

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

a 12th list of substances for food contact materials

**Question N° EFSA-Q-2004-073, EFSA-Q-2006-024,
EFSA-Q-2005-238a, EFSA-Q-2005-238b, EFSA-Q-2005-238c,
EFSA-Q-2006-012, EFSA-Q-2006-027**

Adopted on 26 & 27 September 2006

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.:	45705
Name of the substance:	1,2-cyclohexyldicarboxylic acid, diisononyl ester
CAS number:	166412-78-8
Classified in list:	2
Restriction:	TDI = 1 mg/kg bw/day
Ref. No.:	81500
Name of the substance:	Polyvinylpyrrolidone
CAS number:	9003-39-8
Classified in list:	3
Restriction:	None
Ref. No.:	86432/20, 86432/40 and 86432/60
Name of the substance:	<ul style="list-style-type: none">- Silver containing glass (silver-magnesium-aluminium-phosphate-silicate), silver content less than 2%.- Silver containing glass (silver-magnesium-aluminium-sodium-phosphate-silicate-borate), silver content less than 0.5%- Silver containing glass (silver-magnesium-sodium-phosphate), silver content less than 3 %
CAS number:	-
Classified in list:	3

Restriction: In accordance with other silver biocides these biocides will be subject to a group SML of 0.05 mg Ag/kg food

In accordance with other boron compounds the biocide Ref No 86432/40 will be subject to a group SML of 6 mg B/kg food

Ref. No.: 95020
Name of the substance: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate
CAS number: 6846-50-0
Classified in list: 3
Restriction: 5 mg/kg food

Ref. No.: 95420
Name of the substance: 1,3,5-tris(2,2-dimethylpropanamido)benzene
CAS number: 745070-61-5
Classified in list: 3
Restriction: 0.05 mg/kg food

KEY WORDS

Food Contact Materials, Plastics, Monomers, Additives, REF. No 45705, CAS No 166412-78-8, 1,2-cyclohexyldicarboxylic acid, diisononyl ester, REF. No 81500, CAS No 9003-39-8, Polyvinylpyrrolidone, REF. No 86432/20, Silver containing glass (silver-magnesium-aluminium-phosphate-silicate), silver content less than 2%, REF. No 86432/40, Silver containing glass (silver-magnesium-aluminium-sodium-phosphate-silicate-borate), silver content less than 0.5%, REF. No. 86432/60, Silver containing glass (silver-magnesium-sodium-phosphate), silver content less than 3 %, REF. No 95020, CAS No 6846-50-0, 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate, REF. No 95420, CAS No. 745070-61-5, 1,3,5-tris(2,2-dimethylpropanamido)benzene.

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 food¹.

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

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).

Ref. No.:	45705
Name of the substance:	1,2-cyclohexanedicarboxylic acid, diisononyl ester

CAS number: 166412-78-8

Document reference: EFSA/AFC/FCM/293-Rev.IB/45705 of June 2006

General information: According to the petitioner 1,2-cyclohexanedicarboxylic acid, diisononyl ester is used as a plasticiser in PVC (up to 40%) and as an impact modifier in polystyrene (max 3%). The plasticiser is used in PVC cling films for fresh meat packaging (10%), for aqueous food and fruits and vegetables (35%), artificial corks (35%), sealing gaskets for beverage containers (35%), flexible tubes for beverages, alcoholic and non-alcoholic (40%), conveyor belts for fatty foods (12%) and other foods (12%) and as polystyrene impact modifier (3%). The conditions of contact of the food with the packaging material depend on the food and its required storage conditions.

Previous evaluations (by SCF or AFC): None

Available data used for this evaluation:

Non-toxicity data: - Data on identity, physical/chemical properties, use, authorisation
 - Migration data into food simulants and various foodstuffs
 - Simulation of the migration using mathematical modelling
 - Data on the actual content in the test samples

Toxicity data: - Gene mutation in bacteria
 - *In vitro* mammalian cell gene mutation test
 - *In vitro* mammalian chromosome aberration test
 - *In vivo* micronucleus test
 - Subchronic (3 months) oral toxicity study in rats
 - Prenatal developmental toxicity studies in rats (by gavage)
 - Two-generation reproduction/developmental toxicity studies in rats and rabbits (by dietary administration)
 - Chronic toxicity/carcinogenicity study in rats
 - Biokinetic and metabolism studies in rats
 - Studies on thyroid function, liver enzymes induction and S-phase response in rat liver, thyroid and kidney (by dietary administration).

Ref. No.:	45705
Name of the substance:	1,2-cyclohexanedicarboxylic acid, diisononyl ester

Evaluation:

The specific migration of 1,2-cyclohexanedicarboxylic acid, diisononyl ester (DINCH) from plasticized PVC cling film containing 10 - 17.8 % of DINCH into food simulants and foodstuffs was determined. by a Gas Chromatography/ Mass Spectrometry (GC/MS) method. The method was properly described and validated. The recovery data and precision data showed the reliability of the method. The following migration results were obtained:

Test sample	Food/simulant	Fat content (fresh product) %	Storage conditions	Migration mg/dm ²
Cling film ; thickness 14 µm, 17,8% 1,2-cyclohexanedicarboxylic acid, diisononyl ester	Sunflower oil	100	6 -144 h at 10 and 20°C	29 ± 2 ¹⁾
	Ethanol 10%	0	24 h at 40 °C	0.016 ± 0.002
	Turkey (escalope)	1.0 ± 0.5	5d at 5 °C	0.3 ± 0.1
	Pork (neck)	11.3 ± 2.5	5d at 5 °C	1.2 ± 0.2
	Pork (escalope)	0.7	5d at 5 °C	0.1 ± 0.01
	Pork (liver)	5.0 ± 0.1	5d at 5 °C	0.1 ± 0.02
	High fat cheese	44.3	10d at 5 °C	27.5 ± 2.2
	Low fat cheese	11.4	10d at 5 °C	2.4 ± 0.7
Cling film ; thickness 14 µm 12%	Pork (neck)	14.7 ± 2.9	5d at 5 °C	1.0 ± 0.3
	Pork (bacon)	22.1 ± 2.7	5d at 5 °C	1.4 ± 0.1
Cling film ; thickness 14 µm 10%	Pork (neck)	17.9 ± 0.5	5d at 5 °C	0.5 ± 0.1
	Pork (bacon)	25.8 ± 2.4	5d at 5 °C	0.8 ± 1.5

1) the kinetic curved showed complete migration within 6 h at both 10°C and at 20°C

DINCH migrates quantitatively into foods with high fat content and the overall migration limit of 10 mg/dm² may be exceeded. The migration in foods like fresh meat and low fat cheese is low.

Ref. No.:	45705
Name of the substance:	1,2-cyclohexanedicarboxylic acid, diisononyl ester

Migration of DINCH from bottle closures containing a PVC sealing layer with 37% DINCH was determined in carbonated mineral water, grape fruit juice and orange lemonade.

In all cases migration into the aqueous beverages was low, in the range of 10-30 microg/kg.

Also the migration into 10% ethanol, 50% ethanol and olive oil from a polystyrene sample containing 3% DINCH was determined. For this purpose a LC/MS method was used which was validated for precision and detection limit. Recovery including storage conditions was found to be 97% for 50% ethanol. The following results were obtained:

simulant	Storage conditions	Migration mg/kg
Olive oil	1, 5 and 10 d at 40°C	nd (<0.037)
10% ethanol	1, 5 and 10 d at 40°C	nd (<0.031)
50% ethanol	10 d at 40°C	0.053

The actual content of DINCH in the various polymer samples was determined and was found to be at the intended level.

DINCH was tested in three *in vitro* mutagenicity assays (reversion in bacteria, forward mutation and chromosomal aberration tests in mammalian cells) and in the micronucleus test in mouse bone marrow. Based on the negative results obtained, it is concluded that DINCH is not genotoxic.

In a subchronic (13 weeks) oral toxicity study in Wistar rats given 100, 300 and 1000 mg DINCH/kg bw/day, signs of renal toxicity (haematuria and increased occurrence of degenerated transitional epithelial cells in urine) were observed at high dose (1000 mg/kg bw/day) in males and females, and at mid dose (300 mg/kg bw/day) in males. Significantly increased liver weight, without histological alterations, was observed at high dose (both sexes) and at mid dose (females only). An increased incidence of thyroid hyperplasia was observed in males at all doses and in females at high dose. As marked species differences exist in thyroid cancer related effects (IARC, 1999), the NOAEL for thyroid hyperplasia was considered inappropriate to set a TDI. The NOAEL for kidney effects was 100 mg/kg bw/day.

No evidence of developmental or reproductive toxicity was obtained in prenatal and two-generation toxicity studies in Wistar rats and in

Ref. No.:	45705
Name of the substance:	1,2-cyclohexanedicarboxylic acid, diisononyl ester

rabbits, up to the highest administered dose of 1000 mg/kg bw/day. In rats, the following signs of general toxicity were observed in the F1 generation after 26 weeks of dietary exposure at high and mid doses (1000 and 300mg/kg bw/day): vacuolization of kidney tubular epithelia in males and thyroid hyperplasia in females. For reasons outlined above thyroid hyperplasia was not taken as the critical effect to define the TDI. The NOAEL for general toxicity from the 2 generation study in rats, based on renal toxicity findings, was 100 mg/kg bw/day. No toxic effects were observed in rabbits.

A 2-year chronic toxicity/carcinogenicity study in Wistar rats with dietary administration of DINCH at 40, 200 and 1000 mg/kg bw/day showed no treatment related mortality or increase in malignant neoplasias up to the highest dose of 1,000 mg/kg bw/day. Increased incidences of thyroid adenomas and increased thyroid weight were observed in both sexes at the high dose, and at mid dose in males. High dose females also showed significantly increased platelets counts. A transient increase in the excretion of the degenerated transitional epithelial cells, with no histopathological findings at sacrifice, was observed after 3 months in high dose males. In this study, the NOAEL for thyroid effects was 40 mg/kg bw/day. The NOAEL for other adverse effects was 200 mg/kg bw/day (based on increased platelet counts in females at 1000 mg/kg bw/day).

A biokinetic study in the rat with ¹⁴C-labelled DINCH showed rapid absorption after oral administration and extensive elimination. Tissue concentrations declined after administration, with less than 1% of radioactivity remaining after 1 week. Overall, kinetic data do not indicate a potential for accumulation in man.

The characterisation of metabolites after oral and intravenous administration of DINCH indicates two main pathways: the partial hydrolysis of DINCH to the mono-isononyl ester followed by conjugation to glucuronic acid, which is the most abundant metabolite in bile, or the hydrolysis of the remaining ester bond to yield free cyclohexane dicarboxylic acid, the predominant metabolite in urine.

Considering the absence of genotoxic properties, the induction of follicular cell hyperplasia and adenomas in rat thyroid can be attributed to a non-genotoxic, indirect mechanism. As rodents are far more sensitive than humans to chemical disturbance of thyroid function (IARC, 1999), the effects on thyroid observed in 90 days and chronic toxicity/carcinogenicity studies are not appropriate to set a TDI. To this aim the evidence of renal toxicity observed in the rat subchronic toxicity study and in the 2-generation rat study can be considered as the pivotal effect, for which a NOAEL of 100 mg/kg bw/day has been identified.

Ref. No.:	45705
Name of the substance:	1,2-cyclohexanedicarboxylic acid, diisononyl ester

In view of the absence of genotoxicity, and of the extensive toxicity database available, a Tolerable Daily Intake (TDI) for DINCH can be derived from the NOAEL for renal effects with the application of the default uncertainty factor of 100:

100 mg/kg bw/day (NOAEL) : 100 = 1 mg/kg bw/day (TDI)

Conclusion: Based on the above-mentioned data, the substance is classified:

SCF_List: 2

Restriction: TDI = 1 mg/kg bw/day

Remark for Commission:

- FRF is applicable
- Overall migration limit into high fat content foods may be exceeded.

Needed data or
information None

References:

- Unpublished data submitted by the petitioner in May 2004 and February 2006
- IARC (1999) International Agency for Research on Cancer. *Species Differences in Thyroid, Kidney and Urinary Bladder Carcinogenesis*. C.C. Capen *et al.*, (Eds.). IARC Scientific Publications n.147. IARC, Lyon, 1999.

Ref. No.:	81500
Name of the substance:	Polyvinylpyrrolidone

CAS number: 9003-39-8

Document reference: SDS EFSA/AFC/FCM/641-Rev.0B/81500 of June 2006

General information: According to the petitioner polyvinylpyrrolidone (PVP) is intended to be used as a polymeric additive in polyamide. Maximum percentage in formulation is 0.1%.

Previous evaluations (by SCF or AFC): The SCF evaluated polyvinylpyrrolidone in 1990 (SCF, 1992) for its use as a food additive and the monomer vinylpyrrolidone in 2001 and 2002 (SCF, 2002a and 2002b)

Available data used for this evaluation:

- Non-toxicity data:
- Data on identity and physical and chemical properties
 - Intended application of the substance
 - Authorisation of the substance
 - Data on migration of the substance
 - Data on the residual content of the substance

Toxicity data: This aspect has been evaluated by the Joint FAO/WHO Experts Committee on Food Additives in 1986 (JECFA, 1987) and the SCF in 1990 and 2001 and 2002 (SCF, 1992 and 2002a and 2002b)

Evaluation: In contrast to most polymers, PVP is readily soluble in both water and a large number of organic solvents, such as alcohols, amines, acids, chlorinated hydrocarbons, amides and lactams. On the other hand, the polymer is insoluble in the common esters, ethers, hydrocarbons and ketones. When cross-linked, PVP becomes insoluble in all solvents.

The PVP has a wide molecular weight range, from 25,000 – 2,500,000 D.

The substance meets the purity requirements on food additives as set in Directive 96/77/EC.

Specific migration of PVP was determined in 10% ethanol and Miglyol. A polyamide sample containing 0.1% PVP was tested by total immersion after 4 hours at 100°C and after 10 days at 40°C. Specific migration of PVP was found to be non-detectable under all test conditions applied. The detection limit of the method corresponds to 0.144 mg/kg food.

The migration of the residual monomer N-vinylpyrrolidone (NVP) is calculated to be 0.2 microg/kg into food, based on the specifications for residual monomer and assuming 100% migration.

Ref. No.:	81500
Name of the substance:	Polyvinylpyrrolidone

Polyvinylpyrrolidone (PVP) has been evaluated by the JECFA in 1986 (JECFA, 1987) and it was allocated an ADI of 0-50 mg/kg bw. The substance was also evaluated by the SCF in 1990 (SCF, 1992) and it was considered as toxicologically acceptable for its use as an excipient in vitamin and sweetener preparations.

PVP is an approved food additive included in the positive list of the Council Directive No 95/2 /EC for use in dietary food supplements in tablet and coated tablet form following the *quantum satis* principle.

The Panel endorsed the previous SCF opinions and taking into account that exposure to NVP from the use of PVP in food contact materials is in a similar range to the exposure from its use as excipient in food supplements, the Panel concluded that PVP is acceptable for use in food contact materials provided that the specifications for the food additive are met.

Conclusion: Based on the above-mentioned data the substance is classified:

SCF_List: 3

Restriction: None

Remark for Commission: The substance should meet the purity criteria established for food additives

Needed data or information

References:

- Unpublished data submitted by petitioner on 27/01/2006
- JECFA (1987), 30th report of the Joint FAO/WHO Expert Committee on Food Additives, WHO Technical report series 751, Geneva, 1987
http://whqlibdoc.who.int/trs/WHO_TRS_751.pdf
- European Parliament and Council Directive No 95/2/EC of February 1995 on food additives other than colours and sweeteners.
http://europa.eu.int/eur-lex/en/consleg/pdf/1995/en_1995L0002_do_001.pdf
- Commission Directive 2002/82EC of 15 October 2002 amending directive 96/77/EC laying down the purity criteria on food additives other than colours or sweeteners.
http://europa.eu.int/eur-lex/pri/en/oj/dat/2002/l_292/l_29220021028en00010028.pdf

Ref. No.:	81500
Name of the substance:	Polyvinylpyrrolidone
	<ul style="list-style-type: none"> - SCF (1992), reports, 26th series, second series of food additives of various technological functions, 19 October 1990, published in 1992 http://europa.eu.int/comm/food/fs/sc/scf/reports/scf_reports_26.pdf - SCF (2002a), opinion of the Scientific Committee on Food on the safety of N-vinyl-2-pyrrolidone residues in polyvinylpyrrolidone and polyvinylpolypyrrolidone when used as food additives, expressed on 30 May 2001, corrected on 17 April 2002. http://europa.eu.int/comm/food/fs/sc/scf/out87_en.pdf - SCF (2002b), opinion of the Scientific Committee on Food on the 18th list of monomers and additives for food contact materials. PM REF No. 26230:N-vinyl-2-pyrrolidone, expressed at 134th meeting of the SCF on 24 September 2002. http://europa.eu.int/comm/food/fs/sc/scf/out140_en.pdf

Ref. No.:	86432/20, 86432/40 and 86432/60
Name of the substance:	<ul style="list-style-type: none"> - Silver containing glass (silver-magnesium-aluminium-phosphate-silicate), silver content less than 2%. - Silver containing glass (silver-magnesium-aluminium-sodium-phosphate-silicate-borate), silver content less than 0.5% - Silver containing glass (silver-magnesium-sodium-phosphate), silver content less than 3 %

CAS number: The petitioner has indicated a CAS number, which may not be adequate (CAS for glass in general)

Document reference: SDS EFSA/AFC/FCM604-Rev.0D/86432/20/40/60 of May 2006

General information: According to the petitioner, glass matrices containing silver, magnesium, phosphorus and/or calcium and/or boron and/or aluminium and/or sodium and/or silicon oxides are glasses to be used as additives for food contact plastic materials. The three following defined mixtures were evaluated:
Ref. No. 86432/20: Silver containing glass (silver-magnesium-aluminium-phosphate-silicate), silver content less than 2%.

Ref. No.:	86432/20, 86432/40 and 86432/60
Name of the substance:	<ul style="list-style-type: none"> - Silver containing glass (silver-magnesium-aluminium-phosphate-silicate), silver content less than 2%. - Silver containing glass (silver-magnesium-aluminium-sodium-phosphate-silicate-borate), silver content less than 0.5% - Silver containing glass (silver-magnesium-sodium-phosphate), silver content less than 3 %

Ref. No. 86432/40: Silver containing glass (silver-magnesium-aluminium-sodium-phosphate-silicate-borate), silver content less than 0.5%

Ref. No. 86432/60: Silver containing glass (silver-magnesium-sodium-phosphate), silver content less than 3 %.

The maximum use levels requested were 0.6% for the first 2 and 0.3% for the last one.

When they are incorporated in a food contact material, these silver containing glasses release silver and develop an antimicrobial activity on the surface of the material. The composition of the glasses plays a major role on the silver release capacity.

The materials containing the glass are to be used in a wide range of applications, for any polymer and for any food, for single and for repeated uses.

Previous evaluations (by SCF or AFC): None

Available data used for this evaluation:

Non-toxicity data:

- Identity and composition
- Physical and chemical properties
- Mechanism of action
- Intended use and authorisation
- Migration with samples which do not represent worst case situations

Microbiological data:

- Intended microbiological function
- Spectrum of antimicrobiological activity
- Level of activity (minimum inhibitory concentrations)
- Information on consequences of use
- Efficacy
- Efficacy upon repeated use
- Lack of biocidal activity against microbes on /in food.

Ref. No.:	86432/20, 86432/40 and 86432/60
Name of the substance:	<ul style="list-style-type: none"> - Silver containing glass (silver-magnesium-aluminium-phosphate-silicate), silver content less than 2%. - Silver containing glass (silver-magnesium-aluminium-sodium-phosphate-silicate-borate), silver content less than 0.5% - Silver containing glass (silver-magnesium-sodium-phosphate), silver content less than 3 %

Toxicity data: This aspect has been evaluated for similar substances by the EFSA in 2004 and 2005 (EFSA, 2004 and EFSA, 2005)

Evaluation:

Migration of silver and other ions in glass has been tested for 10 days at 40°C, using properly described methods. Migration was tested in 3% acetic acid, 15% ethanol and in olive oil. For all samples tested, 3% acetic acid gave the highest migration of silver, and can be considered as a worst case test medium for these glasses.

Migration is shown to be proportional to the percentage of silver in the final material, for each glass.

Migration values for silver reported were between 42 and 95 microg/kg food simulant, depending on the glass and of the actual percentages of glass and of silver in the formulations.

Other elements, mainly phosphate, magnesium and boron (in the case of Ref. No. 86432/40) migrated at low levels. Overall migration has not been tested.

The applicant has demonstrated that the three substances, when incorporated into appropriate polymers, have antimicrobial activity against a wide spectrum of microorganisms including Gram positive and negative bacteria, yeasts and moulds. In tests viable counts after 24 hours incubation in their presence were usually 10⁴ to 10⁵ fold less than in their absence. This level of activity was maintained after washing the final products for 16 hours at 50°C or after many wash cycles at 40°C if the biocides were incorporated into fibres.

Virtually all microorganisms that might be expected to be present in a food environment will be sensitive to silver ions so that the problem of selecting populations that are resistant to silver ions appears unlikely. This was supported by the fact that the use of silver compounds in water treatment and medical environments has not so far resulted in the selection of silver-resistant mutants within the sensitive population of microbes.

The applicant provided data on another silver-containing glass (silver-magnesium-calcium-phosphate-borate), Ref No. 86432,

Ref. No.:	86432/20, 86432/40 and 86432/60
Name of the substance:	<ul style="list-style-type: none"> - Silver containing glass (silver-magnesium-aluminium-phosphate-silicate), silver content less than 2%. - Silver containing glass (silver-magnesium-aluminium-sodium-phosphate-silicate-borate), silver content less than 0.5% - Silver containing glass (silver-magnesium-sodium-phosphate), silver content less than 3 %

already evaluated by the EFSA (EFSA, 2004) to demonstrate that the substance incorporated into polymers would not inhibit microbes in food. Since the antimicrobial effect is based on the same principle of the action of silver ions being released from a glass matrix on the surface of a plastic material, this is plausible. No evidence is provided of efficacy under "in-use" conditions i.e. to demonstrate that the use of the substance in food contact materials improves the hygienic state of food preparation areas over and above that of general cleaning procedures although the laboratory experiments reported suggest that might be the case.

The Panel noted that due to the nature of the substances the only ions that might migrate in toxicologically relevant quantities are silver and boron (in the case of Ref. No. 86432/40).

For boron a group restriction of 6 mg B/kg food has already been allocated (Directive 2002/72/EC).

Concerning silver, the EFSA has evaluated in 2004 and in 2005 (EFSA, 2004 and EFSA, 2005) various silver releasing biocides allocating a group specific migration limit (SML) of 0.05 mg Ag/kg food.

The Panel also took note of the WHO "Guidelines for drinking-water quality" (WHO, 2004). According to these Guidelines a total lifetime oral intake of about 10 g of silver (equal to 0.39 mg/day/person) can be considered on the basis of epidemiological and pharmacokinetic knowledge as the human NOAEL.

Based on the data above, a restriction of 0.05 mg/kg of food (as silver) for the substance would limit intake 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.

Conclusion:

Based on the above-mentioned data the substance is classified:

SCF_List: List 3:
Restriction : **In accordance with other silver biocides these biocides will be subject to a group SML of 0.05 mg Ag/kg food**

In accordance with other boron compounds the biocide Ref No

Ref. No.:	86432/20, 86432/40 and 86432/60
Name of the substance:	<ul style="list-style-type: none"> - Silver containing glass (silver-magnesium-aluminium-phosphate-silicate), silver content less than 2%. - Silver containing glass (silver-magnesium-aluminium-sodium-phosphate-silicate-borate), silver content less than 0.5% - Silver containing glass (silver-magnesium-sodium-phosphate), silver content less than 3 %

86432/40 will be subject to a group SML of 6 mg B/kg food

Remark for Commission: - The substances are surface biocides
 - The migration of silver may exceed the relevant restrictions in acidic foods if substances with the maximum silver content are used at the maximum use level requested.

Needed data or information None

- References:**
- Unpublished data submitted by the petitioner, October 2005
 - Commission Directive 2002/72/EC of August 2002, relating to plastic materials and articles intended to come into contact with foodstuffs, L39/2, 13.2.2003
http://europa.eu.int/comm/food/food/chemicalsafety/foodcontact/2002-72_en.pdf
 - EFSA Opinion on a 4th list of substances for food contact materials, adopted by the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food on 26 May 2004
http://www.efsa.eu.int/science/afc/afc_opinions/468_en.html
 - EFSA Opinion on a 7th list of substances for food contact materials, adopted by the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food on 29 March 2005
http://www.efsa.eu.int/science/afc/afc_opinions/890_en.html
 - World Health Organization (2004). Guidelines for drinking-water quality. Third edition.
http://www.who.int/water_sanitation_health/dwq/gdwq3/en/

Ref. No.:	95020
Name of the substance:	2,2,4-Trimethyl-1,3-pentanediol diisobutyrate

Ref. No.:	95020
Name of the substance:	2,2,4-Trimethyl-1,3-pentanediol diisobutyrate

CAS number: 6846-50-0

Document reference: SDS EFSA/AFC/FCM/646-Rev.0C/95020 of September 2006

General information: According to the petitioner 2,2,4-trimethyl-1,3-pentanediol diisobutyrate is used in plasticised PVC single use gloves for contact with food. 2,2,4-trimethyl-1,3-pentanediol diisobutyrate reduces the formation of pinholes during the manufacturing process of single use gloves. The final product, gloves, will come in contact with all kinds of food for a period of not longer than 30 min and at a temperature not exceeding 40°C.

Previous evaluations (by SCF or AFC): None

Available data used for this evaluation:

Non-toxicity data:

- data on identity, physical and chemical properties
- data on intended use and authorisation of the substance
- data on migration of the substance and its main impurity
- data on the residual content of the substance

Toxicity data

- gene mutation in bacteria
- chromosomal aberrations in cultured mammalian cells
- gene mutation in cultured mammalian cells
- subchronic (one 90-day and one 100-day) oral toxicity study in rats and a 90-day oral toxicity study in dogs; additional feeding studies in rats for 50 and 100 days
- reproductive/developmental toxicity “screening” study
- absorption, distribution, metabolism and excretion
-

Evaluation: The specific migration of 2,2,4-trimethyl-1,3-pentanediol diisobutyrate is determined in the food simulants 3% acetic acid, 10% ethanol and olive oil using the test condition of 30 min at 40°C. The analytical gas chromatography-flame ionisation detector (GC-FID) method for the determination of the compound in food simulants is provided and properly validated.

Under the specific conditions applied the migration of 2,2,4-trimethyl-1,3-pentanediol diisobutyrate in 3% acetic acid, 10% ethanol and olive oil is 0.17, 0.14 and 41.1 mg/6 dm² respectively. For single use gloves the following indicative migration levels were calculated for different types of foodstuffs: 0.016 mg/kg for salad, 0.64 mg/kg for cheese, 1.28 mg/kg for mayonnaise-containing salad and 1.20 mg/kg for chicken meat.

Ref. No.:	95020
Name of the substance:	2,2,4-Trimethyl-1,3-pentenediol diisobutyrate

The actual content of 2,2,4-trimethyl-1,3-pentenediol diisobutyrate in the plasticised PVC single use gloves was found to be 0.76%.

2,2,4-trimethylpentenediol-1,3-diisobutyrate did not induce mutagenicity in bacteria and in mammalian cells and did not induce chromosome aberrations in mammalian cells and is thus considered as non-genotoxic. In the only adequate 90-day oral feeding study in rats in which doses of 0, 30, 150 and 750 mg/kg bw/day were given, the liver was identified as a relevant target organ. Based on statistically significant increases in relative liver weights at the higher dose (750 mg/kg bw/day), the NOAEL was 150 mg/kg bw/day. The kidney effects observed in high dose male rats were characterised as hyaline droplet nephropathy and an exacerbation of progressive nephropathy at 750 mg/kg bw/day. Hyaline droplets in the kidney of male rats were also observed at the lower doses. 2,2,4-Trimethylpentenediol-1,3-diisobutyrate is rapidly metabolized in rats, mainly by hydrolysis, and most of a single oral dose is eliminated with urine and faeces within 4 days after administration.

The data from the toxicokinetic study do not suggest a potential for accumulation in man.

From the other available studies no additional relevant information could be gained.

Conclusion: Based on the above-mentioned data the substance is classified:

SCF_List: 3

Restriction: 5 mg/kg food

Remark for Commission: For single use gloves

Needed data or information -

References: - Unpublished data submitted by the petitioner in January and June 2006

Ref. No.:	95420
Name of the substance:	1,3,5-tris(2,2-dimethylpropanamido)benzene

CAS number: 745070-61-5

Document reference: SDS EFSA/AFC/FCM650-Rev.0A/95420 of September 2006

General information: According to the petitioner 1,3,5-tris(2,2-dimethylpropanamido)benzene is requested for use as nucleating agent only in polypropylene (PP) at a maximum level around 0.02%. The products containing the additive are for single and multiple use, for all types of foods, in conditions ranging from refrigerator

Ref. No.:	95420
Name of the substance:	1,3,5-tris(2,2-dimethylpropanamido)benzene

conditions, to prolonged contact at room temperature, up to 100°C for 1 hour.

Previous evaluations (by SCF or AFC): None

Available data used for this evaluation:

Non-toxicity data:

- Data on identity, physical and chemical properties,
- Hydrolysis studies,
- Data on the intended use and authorisation,
- Specific migration tests in 3% acetic acid, 10% ethanol, miglyol,
- Determination of residual content
-

Toxicity data

- Gene mutation in bacteria
- *In vitro* mammalian cell gene mutation test
- *In vitro* mammalian chromosome aberration test
- *In vivo* micronucleus test

Evaluation:

Specific migration tests of 1,3,5-tris(dimethylpropanamido)benzene were performed on PP plaques nominally containing 0.02% of the additive (1 mm thickness, d 0.9 g/cm³), in 10% ethanol, 3% acetic acid, and miglyol, substitute simulant for olive oil, for 1 hour at 100°C and for 10 days at 40°C. Analytical methods, based on High Performance Liquid Chromatography (HPLC) determination and Limit of Quantitation (LOQ) of 9.5 microg/kg food were developed. Validation of the analytical methods was performed with satisfactory results.

In the acetic simulant, no migration of 1,3,5-tris(2,2-dimethylpropanamido)benzene was undetected after 10 days at 40°C. A migration of 9.8 microg/kg was measured after 1 hour at 100°C. In the ethanolic simulant, no migration of the substance was detected after 10 days at 40°C. A migration of 13.0 microg/kg was measured after 1 hour at 100°C. In miglyol the migration of 1,3,5-tris (dimethylpropanamido) benzene was undetectable after 10 days at 40°C. A migration of 25 microg/kg was measured after 1 hour at 100°C.

In order to verify that no pH dependent hydrolysis of 1,3,5-tris(dimethylpropanamido)benzene occurred under physiological conditions, hydrolysis tests in saliva simulant (pH 8.7, 0.5h at 37°C) and in gastric juice simulant (pH 1.14, 4 h at 37 °C) were performed. No primary aromatic amines were detected.

Ref. No.:	95420
Name of the substance:	1,3,5-tris(2,2-dimethylpropanamido)benzene

1,3,5-Tris(2,2-dimethylpropanamido)benzene did not show mutagenic potential in bacteria and in mammalian cells *in vitro*. It did not induce chromosome aberrations *in vitro* or micronuclei in bone marrow cells *in vivo*. Based on the genotoxicity tests performed, there is no evidence for a genotoxic potential of 1,3,5-tris(2,2-dimethylpropanamido)benzene.

Conclusion: Based on the above-mentioned data the substance is classified:

SCF_List: 3

Restriction: 0.05 mg/kg food

Remark for Commission:

Needed data or
information None

References: - Unpublished data submitted by the petitioner, March 2006

SCIENTIFIC PANEL MEMBERS

Fernando Aguilar, Herman Autrup, Sue Barlow, Laurence Castle, Riccardo Crebelli, Wolfgang Dekant, Karl-Heinz Engel, Nathalie Gontard, David Gott, Sandro Grilli, Rainer Gürtler, John Christian Larsen, Jean-Charles Leblanc, Catherine Leclercq, François Xavier Malcata, Wim Mennes, Maria Rosaria Milana, Iona Pratt, Ivonne Rietjens, Paul Tobback, Fidel Toldrá.

ACKNOWLEDGEMENTS

The Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food wishes to thank M.-L. Binderup, A. Feigenbaum, B.E.B. Moseley, A.K. Müller, M.A.H. Rijk, S. Rossi, T.G. Siere, A.A.M. Stolker for their contribution to the draft opinion.

List of abbreviations:

bw	Body weight
D	Dalton
MW	Molecular weight
NOAEL	No observed adverse effect level
SML	Specific migration limit
TDI	Tolerable daily intake

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.