Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request related to

a 14th list of substances for food contact materials

Question N° EFSA-Q-2006-1, EFSA-Q-2006-178, EFSA-Q-2006-116

Adopted on 6 and 7 February 2007

SUMMARY

Within the general task of evaluating substances intended for use in materials in contact with food according to the Regulation (EC) No.1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with foodstuffs, the AFC Panel evaluated the following substances:

Ref. No.:	18455, 18457 for the composing monomers
Name of the substance:	Silicon dioxide coating (SiOx) formed from the monomers hexamethyldisiloxane and hexamethyldisilazane
CAS number:	107-46-0 (hexamethyldisiloxane) and 999-97-3 (hexamethyldisilazane)
Classified in list:	3
Restriction:	0.05 mg/kg of food (measured as hexamethyldisiloxane) Only to be used as a surface treatment agent on PET
Ref. No.:	38875
Name of the substance:	Bis(2,6-diisopropylphenyl)carbodiimide
CAS number:	2162-74-5
Classified in list:	3
Restriction:	0.05 mg/kg food For use behind a PET layer
Ref. No.:	89120 (stearic acid, butyl ester) & 70480 (palmitic acid, butyl ester)
Name of the substance:	Mixture of 40-60% stearic acid, butyl ester and 60-40% palmitic acid, butyl ester
CAS number:	123-95-5 & 111-06-8
Classified in list:	3
Restriction:	None

KEYWORDS

Food Contact Materials, Plastics, Monomers, Additives, REF. No 18455, 18457, CAS No. 107-46-0 (hexamethyldisiloxane) and 999-97-3 (hexamethyldisilazane), silicon dioxide coating (SiOx) formed from the monomers hexamethyldisiloxane and hexamethyldisilazane, REF. 38875, CAS No. 2162-74-5, Bis(2,6-diisopropylphenyl)carbodiimide, REF. No 89120&70480, CAS No 123-95-5 & 111-06-8, mixture of 40-60% stearic acid, butyl ester and 60-40% palmitic acid, butyl ester.

BACKGROUND

Before a substance is authorised to be used in food contact materials and is included in a positive list EFSA´s opinion on its safety is required. This procedure has been established in Articles 8 and 9 of the Regulation (EC) No. 1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food[1].

TERMS OF REFERENCE

The EFSA is required by Article 10 of Regulation (EC) No. 1935/2004 of the European Parliament and of the Council on materials and articles intended to come into contact with food to carry out risk assessments on the risks originating from the migration of substances from food contact materials into food and deliver a scientific opinion on:

1. new substances intended to be used in food contact materials before their authorisation and inclusion in a positive list;
2. substances which are already authorised in the framework of Regulation (EC) No. 1935/2004 but need to be re-evaluated.

ASSESSMENT

Within this general task the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) evaluated the following substances used in food contact materials.

The substances examined are listed in ascending order of their Reference Number (REF No.), with their chemical name, Chemical Abstract Number (CAS No.) and classification according to the “SCF list”. (Since in the past the evaluation of substances used in food contact materials was undertaken by the Scientific Committee on Food (SCF), the same system of classification into a “SCF list” is retained for uniformity purposes). The definitions of the various SCF lists and the abbreviations used are given in the appendix.

The studies submitted for evaluation followed the SCF guidelines for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation (http://ec.europa.eu/food/fs/sc/scf/out82_en.pdf)

[1] This Regulation replaces Directive 89/109/EEC of 21 December 1988, OJ L 40, 11.2.1989, P.38

Ref. No.:	**18455, 18457 for the composing monomers**
Name of the substance:	**Silicon dioxide coating (SiOx) formed from the monomers hexamethyldisiloxane and hexamethyldisilazane**
CAS number:	107-46-0 (hexamethyldisiloxane) and 999-97-3 (hexamethyldisilazane)
Document reference:	SDS EFSA/AFC/FCM/816-Rev.IA/SiOx of January 2007
General information:	According to the petitioner, the monomers hexamethyldisiloxane and hexamethyldisilazane are used to make a silicon dioxide coating *in situ* on the inner surface of PET articles. The coating is intended to provide gas barrier properties and the maximum thickness is 100 nm. Final articles are intended for all types of food, including hot fill and pasteurisation at temperatures up to 95°C and long term storage at room temperature.
Previous evaluations (by SCF or AFC):	None (new substance)
Available data used for this evaluation:	
Non-toxicity data:	- Data on identity - Data on physical and chemical properties - Hydrolysis studies - Data on use and authorisation - Analysis for migrateable oligomers or other reaction products - Determination of residual content
Toxicity data	- Gene mutation in bacteria (2 assays) - *In vitro* mammalian cell gene mutation test - Chromosome aberration tests (2 assays) - Alkaline elution assay - Sister chromatid exchange assay - *In vivo* mammalian bone marrow chromosome aberration test - Cytotoxicity test in mouse lymphoma cells
Evaluation:	It was demonstrated that hexamethyldisilazane is not stable in moist air or in aqueous media and is converted rapidly into hexamethyldisiloxane. The residual content of hexamethyldisiloxane in PET bottles treated with both monomers to give a 43 nm barrier coating was 0.9 microg per 6 dm^2. No other constituents with a molecular mass below 1000 g/mol were detected, using liquid chormatography coupled to mass spectroscopy. Overall migration was not determined but given the very low thickness of the coating this information is not required

Ref. No.:	**18455, 18457 for the composing monomers**
Name of the substance:	**Silicon dioxide coating (SiOx) formed from the monomers hexamethyldisiloxane and hexamethyldisilazane**
	The applicant has submitted toxicity data on hexamethyldisiloxane (HMDSO). Gene mutation tests in bacteria were negative. A limited gene mutation test in mammalian cells *in vitro* with no adequate reduction of relative total growth under activation conditions did not show increased mutation frequencies. Two chromosome aberration tests were submitted: The most recent one, performed according to current guidelines, is clearly negative and the other one is equivocal. An *in vitro* sister chromatid exchange assay and an alkaline elution assay, which provide supplementary information on DNA damaging activity, were both negative. An *in vivo* bone marrow chromosome aberration assay was negative. On the basis of the results presented, the tested substance is considered to be non genotoxic.
Conclusion:	Based on the above-mentioned data the substance is classified:
SCF_List:	**3**
Restriction:	**0.05 mg/kg of food (measured as hexamethyldisiloxane)** **Only to be used as a surface treatment agent on PET**
Remark for Commission:	Only a method of analysis for the determination of the residual content of hexamethyldisiloxane on the treated surface is provided
Needed data or information	None
References:	- Unpublished data submitted by the petitioner, January and December 2006

Ref. No.:	**38875**
Name of the substance:	**Bis(2,6-diisopropylphenyl)carbodiimide**
CAS number:	
Document reference:	EFSA/AFC/FCM/857-Rev.0A of January 2007
General information:	According to the petitioner, bis(2,6-diisopropylphenyl)carbodiimide (CDI) is an additive for the manufacturing of polyglycolic acid (PGA) layer, which is intended to be used as an inner layer of multi-layer structure, PET/PGA/PET, destined to be in contact with aqueous food , acidic food and alcoholic (up to 15% ethanol) beverages.
Previous evaluations (by SCF or AFC):	None (new substance)

Ref. No.:	**38875**
Name of the substance:	**Bis(2,6-diisopropylphenyl)carbodiimide**
Available data used for this evaluation:	
Non-toxicity data:	- Data on identity - Data on physical and chemical properties, - Data on the intended use and authorisation, - Overall migration - Data on residual content of the substance - Worst case calculation of the migration of the substance - Residual amount of oligomers and migration of theoretical breakdown products
Toxicity data	- Gene mutation in bacteria, - *In vitro* mammalian cell gene mutation test, - *In vitro* mammalian chromosome aberration test
Evaluation:	Specific migration of CDI was not determined but worst case migration was calculated from the measured residual amount in multilayer bottles prepared with PGA treated with CDI, and was 48 microg/kg food. Overall migration from the multilayer bottles in 3% acetic acid and 10% ethanol for 10 days at 40°C was not detectable (detection limit 0.3 mg/dm^2) The residual amount of CDI in PGA was 37 microg/6 dm^2. No residual amount of oligomers and reaction products of CDI in PGA were detected (detection limit 29 µg/6 dm^2). No migration of the theoretical breakdown product 2,6-diisopropylaniline was detected (detection limit 4 microg/kg food) after 10 days at 40°C (3%acetic acid or 10% ethanol) and after 30 days at 40°C in 10% ethanol. Bis(2,6-diisopropylphenyl)carbodiimide did not show mutagenic potential in bacteria or in mammalian cells and it did not induce chromosome aberrations *in vitro*. Based on the three performed *in vitro* tests there is no evidence for a genotoxic potential of bis(2,6-diisopropylphenyl)carbodiimide.
Conclusion:	Based on the above-mentioned data the substance is classified:
SCF_List:	**3**
Restriction:	**0.05 mg/kg food** **For use behind a PET layer**
Remark for Commission:	Since the substance may react with food only a method of analysis in the polymer is available.
Needed data or information	None

Ref. No.:	**38875**
Name of the substance:	**Bis(2,6-diisopropylphenyl)carbodiimide**
References:	- Chemical Reviews, vol 67, n 2 March 27, 1967, pag 123-127 - Unpublished data submitted by the petitioner, December 2006

Ref. No.:	**89120 (stearic acid, butyl ester) & 70480 (palmitic acid, butyl ester)**
Name of the substance:	**Mixture of 40-60% stearic acid, butyl ester and 60-40% palmitic acid, butyl ester**
CAS number:	123-95-5 & 111-06-8
Document reference:	EFSA/AFC/FCM/754-Rev.0C/89120&70480 of January 2007
General information:	According to the petitioner n-butyl stearate is primarily a mixture of two fatty acid esters derived from commercial grades of stearic acid, i.e. a mixture of 40-60% stearic acid, butyl ester and 60-40% palmitic acid, butyl ester. This mixture is commonly referred to as n-butyl stearate despite the fact that it also contains esters derived from palmitic acid. The substance may be used as a lubricant during processing in several polymers. These are intended for contact with all food types, for repeat use, short-term and long-term at ambient temperatures or below.
Previous evaluations (by SCF or AFC):	
Available data used for this evaluation:	
Non-toxicity data:	- Data on identity - Data on physical and chemical properties - Hydrolysis studies - Data on use and authorisation - Data on overall migration - Data on residual content of the substance
Toxicity data	- Bacterial reverse mutation assay (Ames test) with butyl stearate - Two-year oral toxicity study in rat with butyl stearate (only summary) - Two generation toxicity study in rat with butyl stearate (only summary) - Literature data on other esters of linear aliphatic saturated carboxylic acids

Ref. No.:	**89120 (stearic acid, butyl ester) & 70480 (palmitic acid, butyl ester)**
Name of the substance:	**Mixture of 40-60% stearic acid, butyl ester and 60-40% palmitic acid, butyl ester**
Evaluation:	Specific migration into aqueous food simulants and olive oil was not determined because of insolubility and analytical difficulties, respectively. In 95% ethanol and iso-octane specific migration was below 200 microg/l under unrealistically severe test conditions (24 hours at 70°C). The residual content of the additive in the polymethylmethacrylate sample tested was found to be only 2% of the initial content (0.15% w/w). The extent of hydrolysis of n-butyl stearate and n-butyl palmitate, in digestive fluid simulants was determined and it was observed that there was significant hydrolysis in intestinal fluid simulant (pH 7.5) over a period of 4 hours. Butyl stearate did not induce gene mutations in bacteria, with or without metabolic activation. No further information on the genotoxic activity of butyl esters of stearic and palmitic acid is available, while uniformly negative results in bacterial and cytogenetic assays are reported in the literature for other fatty acid esters. Based on these findings, and on the lack of structural alerts for genotoxicity, the test material can be considered as non-genotoxic. Aliphatic linear esters of aliphatic linear saturated carboxylic acids are regarded as a class with low toxicity, being metabolised to the corresponding alcohols and carboxylic acids (JECFA, 1998). There is extensive, although not complete hydrolysis of butyl stearate and butyl palmitate in intestinal fluid simulant into n-butyl alcohol, stearic and palmitic acid. All hydrolysis products are listed without restrictions in Commission Directive 2002/72/EC (Commission, 2002). The limited experimental data available indicate that butyl stearate has very low acute and repeated-dose toxicity in mammals. Based on the information available on toxicity and residual content in food contact materials, it is concluded that the use of the substance as additive in the manufacture of plastic polymers is toxicologically acceptable.
Conclusion:	Based on the above-mentioned data the substance is classified:
SCF_List:	**3**
Restriction:	**None**
Remark for Commission:	

Needed data or information	None
References:	- Unpublished data submitted by the petitioner in August 2006 - Commission Directive 2002/72/EC, relating to plastic materials and articles intended to come into contact with foodstuffs http://europa.eu.int/eur-lex/pri/en/oj/dat/2002/l_220/l_22020020815en00180058.pdf - Hachiya, N. (1987) Evaluation of chemical genotoxicity by a series of short-term tests. Akita J. Med. 14: 269-292. - Joint FAO/WHO Expert Committee on Food Additives (JECFA) Esters of primary acyclic primary alcohols with aliphatic linear saturated carboxylic acids. The forty-ninth JECFA meeting, WHO 1998. - Smith. C.C. (1953) Toxicity of butyl stearate, dibutyl sebacate, dibutyl ohthalate and methoxyethyl oleate. AMA Arch. Ind. Hyg. Occup. Med. 7: 310-318. - High Production Volume (HPV) Chemical Challenge Program for Monoesters - Section 8. Appendix "Robust Summaries for Substances in the HPV Test Plan for the Monoesters Category of the Aliphatic Esters Chemicals". American Chemistry Council, November 2003.

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APPENDIX

DEFINITION OF THE SCF LISTS

The classification into a SCF_List is a tool used for tackling authorisation dossiers and do not prejudice the management decisions that will be taken on the basis of the scientific opinions of the AFC Panel and in the framework of the applicable legislation

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 need not be established for this purpose.

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.

List 2 Substances for which this Committee has established a TDI or a t-TDI.

List 3 Substances for which an ADI or a TDI could not be established, but where the present use could be accepted.

Some of these substances are self-limiting because of their organoleptic properties or are volatile and therefore unlikely to be present in the finished product. For other substances with very low migration, a TDI has not been set but the maximum level to be used in any packaging material or a specific limit of migration is stated. This is because the available toxicological data would give a TDI, which allows that a specific limit of migration or a composition limit could be fixed at levels very much higher than the maximum likely intakes arising from present uses of the additive.

Depending on the available toxicological studies a restriction of migration into food of 0.05 mg/kg of food (3 mutagenicity studies only) or 5 mg/kg of food (3 mutagenicity studies plus 90-day oral toxicity study and data to demonstrate the absence of potential for bio-accumulation in man) may be allocated.

List 4 **(for monomers)**

4A Substances for which an ADI or TDI could not be established, but which could be used if the substance migrating into foods or in food simulants is not detectable by an agreed sensitive method.

4B Substances for which an ADI or TDI could not be established, but which could be used if the levels of monomer residues in materials and articles intended to come into contact with foodstuffs are reduced as much as possible.

List 4 **(for additives)**

Substances for which an ADI or TDI could not be established, but which could be used if the substance migrating into foods or in food simulants is not detectable by an agreed sensitive method.

List 5	Substances that should not be used.
List 6	Substances for which there exist suspicions about their toxicity and for which data are lacking or are insufficient. The allocation of substances to this list is mainly based upon similarity of structure with that of chemical substances already evaluated or known to have functional groups that indicate carcinogenic or other severe toxic properties.
6A	Substances suspected to have carcinogenic properties. These substances should not be detectable in foods or in food simulants by an appropriate sensitive method for each substance.
6B	Substances suspected to have toxic properties (other than carcinogenic). Restrictions may be indicated.
List 7	Substances for which some toxicological data exist, but for which an ADI or a TDI could not be established. The required additional information should be furnished.
List 8	Substances for which no or only scanty and inadequate data were available.
List 9	Substances and groups of substances which could not be evaluated due to lack of specifications (substances) or to lack of adequate description (groups of substances). Groups of substances should be replaced, where possible, by individual substances actually in use. Polymers for which the data on identity specified in "SCF Guidelines" are not available.
List W	"Waiting list". Substances not yet included in the Community lists, as they should be considered "new" substances, i.e. substances never approved at national level. These substances cannot be included in the Community lists, lacking the data requested by the Committee.

List of abbreviations:

CDI	Bis(2,6-diisopropylphenyl)carbodiimide
DL	Detection limit
FAO	Food and Agrculture Organization of the United Nations
HMDSO	Hexamethyldisiloxane
HPV	High Production Volume
JECFA	Joint expert Committee on food additives
OECD	Organisation for economic co-operation and development
PET	Polyethyleneglycol terephthalate
PGA	Polyglycolic acid
SCF	Scientific Committee on food
TDI	Tolerable daily intake
WHO	World Health Organisation