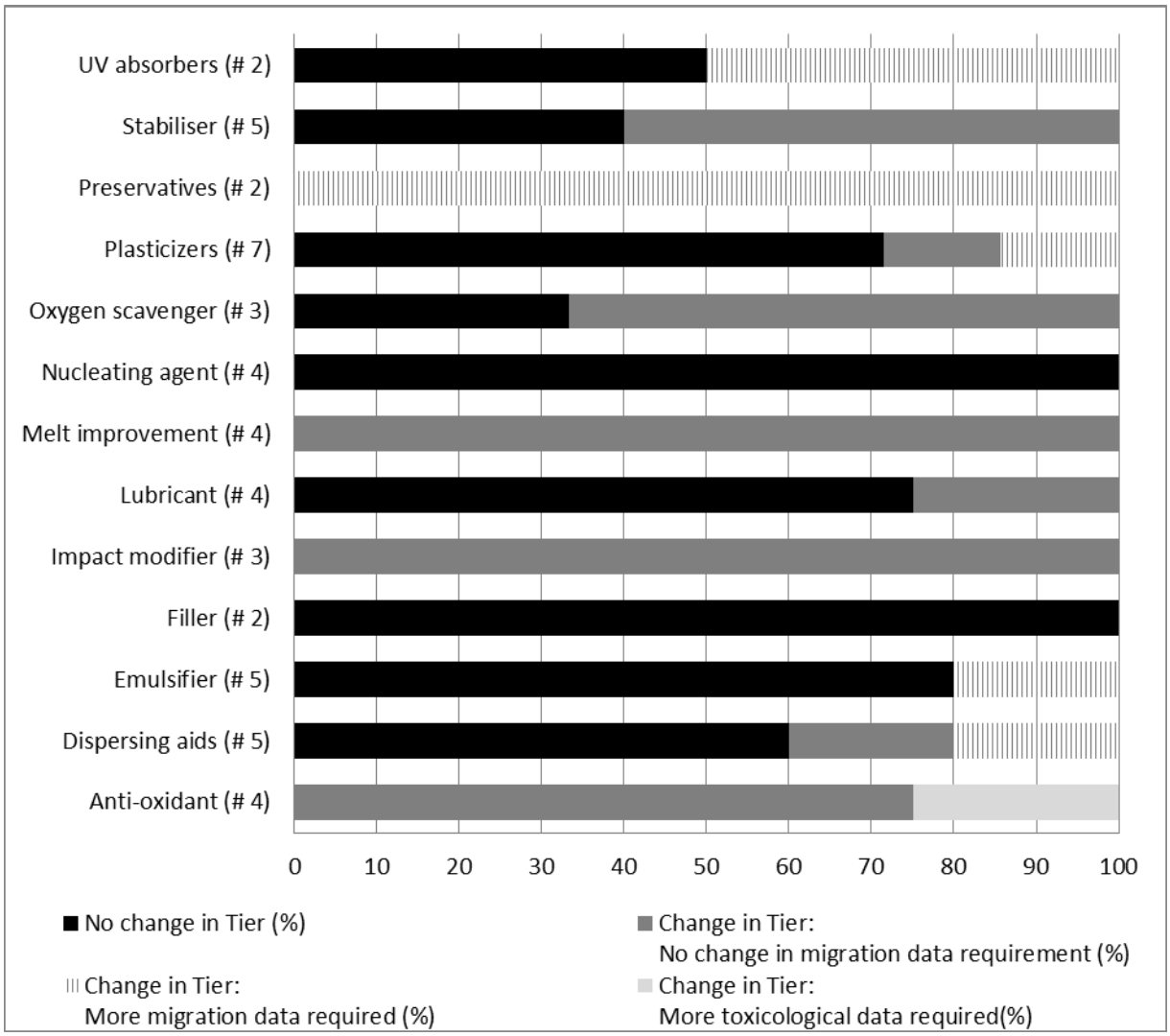

Figure 36: Overview of the impact of the revised guidelines on the data requirements for the different subcategories of additives (based on the detailed technological function) taking into account the assumptions related to a too high limit of detection and exposure values close to the thresholds.

The data presented in Figure 36 indicate that when the assumptions discussed above are taken into account, more adequate migration data were not required for additives used as a stabiliser, oxygen scavenger, nucleating agent, lubricants, melt improvement or impact modifier. Furthermore, more adequate migration data were needed for all additives used as preservative.

Based on these data, the following subcategories of additives can be proposed as indicators:

- Stabilisers
- Oxygen scavenger
- Nucleating agents,
- Lubricants,
- Melt improvement,
- Impact modifier

- Preservatives

However, these indicators should only be applied with extreme caution as they are based on a limited number of substances.

Nature of the foodstuffs in contact

Next, the potential relationship between the need for more adequate migration data after applying the two assumptions and the nature of the intended contact food was investigated (Figure 37).

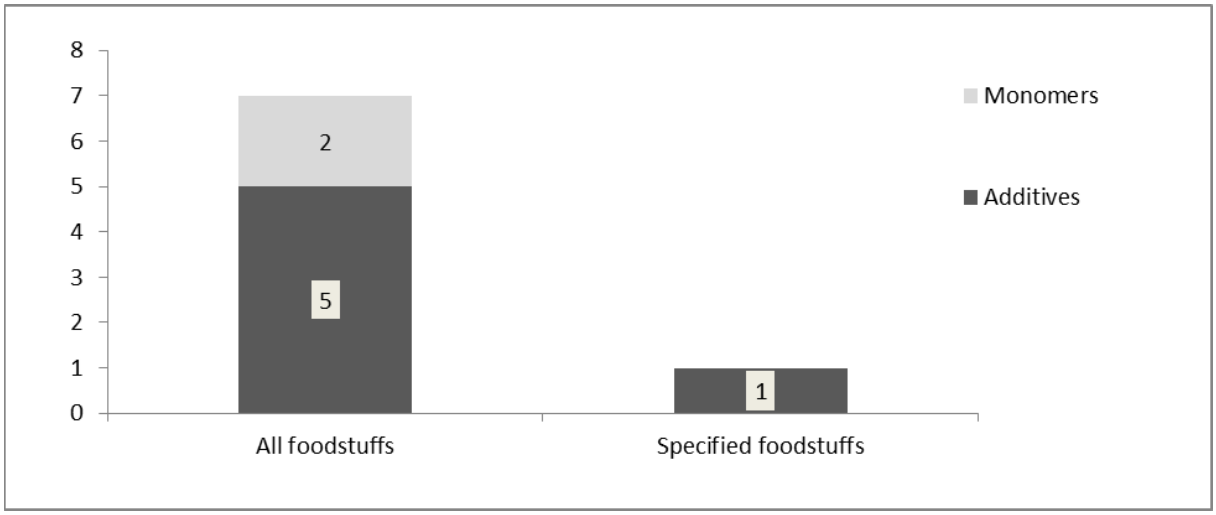

Figure 37: Overview of the number of monomers and additives requiring more adequate migration data taking into account the assumptions related to a too high limit of detection and exposure values close to the thresholds, as a function of the intended contact food.

Figure 37 illustrates that 7 (5 additives and 2 monomers) out of the 8 substances requiring more adequate migration data were intended to be used in contact with 'all foodstuffs'. When the intended food contact was more specified, adequate migration data were only requested for 1 additive. These data indicate that the combination of intended contact food contact with the technological function of the substance, can still not be used as indicator to identify substances for which more adequate migration data according to the revised guidelines.

Use of the substances

A re-assessment of 'the use of the substance' as an indicator was performed (Figure 38).

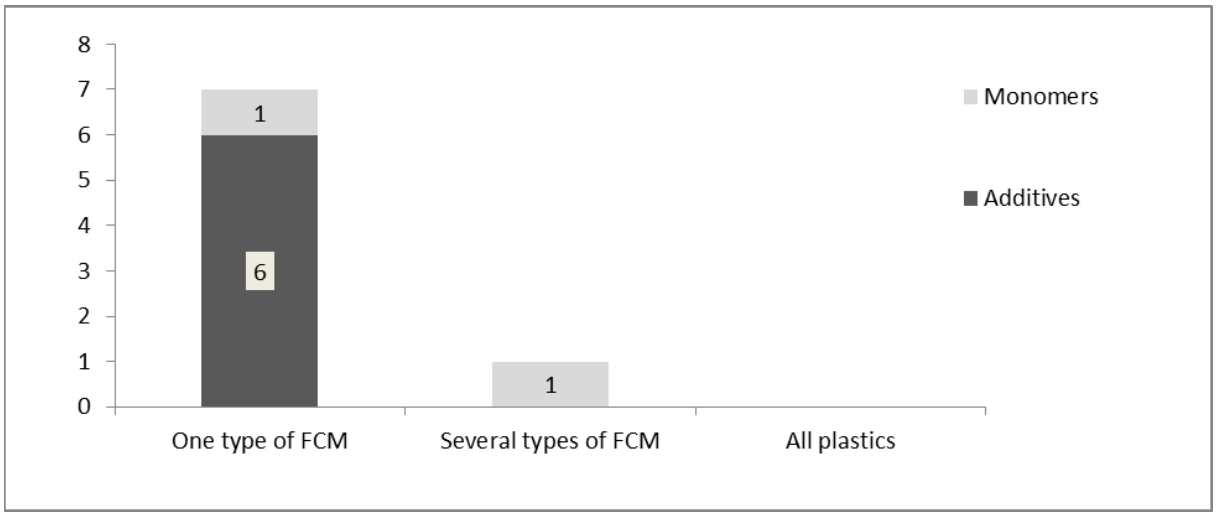

Figure 38: Overview of the number of monomers and monomers requiring more adequate migration data taking into account the assumptions related to a too high limit of detection and exposure calculations close to the thresholds, as a function of the use of the substance

The data presented in Figure 38 indicate that 7 (6 additives and 1 monomers) out of the 8 substances requiring more adequate migration data are used in only one type of FCM. Only one substance for which more adequate migration data were needed according to the revised guidelines was used in several types of FCM, whereas none of the substances was intended to be used in all types of plastic. Consequently, the combination of use of the substance and the technological function is not a good indicator, even when the two assumptions discussed above were taken into account.

The specific information on the use of the substance for those intended to be used in only one type of FCM was also re-evaluated as indicator. An overview of the results is given in . However, it should be noted that only the FCM covered by more than one substance are taken into account.

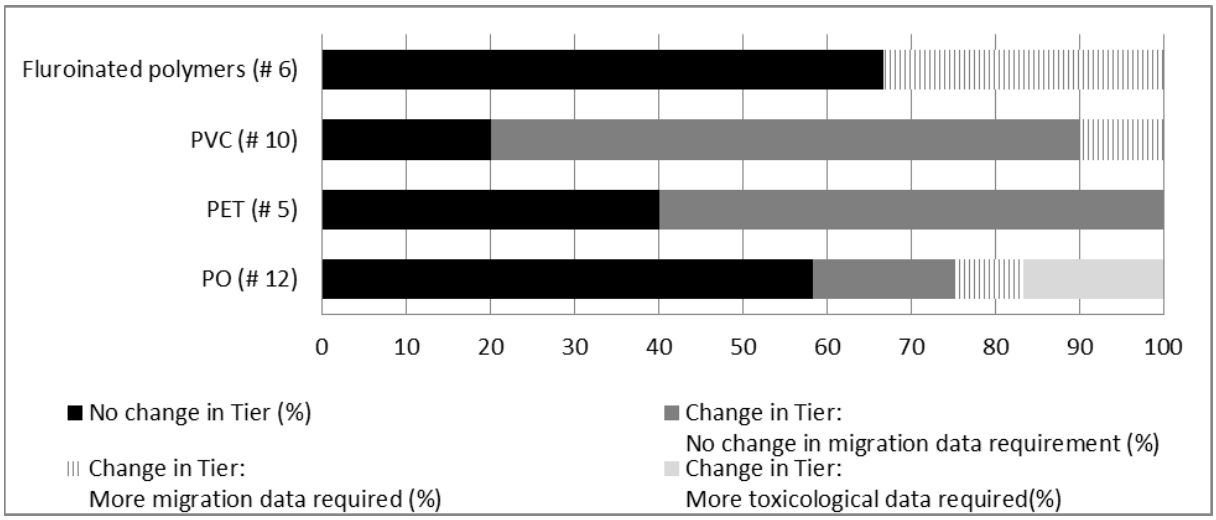

Figure 39: Overview of the impact of the revised guidelines on the data requirements for the different single types of FCM covered by more than one substance (# 33), taking into account the assumptions related to a too high limit of detection and exposure values close to the thresholds.

This figure indicates that when the assumptions discussed above are taken into account, more adequate migration and/or toxicological data were not required for substances intended to be used in PET. Consequently, this could be used as an indicator. However, this should be applied with extreme caution as they are based on a limited number of substances (only 5) and the assumptions related to a too high detection limit and exposure values close to the thresholds.

Type of restriction

Finally, the relation between the need for more adequate migration data and the combination of the technological function and the type of restriction was investigated when the assumptions discussed above were taken into account (Figure 40).

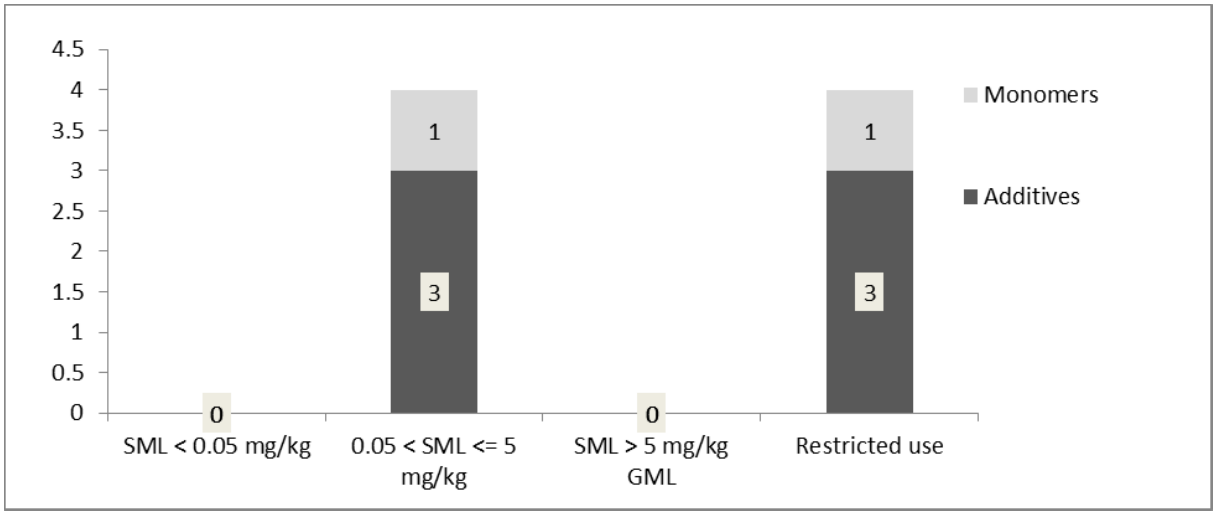

Figure 40: Overview of the number of monomers and additives requiring more adequate migration data taking into account the assumptions related to a too high limit of detection and exposure calculations close to the thresholds as a function of the type of restriction.

Figure 40 clearly shows that substances covered by an SML ≤ 0.05 mg/kg or by an SML > 5 mg/kg or GML are no longer requiring more adequate migration data when the above mentioned assumptions are taken into account. For substances covered by an SML > 5 mg/kg or GML, the lack of a need for more adequate migration data was already discussed under 4.2.1. For the other types of restriction, no clear correlation could be made between the combination of the technological function and the type of restriction of the substance.

The results discussed above reveal that an extra indicator to identify substances that will not require more adequate migration data according to the revised guidelines can be defined when a certain degree of uncertainty is accepted. Indeed, for substances covered by an SML ≤ 0.05 mg/kg that changed in tier, the change in tier was triggered by the use of a too high LOD for exposure calculations (or a result of the migration expressed as 'smaller than') or the calculated exposure value was very close to the threshold values. However, this indicator is based on some uncertainties and should therefore be applied with caution.

4.3.2. Indecisive indicators based on the NOAEL-values

If a certain degree of uncertainty is accepted, more adequate migration data are only required for eight out of the 73 model substances. Six out of these eight substances were classified as Tier 2 according to the current guidelines, and consequently, data on subchronic toxicity study and on the absence of a potential for accumulation in man had to be included in the submitted dossiers. For some of the substances, results of reproductive and/or developmental toxicity studies were also available. Based on the results of the 90d subchronic and/or developmental and reproductive toxicity studies, a NOAEL was set. These NOAEL values could be used to roughly evaluate whether changing the restriction according to the revised guidelines would trigger a toxicological concern.

First, the NOAELs of all substances classified as Tier 2 or Tier 3 according to the current guidelines, and for which data of a 90d-study and/or a developmental toxicity test were submitted, were investigated in more detail (Annex C).

As discussed under 3.3, the NOAEL-values can be used to evaluate whether a proposed SML would trigger a toxicological concern or not. In general, a TDI is calculated based on the NOAEL by applying a safety factor of 100 to correct for inter- and intraspecies variability. However, as no chronic toxicity data were available for the substances classified in Tier 2, an extra safety factor of 5 was applied to estimate the TDI. The TDI values were then used to calculate the potential migration limits for the FCM substances (Annex C).

Afterwards, the potential migration limits were compared to the migration limits according to the revised guidelines Table 10. Since the value of the migration limit depends of the food group category, the food group categories responsible for the highest calculated exposure were also included in Annex C. Although all three food group categories could contain the highest exposure value, none of the FCM substances with a highest exposure in food group category 2 or 3 changed in Tier. Consequently, the migration limit for food group category 1 in Tier 3 was used for the evaluation, i.e. 6.67 mg/kg.

For all substances that changed in tier due to the application of the revised guidelines, the potential SML was always higher than the threshold values of the revised guidelines. This is not surprising as the SML of 6.67 mg/kg is close to the maximum migration limit that could be set for substances classified in Tier 2 according to the current guidelines, i.e. 5 mg/kg. However, for the substances that did not change in tier, the available NOAEL-values would also not allow a higher tier classification.

These results indicate that for substances covered by an SML between 0.05 and 5 mg/kg according to the current guidelines which change in tier, in all cases, the available NOAEL-values indicate no direct toxicological concern when the SML according to the revised guidelines is set. However, it should be noted that only for some of the substances reproductive and/or developmental toxicity data were available. Furthermore, in case of extrapolation to the Union list, it would be recommended to evaluate the NOAEL-values of the substances covered by an SML between 0.05 and 5 mg/kg according to the current guidelines.

4.3.3. Conclusion

An indecisive indicator to identify substances for which the application of the revised guidelines will not require more adequate migration data could be defined, i.e. substances covered by an SML ≤ 0.05 mg/kg. This indicator contained a certain degree of uncertainty as it was based on two assumptions:

- **the real migration of substances for which a too high LOD was used to calculate exposure substances was assumed to be low enough to ensure that no additional toxicological data were required.**

- **the real migration of substances for which the exposure values were close to the lower threshold of the toxicological tier was assumed to be low enough to ensure that no additional toxicological data were required.**

An indecisive indicator to identify substances for which the application of the revised guidelines will not require more toxicological data could also be defined, i.e. substances covered by an SML between 0.05 and 5 mg/kg. This indicator contained a higher degree of uncertainty as its was based on the additional assumption that no direct toxicological concern occurs when the SML according to the revised guidelines is applied. The assumption was based on the observation that the NOAELs of all substances with an SML between 0.05 and 5 mg/kg that changed in tier allowed to set the SML according to the revised guidelines. This is not surprising as the SML of 6.67 mg/kg of food group category 1 combined with Tier 3 is close to the maximum migration limit that could be set for substances classified in Tier 2 according to the current guidelines, i.e. 5 mg/kg. Indecisive indicators should be applied with caution as they contain a certain amount of uncertainty.

5. EXTRAPOLATION OF THE RESULTS TO THE SUBSTANCES INCLUDED IN THE UNION LIST OF EU REGULATION 10/2011

The Union list of monomers, other starting substances and additives which may be used in the manufacture of plastic materials and articles, present in Annex I of EU Regulation 10/2011 has already been amended and corrected by Commission Regulation 1282/2011, 1282/2012 and 202/214. In total 861 substances are present in the Union list, of which 63 were included as a model substance in this project (see also Figure 3).

5.1. Information present in the EU Regulation 10/2011

The EU Regulation 10/2011 describes whether the FCM substance can be used as additive or polymer production aid or as monomer or other starting substance. The technological function of all substances included in the Union list could be easily collected from the database on substances known and used in FCM and an overview is provided in Figure 41.

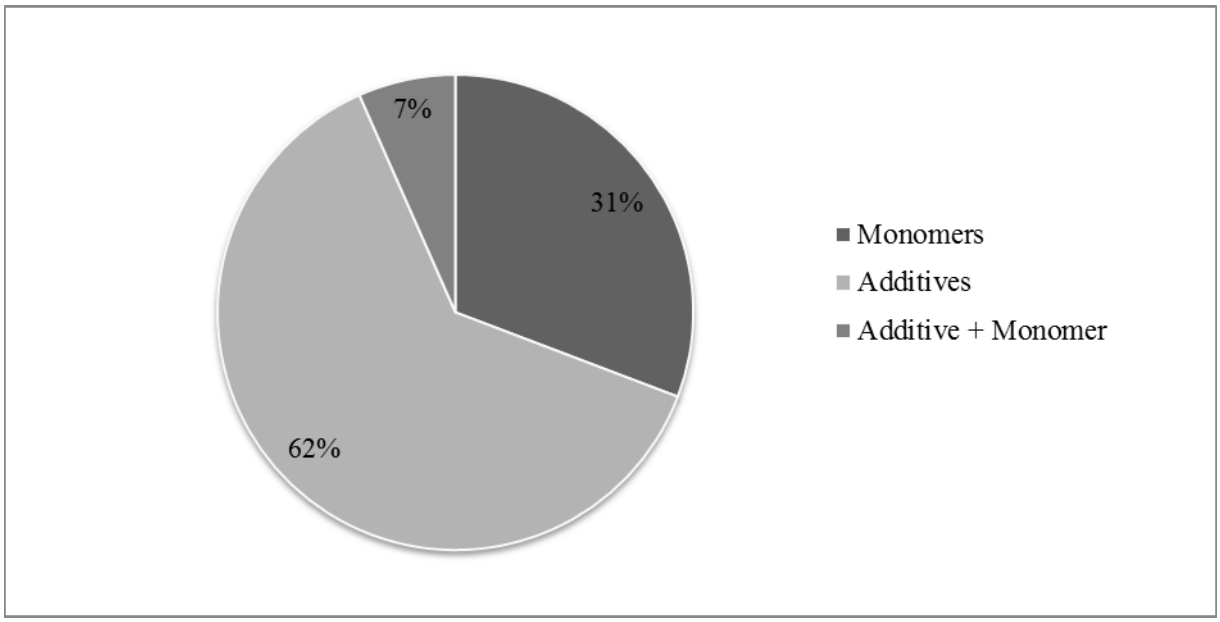

Figure 41: Overview of the technological function of the substances present in the Union list

Most of the substances from the Union list are used as additives (62%, corresponding to 539 out of 861 substances). Furthermore, 57 substances (corresponding to 7%) are authorised both as monomer and as additive.

In addition, an overview of the different types of restrictions of substances present in the Union list is given in Figure 42.

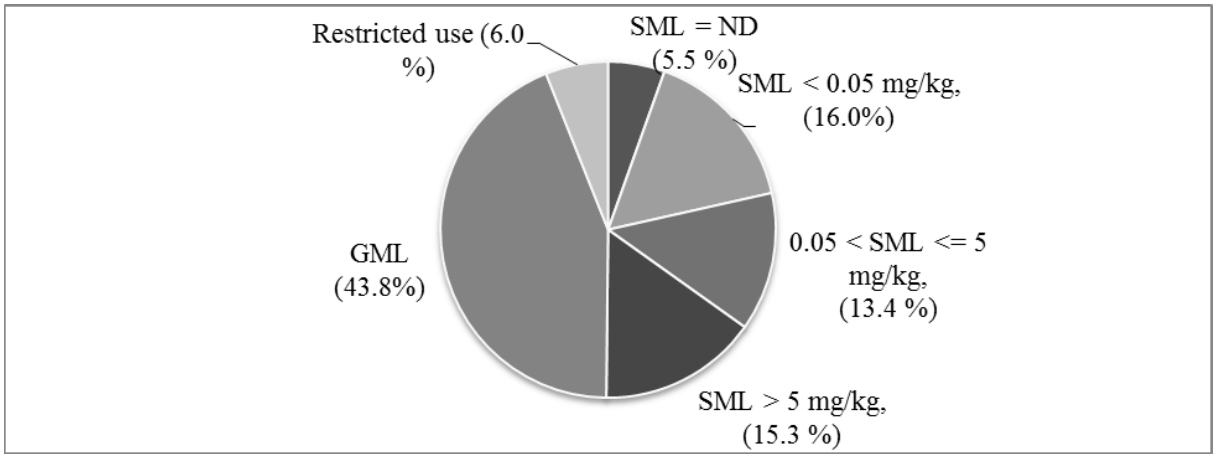

Figure 42: Overview of the restrictions of the substances present in the Union list of EU Regulation 10/2011.

Most of the substances present in the Union list of EU Regulation 10/2011, are covered by the generic migration limit (GML), followed by a specific migration limit higher than 5 mg/kg. Finally, Figure 42 illustrates that only a limited number of substances is regulated by a restricted use (6%), while the others are covered by a migration limit (specific or generic) ranging from 'not detected' to 60 mg/kg.

The information present in the Union list was used to evaluate the impact of the revised guidelines on the restriction and/or data requirement of all substances included in this list.

5.2. Evaluation of the impact of the revised guidelines on the data requirement

The SML values of all substances of the Union list covered by migration limit will change, even when the data requirements are not altered after application of the revised guidelines. However, this issue has been extensively discussed under 3.3.2 and consequently, the section below relates only to the impact of the revised guidelines on the data requirements for the substances included in the Union list.

5.2.1. Impact of the revised guidelines on the toxicological data requirement

As for many of the 73 model substances evaluated in the project adequate migration data were not available, indicators to identify substances for which the data requirements change according to the revised guidelines could not be defined. However, as discussed in section 4.2.1, several indicators were proposed to identify substances for which the application of the revised guidelines will not change the toxicological requirements. These indicators were applied to the 861 substances present in the Union List.

Substances classified in SCF-List '0' or '1'

As described above, the toxicological requirements of substances classified in list '0' and '1', are not influenced by the revised guidelines. In the Union list, 133 substance are classified in SCF list 0 or 1. Most of these substances (127 out of 133) are also covered by the GML or by an SML higher than 5 mg/kg. However, substances covered by the GML or an SML higher than 5mg/kg were also reported to be unaffected by the application of the revised guidelines. For substances allocated to SCF list 1 that are classified in tier 3 according to the current guidelines, the ADI or equivalent value can be used to evaluate whether changing the migration limit according to the revised guidelines will trigger a toxicological concern.

Substances SML = Not detected

In the Union list of the EU Regulation 10/2011, 47 substances are covered by a specific migration limit stating that the substance may not be detected with an LOD of 10 µg/kg. The migration limit of these substances will not be influenced by the revised guidelines since they will remain 'not detected'.

Substances covered by SML > 5 mg/kg or GML

Substances classified as Tier 3 according to the current guidelines, will remain in Tier 3 when the exposure based approach as described in the revised guidelines is followed. Consequently, the application of the revised guidelines has no impact on the data requirements of the substances covered by a migration limit higher than 5 mg/kg. In the Union list 509 substances are covered by the GML (377 substances) or an SML > 5 mg/kg (132 substances), and will thus not be influenced by the application of the revised guidelines. As discussed above, 127 out of the 509 substances are also classified in SCF-list 0 or 1.

The impact of the revised guidelines on the toxicological data requirement of all substances included in the Union list is illustrated in Figure 43.

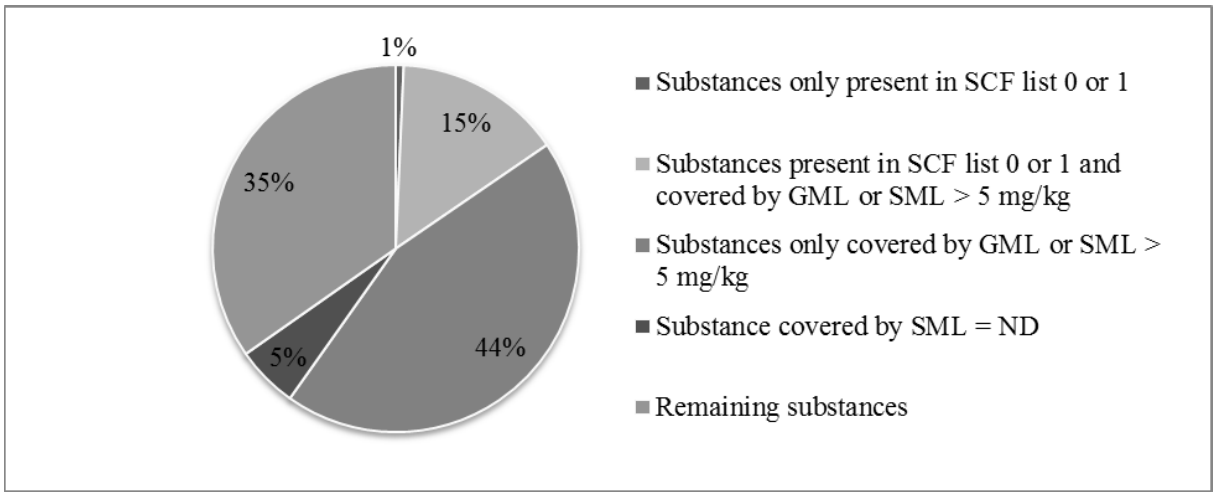

Figure 43: Overview of the impact of the revised guidelines on the data requirements for all 861 substances included in the Union list

The results presented in Figure 43 indicate that for 65% of the substances, the application of the revised guidelines will not influence the data requirements. However, the impact of the revised guidelines on the remaining 35% of the substances should be further evaluated.

5.2.2. Impact of the revised guidelines on the migration data requirement using reliable indicators

Although application of the proposed indicators allowed to identify 562 substances (65%) for which the data requirements will not change according to the revised guidelines, the impact on the data requirements remains unclear for 299 substances (35%) present in the Union list.

As discussed under section 4.2.2, no straightforward indicators to identify substances for which more adequate migration data will be required after the application of the revised guidelines could be defined. Consequently, indicators containing a certain degree of uncertainty ('indecisive') were proposed to further identify substances for which the application of the revised will not require more adequate migration data.

5.2.3. Impact of the revised guidelines on the migration data requirement using indecisive indicators

In section 4.3, some indecisive indicators were discussed. Application of these indicators to evaluate the impact of the revised guidelines on the substances present in the Union list should however be done with caution as they imply a certain degree of uncertainty.

Indecisive indicator: Substances covered by an SML ≤ 0.05 mg/kg will not require more data when they change in Tier.

The results of the evaluation of the 73 model substances indicated that for substances that change in tier and were covered by an SML ≤ 0.05 mg/kg according to the current guidelines, the change in tier was triggered by the use of a too high LOD for exposure calculations (or a result of the migration expressed as 'smaller than') or the calculated exposure value was very close to the threshold values. Consequently, for the 138 substances of the Union list of EU Regulation 10/2011 covered by an SML ≤ 0.05 mg/kg, the data requirements will not change according to the revised guidelines. One of the 138 substances, i.e. 1,2-Propyleneglycol distearate (FCM No. 491), was allocated to the SCF list 1 and was thus already identified as a substance for which the data requirements will not change according to the revised guidelines. As for this substance a previously established ADI or equivalent value exist, it would be interesting to evaluate whether changing the migration limit according to the revised guidelines will trigger a toxicological concern. Application of this indicator further decreased the number of substances for which the application of the revised guidelines alters the data requirements as 16% of the substances present of the substances present in the Union list (corresponding to 137 substances) are covered by an SML ≤ 0.05 mg/kg. Consequently, the application of the revised guidelines will have no impact on 81% of the substances present in the Union list. However, for 19% of the substances, the impact of the revised guidelines remains unclear.

Indecisive indicator: The NOAEL-values indicate no direct toxicological concern for the substances covered by an SML between 0.05 and 5 mg/kg.

Based on the available NOAEL-values for the substances that change in tier and that are covered by an SML between 0.05 and 5 mg/kg according to the current guidelines, there appeared to be no direct toxicological concern when the SML according to the revised guidelines was set. These results should however be considered with caution as only for some of the substances reproductive and/or developmental toxicity data were available. Nevertheless, for substances with the highest exposure value in food group category 1 and classified as Tier 3 according to the revised guidelines, the SML according to the revised guidelines will be 6.67 mg/kg, which is only slightly higher than the highest SML associated with Tier 2 according to the current guidelines, i.e. 5 mg/kg.

In the Union list of EU Regulation 10/2011, 115 substances are covered by an SML between 0.05 and 5 mg/kg. Two of these substances, Sodium Iodide (FCM No. 513) and 2,6-di-t-butylphenol-p-cresol (FCM No. 315) were allocated to SCF list 1, and were thus already identified as substances for which the data requirements will not change according to the revised guidelines. Again, an evaluation of the safety margin between the ADI or equivalent value and the migration limit according to the revised guidelines would be interesting. Application of the proposed indicator will thus identify 113 substances present in the Union list (13%) for which no more data will be required when the revised guidelines are applied. Consequently, the application of the revised guidelines will have no impact on 94% of the substances present in the Union list.

An overview of the impact of the application of these indecisive indicators is given in Figure 44.

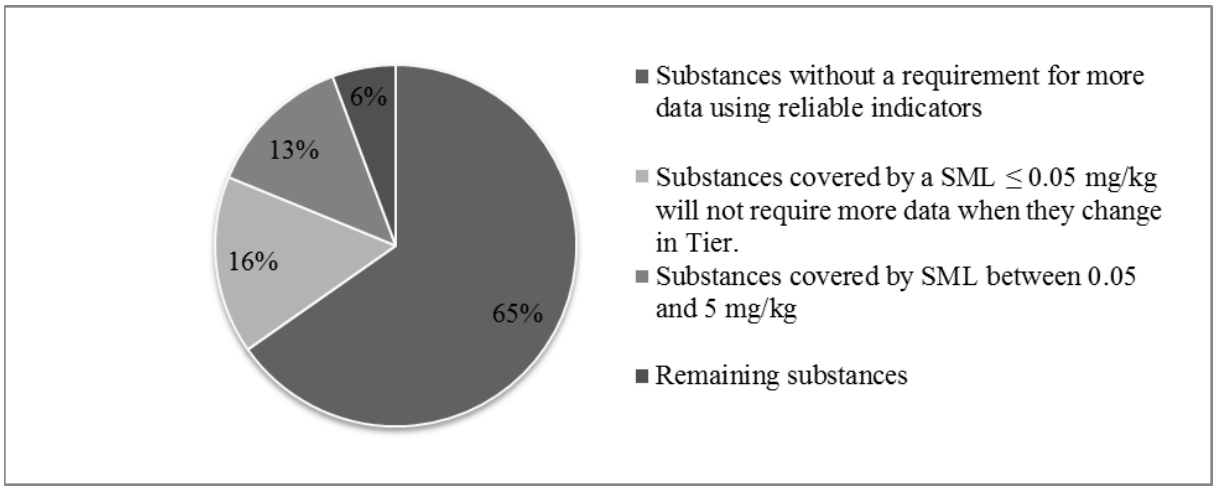

Figure 44: Overview of the impact of the revised guidelines on the data requirements for the substances of the Union list after application of the indecisive indicators

Figure 44 illustrates that the application of the revised guidelines will have an impact on the data requirements of 6% of the substances present in the Union list.

5.2.4. Evaluation of the data requirements for the remaining substances

Only for 6% of the substances present in the Union list of EU Regulation 10/2011, application of the revised guidelines will have an impact on the data requirements. This corresponds to 49 substances of which 25 substances were already included in the 73 model substances, resulting in 24 substances for which the impact of the revised guidelines is unknown.

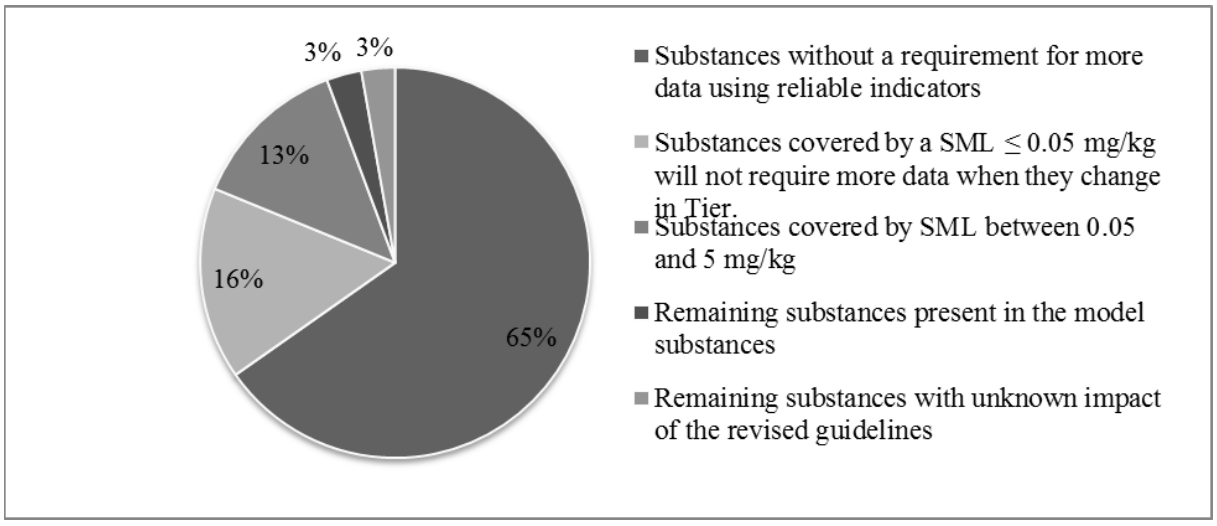

Figure 45: Overview of the impact of the application of the revised guidelines on the data requirement of the substances present in the Union list of EU Regulation 10/2011.

An overview of the 24 substances for which the impact of the application of the revised guidelines is unknown, is given in Table 18.

Table 18: Overview of the substances for which the impact of the revised guidelines on the data requirement is unknown.

FCM No.	*Substance*
65	Mixture of 4-(2-Benzoxazolyl)-4'-(5-methyl-2-benzoxazolyl)stilbene, 4,4'-bis(2-benzoxazolyl) stilbene and 4,4'-bis(5-methyl-2-benzoxazolyl)stilbene
94	Waxes, refined, derived from petroleum based or synthetic hydrocarbon feedstocks, high viscosity
95	White mineral oils, paraffinic, derived from petroleum based hydrocarbon feedstocks
97	Petroleum hydrocarbon resins (hydrogenated)
205	Triallylamine
411	Carbon black
419	Tannic acids
426	2,2-Bis(4-Hydroxyphenyl)propane bis(2,3-epoxypropyl) ether (=BADGE)
468	Perfluorooctanoic acid, ammonium salt
552	Polyvinylpyrrolidone
575	Polydimethylsiloxane
607	Iron phosphide
642	Maleic anhydride-styrene, copolymer, sodium salt
649	Dibutylthiostannoic acid polymer [= thiobis(butyl-tin sulphide), polymer]
713	Charcoal, activated
724	Syrups, hydrolysed starch, hydrogenated
730	Methylsilsesquioxane
744	3-Hydroxybutanoic acid-3-hydroxypentanoic acid, copolymer
768	Amines, bis(hydrogenated tallow alkyl) oxidised
776	Polydimethylsiloxane, 3-aminopropyl terminated, polymer with dicyclohexylmethane- 4,4'-diisocyanate
777	Acrylic acid, methyl ester, telomer with 1-dodecanethiol, C16-C18 alkyl esters
782	Polydimethylsiloxane, 3-aminopropyl terminated, polymer with 1-isocyanato-3-isocyanatomethyl-3,5,5-trimethylcyclohexane
800	triethyl phosphonoacetate
804	Poly(3-nonyl-1,1-dioxo-1-thiopropane-1,3-diyl)-block-poly(x-oleyl-7-hydroxy-1,5-diiminooctane-1,8-diyl), process mixture with x=1 and/ or 5, neutralised with dodecylbenzenesulfonic acid

Since the impact of the revised guidelines is unknown for the 24 substances listed in this table, the submitted dossiers should be re-evaluated more in detail in order to conclude whether more adequate migration data and toxicological data are indeed needed.

5.3. Evaluation of the impact of the revised guidelines on the restrictions

Finally, it should also be mentioned, that even when no extra data are required, the revised guidelines will have an influence on the applied restrictions. This is further discussed in section 3.3.

5.4. Conclusion on the impact of the revised guidelines

After application of the proposed indicators, 97% of the substances present in the Union list in EU Regulation 10/2011 were identified as substances for which no more adequate migration data or toxicological data will be required according to the revised guidelines. It should however be noted that this extrapolation contains some uncertainties. The impact on the data requirements of the remaining 3% of the substances of the Union list should also be further evaluated. In addition, the revised guidelines will have an influence on most of the restrictions of substances covered by a migration limit and for substances covered by a restricted use, the intended contact food should be considered when the restriction according to the revised guidelines is set.

Lastly, it should be emphasized that this study, the impact assessment and the conclusions, have used the information that was provided by applicants for substances within the framework of the existing guidelines. It seems likely that the impact (if any, where identified for particular substances) may change – probably lessened but could in principle increase – if the specific uses of the materials and their substances were in the future, better defined and thus realigned to the proposed new guidelines by the producers or users of those substances and materials.

CONCLUSIONS

This project aimed to evaluate the impact of the revision of the guidelines, by applying the current and the revised guidelines to a selection of 73 model substances. First, a database was developed that structurally summarised all relevant information from the different data sources. The database contained, amongst others, information related to the type of food contact material, the technological function, the intended contact food, migration data (specific migration, overall migration, total mass transfer or modelling) and the available toxicological data, and was used as a working tool during the project.

Interpretation of the restrictions according to the current guidelines:

Migration data:

- For most of the substances and related migrants, specific migration data were provided by the applicant. While simulants A, B and D2 (or its substitutes) were often used, migration data for simulant D1 were only present for 14 substances.
- If no specific migration data were present, total mass transfer or modelling was applied to estimate migration.
- Total mass transfer calculations were usually based on the residual content. In contrast, data used for modelling were more frequently based on the nominal content.
- Overall migration was never used as a single technique for the determination of the migration, but rather as an indication for the migration of the low molecular weight fraction.

Toxicological data

- Most substances and there related migrants were allocated to Tier 1, followed by Tier 2. Only seven out of the 73 model substances were classified as Tier 3.
- All substances classified as Tier 3 were additives. Only for one substance classified in Tier 3, chronic toxicity data were available. However, for all but one of the other substances, the lack of the chronic toxicity data could be justified.
- For most of the substances classified in Tier 1 and Tier 2, the toxicological data provided were in accordance with the toxicological requirements. In case more or less data were available, the rationale behind this deviation was clarified. However, for two substances, the toxicological data submitted by the applicant were considered insufficient.
- For 17 out of the 73 model substances, no toxicological data were required. Most of these substances were polymeric additives, classified in Tier 1. For these polymeric substances, no toxicological data were required as read-across could be applied between the low molecular weight fraction of these polymers and the authorised non-genotoxic monomers. Other substances for which no toxicological data were required included substances that had previously been evaluated or that readily hydrolyse in components that have been toxicologically evaluated, and substances for which no migration is expected.

Interpretation of the restriction

- Two groups of substances could be distinguished: substances covered by a specific or generic migration limit and substances covered by a restricted use. Some substances were covered both by a migration limit and a restricted use.
- Substances covered by a migration limit could be divided into substances covered by the generic migration limit and substances covered by a specific migration limit. Based on the value of the SML, the latter group could be further subdivided in three categories: (i) substances with an SML lower than or equal to 0.05 mg/kg (i) substances with an SML higher than 0.05 and lower than or equal to 5 mg/kg or (iii) substances with an SML between 5 and 60 mg/kg. Most of the substances had an SML higher than 0.05 and lower than or equal to 5 mg/kg.
- Different types of restrictions could be distinguished for substances covered by a restricted use: (i) restrictions excluding certain types of food, (ii) restrictions on the concentration used and (iii) restrictions on the type of plastic. For substances only covered by a restricted use, restrictions were mostly based on the type of plastic, whereas for substances covered both by a migration limit and a restricted use, restrictions were mainly related to the intended contact food.
- Many of the substances covered by a restricted use were polymeric additives composed of authorised monomers.
- The rationale behind the restriction was clarified for all 73 model substances.

Determination of the restrictions according to the revised guidelines:

Exposure calculations:

- For most of the substances, the intended contact foods could only be covered by a combination of all three food group categories. Only for two substances, one (food group category 1) or two (food group category 1 and 3) food group categories were sufficient to cover the intended contact foods, i.e. fresh fruit and all foodstuffs excluding beer and beverages, respectively.
- In most cases, specific migration data were used to calculate exposure. However, an adequate simulant for all requested food group categories was only available for a minority of FCM substances and related migrants.
- For most substances, the highest exposure value was present in food group category 1.

Toxicological data

- According to the revised guidelines, most substances and their related migrants were allocated to Tier 2, followed by Tier 3. Only sixteen substances were classified as Tier 1, including 10 additives and 6 monomers.
- Forty-nine % of the 73 FCM model substances changed in tier when the revised guidelines were applied. For these substances, a change in tier was observed for the substance and/or one or more of its related migrants. Interestingly, both for monomers and additives, about half of the substances was allocated to a different tier according to the revised guidelines.

- Most of the substances and/or the related migrants, shifted from Tier 1 to Tier 2. No shift from Tier 1 to Tier 3 was observed.
- For many substances that shifted in tier, exposure might have been calculated with migration data that significantly overestimated migration. Factors contributing to overestimation of migration include the type of migration experiments, the adequacy of the simulants, the migration conditions and the use of an LOD to calculate exposure.
- Type of migration experiments: For some substances and related migrants with a change in tier, migration data obtained with modelling and total mass transfer were used. This may have caused an overestimation of the migration.
- Adequacy of simulants: For the majority of the substances and related migrants with a change in tier, migration data were obtained through specific migration studies. An adequate simulant for all the food group categories covering the intended contact foods was however only available in a minority of cases. When migration data were obtained with an non-adequate simulant, migration might have been overestimated.
- Migration conditions: For some of the FCM substances and related migrants with adequate migration data, migration conditions might have been too severe, thereby overestimating the migration.
- Use of a too high LOD: For non-detected substances and related migrants with an LOD between 10 and 50 µg/kg, the tier shifted from Tier 1 to Tier 2 when the revised guidelines were applied. For these substances and related migrants, the revision of the guidelines thus triggered new toxicological requirements, while it is not even sure that migration will exceed 10 µg/kg.

Determination of the restriction

- Revision of the guidelines had no effect on the toxicological requirements of substances for which an ADI does not need to be established or for which a previously established ADI or equivalent value was considered acceptable. In case an ADI was available, the safety margin between this ADI and the exposure to the substance related to its use in FM needed to be evaluated.
- Substances covered by a migration limit:
    - The exposure limits of the toxicological tiers needed to be translated into migration limits. Consequently, 9 different migration limits could be derived, three for each food group category. The values of the migration limits ranged from 0.01 mg/kg (Tier 1 in combination with food group category 1) to 50 mg/kg (Tier 3 in combination with food group category 3).
    - As only for substances classified as Tier 2 with a highest exposure value found in food group category 3 the migration limit did not change, the restriction of almost all substances covered by a migration limit was different according to the revised guidelines, regardless a change in tier.
    - For substances without a change in tier, no additional toxicological data were required to set the new restriction. The value of the new restriction depended of the food group category containing the highest exposure value.

- For all substances covered by an SML ≤ 0.05 mg/kg without a change in tier, the new SML was set at 0.01 mg/kg as the highest exposure value was in all cases found in food group category 1.
- For most of the substances covered by an SML between or equal to 0.05 mg/kg and 5 mg/kg, the highest exposure value was also found in food group category 1 and consequently, the new SML value was set at 0.67 mg/kg. Only for one substance, the SML remained at 5 mg/kg since for this substance, the third food group category delivered the highest exposure value.
- None of the substances covered by a migration limit > 5 mg/kg, changed in tier and consequently, the new migration limit could just be set by identifying the food group category containing the highest exposure value. For all substances in this category, an SML of 6.67 mg/kg was set as category 1 was responsible for the highest exposure.
- For substances with a change in tier, additional toxicological data were required to set the restriction. However, exposure calculations were often performed with data overestimating migration. For this reason, the migration data were first further studied. In many cases, overestimation could indeed be expected.
- For all eight substances covered by an SML ≤ 0.05 mg/kg that changed in tier, overestimation of migration due to the use of an non-adequate simulant, the use of a too high LOD or too severe migration conditions can be assumed.
- For all but one of the seven substances covered by an SML between or equal to 0.05 mg/kg and 5 mg/kg, overestimation of migration due to the use of an non-adequate simulant that changed in tier, the use of a too high LOD or too severe migration conditions can be assumed. Only for the substance 3,3',5,5'-tetrakis(tert-butyl)- 2,2'-dihydroxybiphenyl, cyclic ester with [3-(3-tert-butyl-4-hydroxy-5- methylphenyl)propyl] oxyphosphonous acid (EFSA-Q-2008-678, FCM No. 792), migration data were expected to be adequate.
- In case migration of the substance and related migrants was overestimated, more adequate migration data could first be requested from the applicant. If the results of new migration experiments confirm the change in tier, more toxicological data will be needed to set the restriction according to the revised guidelines.

- Substances covered by a restricted use:
  - For substances without a change in tier, no additional toxicological data were required and the restriction did not change.
  - For substances with a change in tier, additional toxicological data were required to evaluate if the restricted use could be maintained according to the revised guidelines. However, as for the substances covered by a migration limit, exposure calculations were often performed with data overestimating migration. For this reason, the migration data were first further studied. In many cases, overestimation could indeed be expected.
  - For all 19 substances with a restricted use that changed in tier, migration could have been overestimated. Consequently, more adequate migration data could first

be requested from the applicant. If the results of new migration experiments confirm the change in tier, more toxicological data will be needed to set the restriction according to the revised guidelines.

Evaluation of the impact of the revised guidelines

Reflections of the impact of the revised guidelines

- Migration data used to calculate exposure: For most substances with adequate migration data (obtained from specific migration experiments with adequate simulants and under appropriate migration conditions), no change in toxicological requirements was observed when the revised guidelines were applied.
- Intended contact food: For future evaluations of substances covered by a restricted use, the intended contact food should be considered when setting the restriction.

Identification of potential indicators

- Reliable indicators to identify substances for which the application of the revised guidelines will require additional toxicological data could not be defined as only one substance with adequate migration data changed in tier.
- Reliable indicators to identify substances for which the application of the revised guidelines will not require additional toxicological data could be defined:
    - Substances for which an ADI did not need to be established or for which a previously established ADI or equivalent value was considered acceptable.
    - Substances SML = Not detected
    - Substances covered by SML > 5 mg/kg or GML
- Reliable indicators to identify substances for which application of the revised guidelines will trigger the need for more adequate migration data could not be defined.
- An indecisive indicator to identify substances for which the application of the revised guidelines will not require more adequate migration data could be defined, i.e. substances covered by an SML $\leq$ 0.05 mg/kg. This indicator contained a certain degree of uncertainty as it was based on two assumptions:
    - The real migration of substances for which a too high LOD was used to calculate exposure substances was assumed to be low enough to ensure that no additional toxicological data were required.
    - The real migration of substances for which the exposure values were close to the lower threshold of the toxicological tier was assumed to be low enough to ensure that no additional toxicological data were required.
- An indecisive indicator to identify substances for which the application of the revised guidelines will not require more toxicological data could be defined, i.e. substances covered by an SML between 0.05 and 5 mg/kg. This indicator contained a higher degree of uncertainty as its was based on the additional assumption that no direct toxicological concern occurs when the SML according to the revised guidelines is applied. The assumption was based on the observation that the NOAELs of all substances with an SML between 0.05 and 5 mg/kg that changed in tier allowed to set the SML according to the revised guidelines. This is not surprising as the SML of 6.67 mg/kg of food group category 1 combined with Tier 3 is close to

the maximum migration limit that could be set for substances classified in Tier 2 according to the current guidelines, i.e. 5 mg/kg.

- Indecisive indicators should be applied with caution as they contain a certain amount of uncertainty.

Extrapolation of the results to the EU Regulation

- After application of the reliable indicators, 65% of the substances present in the Union List in EU Regulation 10/2011 were identified as substances for which no more toxicological data will be required according to the revised guidelines. The remaining 35% can further be reduced by the application of the indecisive indicators. Finally, 97% of the substances present in the Union list in EU Regulation 10/2011 were identified as substances for which no more adequate migration data or toxicological data will be required according to the revised guidelines. It should however be noted that this extrapolation contains some uncertainties. The impact on the data requirements of the remaining 3% of the substances of the Union list should also be further evaluated. In addition, the revised guidelines will have an influence on most of the restrictions of substances covered by a migration limit and for substances covered by a restricted use, the intended contact food should be considered when the restriction according to the revised guidelines is set.

Lastly, it should be emphasized that this study, the impact assessment and the conclusions, have used the information that was provided by applicants for substances within the framework of the existing guidelines. It seems likely that the impact (if any, where identified for particular substances) may change – probably lessened but could in principle increase – if the specific uses of the materials and their substances were in the future, better defined and thus realigned to the proposed new guidelines by the producers or users of those substances and materials.

ABBREVIATIONS

ADI	Acceptable Daily Intake
ADME	Absorption, distribution, metabolism and excretion
AFC Panel	Scientific Panel on food additives, flavourings, processing aids and materials in contact with food
BFDGE	Bisphenol F diglycidyl-ether
CAS nr	Chemical Abstracts Service nr
Cat. 1, 2, 3	Food group category as established in the revised guidelines
CEF Panel	Scientific Panel on Food Contact Materials, Enzymes, Flavourings, and Processing Aids
CHDA	1,4-Cyclohexanedicarboxylic acid
Da	Dalton
DELA	Diethanolamine
EtOH	Ethanol
Exp	Exposure
FCM	Food contact material
FRF	Fat consumption reduction factor
GML	Generic migration limit (mg/kg)
HPMA	2-Hydroxypropylmethacrylate
JECFA	Joint FAO/WHO expert committee on food additives
kg bw	kilogram body weight
LMWF	Low molecular weight fraction
LO(A)EL	Lowest observed (adverse) effect level
LOD	Limit of detection
Log Po/w	Octanol/water partition
LPDE	Low density polyethylene
Model	Migration modelling
MTDI	Maximum tolerable daily intake
MW	Molecular weight
NC	Nominal content
NO(A)EL	No observed adverse effect level
NP-2018	"3,3',5,5'-tetrakis(t-butyl)-2,2'-dihydroxibiphenyl, cyclic ester with [3-(3-t-butyl-4-hydroxy-5-methylphenyl)propyl]phosphate
OM	Overall migration
PC	Polycarbonate
PEIT	Poly(ethylene-co-isosorbide terephthalate)
PET	Polyethylene terephthalate
PHSA	Poly(12-hydroxystearic acid)
PMTDI	Provisional maximum tolerable weekly intake
PO	Polyolefins
PP	Polypropylene
PPA	Polymer production aid
P-SDS	Petitioner summary data sheet

PTWI	Provisional tolerable weekly intake
PVC	Polyvinyl chloride
QM	Maximum permitted quantity of the substance in the finished article (mg/kg)
RC	Residual content
S9	Metabolic activation system, +S9/-S9: presence or absence of the metabolic activation system
SCF	Scientific Committee on Food
SDS	Summary data sheet
SM	Specific migration
SM_N	Specific migration with non-adequate simulant
SML	Specific migration limit (mg/kg)
t/T conditions	Time temperature conditions
t-ADI	Temporary acceptable daily intake
TDI	Tolerable daily intake
TMCD	2,24,4-tetramethyl-cyclobutane-1,3diol
TMT	Total mass transfer calculations
TTC	Threshold of toxicological concern
WHO	World Health Organisation

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