



EUROPEAN COMMISSION

HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions

C2 - Management of scientific committees; scientific co-operation and networks

SCIENTIFIC COMMITTEE ON FOOD

SCF/CS/PM/GEN/M89 final

24 Sept 2002

Opinion of the Scientific Committee on Food on the 18th additional list of monomers and additives for food contact materials

- **PM/REF No. 10599/90A (acids fatty, unsaturated C18, dimers, distilled);
CAS no. 61788-89-4**
- **PM/REF No. 10599/91 (acids fatty, unsaturated C18, dimers, non-distilled);
CAS no. 61788-89-4**
- **PM/REF No. 10599/92A (acids fatty, unsaturated C18, dimers, hydrogenated,
distilled); CAS no. 68783-41-5**
- **PM/REF No. 10599/93 (acids fatty, unsaturated C18, dimers, hydrogenated,
non-distilled); CAS no. 68783-41-5**
- **PM/REF No. 13323 (1,3-bis (2-hydroxyethoxy) benzene); CAS no. 102-40-9**
- **PM/REF No. 18700 (1,6-hexanediol); CAS no. 629-11-8**
- **PM/REF No. 21970 (N-methylolmethacrylamide); CAS no. 923-02-4**
- **PM/REF No. 22330/50 (mixture of (80%) 2,4-diamino-3, 5-diethyltoluene and
(20%) 2,6-diamino-3, 5-diethyltoluene); CAS no. 68479-98-1**
- **PM/REF No. 26230 (N-vinyl-2-pyrrolidone); CAS no. 88-12-0**
- **PM/REF No. 45450 (p-Cresol-dicyclopentadiene/isobutylene, copolymer);
CAS no. 68610-51-5**
- **M REF No. 94400 (Triethyleneglycol bis [3-(3-tert-butyl-4-hydroxy-5-
methylphenyl) propionate]; CAS no. 36443-68-2**

(opinion expressed by the SCF on 24 September 2002)

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**Opinion of the Scientific Committee on Food
on the 18th additional list of monomers and additives for food contact materials**

(opinion expressed by the SCF on 24 September 2002)

The Committee (re)evaluated a number of monomers and additives for food contact materials. The substances examined are listed in alphabetical order in the Table, with their Reference Number (REF No.), Chemical Abstract Number (CAS No.) and classification in a SCF list. The definition of the SCF lists is given in the Appendix 1. The opinion of the Committee on each of the substances is shown in the same table. Where appropriate quantitative restrictions (R) on migration in foodstuffs or in the residual quantity in finished products appear in the Table.

Assessment Tables

Identification of substance/ compound	Assessment
<p>PM/REF_n.: -10599/90A -10599/91 -10599/92A -10599/93</p> <p><u>Name of the substance:</u> - Acids fatty, unsaturated C18, dimers, distilled - Acids fatty, unsaturated C18, dimers, non-distilled - Acids fatty, unsaturated C18, dimers, hydrogenated distilled - Acids fatty, unsaturated C18, dimers, hydrogenated, non-distilled</p>	<p style="text-align: right;">SDS CS/PM/2901 REV. I/ 10599 August 2001</p> <p><u>General information</u> According to petitioner, acids fatty, unsaturated C18, dimers, distilled or non-distilled and/or hydrogenated are requested as monomers with dicarboxylic function in the production of high solid resins for coatings, modified polyesters and modified polyamides (nylons).</p> <p><u>Previous evaluations (by SCF)</u> The substance was first evaluated in 1996 (SCF, 1996) on the basis of partial migration data and on a gene mutation assay in bacteria, a chromosomal aberration assay in cultured mammalian cells, a gene mutation assay in cultured mammalian cells and a 13 week oral feeding study in rat, The substance was classified in SCF_List 7 because migration data for hydrogenated, distilled dimers were lacking. These data are now provided.</p> <p>Overall migration was determined into water, 8% and 50% ethanol. However, this is not a measure of the migration of the monomer but only for the migration of oligomers. Values of 6.1 mg/dm² were found in 8% ethanol (24 h at 121°C) and 52.3 mg/dm² in 50% ethanol (240 h at 121°C). Specific migration could not be determined due to a lack of a sensitive method.</p> <p>A modified polyester coating was tested for residual content. The polyester was made using 7% of dimeric C18 (un) saturated fatty acids, hydrogenated and distilled. The residual content was 18.4-µg/6 dm² for a coating weight of 127 mg/dm², which, for the conventional mass/area ratio, would be equivalent to a worst-case migration of 18.4 µg/kg food.</p> <p>The toxicity studies were all carried out using the non-distilled dimer (REF_n. 10599/91). In a gene mutation assay in bacteria no cytotoxicity was observed. The test substance did not induce gene mutations in any of the four Salmonella strains used in the assay. In a chromosomal aberration test in cultured mammalian cells, cytotoxicity was observed at a concentration of 150 µg/ml without S9 mix and precipitation with S9 mix at 300µg/l. However, the substance did not induce an increase in the number of cells with chromosomal aberrations. In gene mutation assays in cultured mammalian cells cytotoxicity was</p>

Identification of substance/ compound	Assessment
<p><u>CAS number:</u> - 61788-89-4 - 61788-89-4 - 68783-41-5 - 68783-41-5</p>	<p>observed at 225 and 250 µg/ml (viability of 47% and 59% respectively) in the absence of S9, and in two tests at a maximum dose of 225 µg/ml (viability of 51% and 18%) in the presence of S9. The test substance did not induce mutations at the TK+/- locus in mouse lymphoma cells. It is concluded that the substance is non-genotoxic.</p> <p><u>Conclusion</u></p> <p>Based on the above mentioned data the substance is classified: SCF_list: 3 Group restriction: 0.05 mg/kg of food (for 10599/90A-10599/91-10599/92A and 10599/93). Based on the reduced core set of toxicological data according to the migration level. Remark for Commission: only a method for residual content is available. A QMA-limit is applicable.</p> <p>Needed data or information: None.</p> <p><u>References</u></p> <ul style="list-style-type: none"> - Unpublished data submitted by the petitioner. - Scientific Committee for Food, 1996. In "Compilation of the evaluations of the Scientific Committee for Food on certain monomers and additives used in the manufacture of plastic materials intended to come into contact with foodstuffs until the 21 March 1997". 42nd Series of Reports of the Scientific Committee for Food. Office of Official Publications of the European Communities, Luxembourg, 2000 <p>(Opinion expressed by the SCF on 24 September 2002, 134th meeting of the SCF)</p>

Identification of substance/ compound	Assessment
<p>PM/REF_n.: 13323</p> <p>Name of the substance: 1,3-bis(2-hydroxyethoxy) benzene (BHEB)</p> <p>CAS number: 102-40-9</p>	<p style="text-align: right;">SDS CS/PM/2643 REV. IV/ 13323 Nov 2001</p> <p><u>General information</u></p> <p>According to petitioner, BHEB is used as monomer in the production of polyethylene terephthalate (PET). PET is used for the production of bottles with specific technical properties.</p> <p><u>Previous evaluations (by SCF)</u></p> <p>The substance was first evaluated in 1995 (SCF; 1995) on the basis of adequate migration data and on a gene mutation assay in bacteria, a chromosomal aberration assay in cultured mammalian cells and a gene mutation assay in cultured mammalian cells. The substance was evaluated by the Committee as being genotoxic and was classified in SCF_list 5. Further genotoxicity studies were submitted by the petitioner, i.e. repeated tests for chromosome aberration in vitro, gene mutation assay in mammalian cells and a mouse bone marrow micronucleus test. Based on equivocal results in the micronucleus test the Committee concluded again in 2000 the substance to be genotoxic and retained it in SCF_list 5 (Opinion of SCF on the 10th additional list of monomers and additives for food contact materials).</p> <p>The substance was re-evaluated in 2001 and moved from SCF_List 5 to SCF_List 7 because further data provided by the petitioner showed that the substance did not induce genotoxic effects in vivo. However, data on the levels of BHEB and related compounds in blood in a rat cytogenetic study still needed to be provided. These data are now available.</p> <p><u>Evaluation</u></p> <p>Specific migration of BHEB was determined into water, 3% acetic acid, 15% ethanol and olive oil after a contact period of 2h at 70°C or 10d at 40°C. No migration into the food simulants was observed at a detection limit of <0.05 mg/kg food simulant. The residual content in the BHEB co-monomer was found to be 10 mg/kg polymer, corresponding to a concentration in a final product of about 3-mg/kg polymer blend.</p> <p>BHEB applied at high concentrations (5000µg/ml, equivalent to 25mM) and for extended treatment times, was strongly clastogenic in experiments in vitro in the absence of metabolic activation. Gene mutation assays in bacteria and in mammalian cells were negative. Equivocal results were reported from a mouse bone marrow micronucleus test by the oral</p>

Identification of substance/ compound	Assessment
	<p>route, where an increase of micronuclei, within the historical control range, was only observed in animals of both sexes treated at the middle of dose (1000mg/kg). A further in vivo cytogenetic test in rats receiving repeated oral administrations of BHEB produced clearly negative results, with evidence of internal exposure provided by chemical analyses of rat plasma samples. On this basis it is concluded that BHEB, given by the oral route, does not induce genotoxic effects in vivo.</p> <p><u>Conclusion</u></p> <p>Based on the above mentioned data the substance is classified: SCF_list: 3 Restriction: 0.05 mg/kg of food. Based on the reduced core set of toxicological data according to the migration level. Remark for Commission: none.</p> <p>Needed data or information: None.</p> <p><u>References</u></p> <ul style="list-style-type: none"> - Unpublished data submitted by the petitioner. - Scientific Committee for Food, 1995. In "Compilation of the evaluations of the Scientific Committee for Food on certain monomers and additives used in the manufacture of plastic materials intended to come into contact with foodstuffs until the 21 March 1997". 42nd Series of Reports of the Scientific Committee for Food. Office of Official Publications of the European Communities, Luxembourg, 2000 <p>(Opinion expressed by the SCF on 24 September 2002, 134th meeting of the SCF)</p>

Identification of substance/ compound	Assessment
<p>PM/REF_n.: 18700</p> <p>Name of the substance: 1,6-hexanediol</p> <p>CAS number: 629-11-8</p>	<p style="text-align: right;">SDS CS/PM/2087 REV. II/ 18700 August 2001</p> <p><u>General information</u></p> <p>According to petitioner 1,6-hexanediol is used as monomer in the manufacture of coating materials polyester, polyurethane and polyester-melamine resin.</p> <p><u>Previous evaluations (by SCF)</u></p> <p>The substance was first evaluated in 1996 (SCF, 1996) on the basis of an adequate gene mutation assay in bacteria, a chromosomal aberration assay in cultured mammalian cells and a gene mutation assay in cultured mammalian cells. However, the substance was classified in SCF_list 7 because of inadequate analytical and specification data for the substance. The substance was re-evaluated in 1998 (SCF, 1998) but again classified in SCF_List 7 because of still improperly described analytical methods. These data are now available.</p> <p><u>Evaluation</u></p> <p>Specific migration of 1,6-hexanediol into the food simulants was not detectable at a level of 20-µg/kg food using an appropriate method of analysis.</p> <p>In a gene mutation assay in bacteria no reproducible or dose-related increase of revertant colony number was observed, either in the presence or in the absence of S9. No bacteriotoxic effect was observed at any tested dose (up to 5000 µg/plate). In a chromosomal aberration assay in cultured mammalian cells no significant increase of cells with structural aberration was observed at any tested concentration (0.6, 0.3 and 1.2 mg/ml). In a gene mutation assay in cultured mammalian cells, no reproducible, dose-related increase in mutant frequencies was observed in the treated cultures. Up to the highest concentration (5mg/ml) no reduction of plating efficiency was observed. It is concluded that substance is not genotoxic.</p> <p><u>Conclusion</u></p> <p>Based on the above mentioned data the substance is classified: SCF_list: 3 Restriction: 0.05 mg/kg of food. Based on the reduced core set of toxicological data according to the migration level.</p>

Identification of substance/ compound	Assessment
	<p>Remark for Commission: none.</p> <p>Needed data or information: None</p> <p><u>References</u></p> <ul style="list-style-type: none"> - Unpublished data submitted by the petitioner. - Scientific Committee for Food, 1996. In "Compilation of the evaluations of the Scientific Committee for Food on certain monomers and additives used in the manufacture of plastic materials intended to come into contact with foodstuffs until the 21 March 1997". 42nd Series of Reports of the Scientific Committee for Food. Office of Official Publications of the European Communities, Luxembourg, 2000 - Scientific Committee on Food, 1999. Opinion on an additional list of monomers and additives for Food Contact Materials (expressed on 10 december 1998), at the 114th SCF meeting); see internet address: http://europa.eu.int/comm/food/fs/sc/scf/out20_en.html <p>(Opinion expressed by the SCF on 24 September 2002, 134th meeting of the SCF)</p>

Identification of substance/ compound	Assessment
<p>PM/REF_n.: 21970</p> <p>Name of the substance: N-methylol-methacrylamide</p> <p>CAS number: 923-02-4</p>	<p style="text-align: right;">SDS CS/PM/3442 REV.III/21970 August 2001</p> <p><u>General information</u></p> <p>According to petitioner, N-methylol-methacrylamide is used as monomer in dispersions for the finishing of packaging materials for sausage and cheese, filters, paper-based and textile based packaging materials, latex production.</p> <p><u>Previous evaluations (by SCF)</u></p> <p>The substance was first evaluated in 1999 (SCF, 1999) on the basis of hydrolysis data, migration data and on a gene mutation assay in bacteria, a chromosomal aberration assay in cultured mammalian cells and a gene mutation assay in cultured mammalian cells. The substance was classified in SCF_list 7 because data on the estimation of residual N-methylol-methacrylamide and an assay for chromosomal damage in rodents bone marrow were missing.</p> <p><u>Evaluation</u></p> <p>Migration of the substance into food is calculated assuming the complete transfer of the residual monomer. A value of 8 µg/dm² was found. This value is equivalent to 48 µg/kg food.</p> <p>The substance did not induce gene mutations in a gene mutation assay in bacteria. In a chromosomal assay in cultured mammalian cells, with and without metabolic activation, the highest doses of the test substance (1000 µg/ml and 300 µg/ml respectively) reduced the mitotic indices. The frequency of structural aberrations was dose-dependent and increased at both fixation intervals. However, no increase in micronuclei was seen in an <i>in vivo</i> micronucleus test in NMRI mice. It is concluded that the substance is not genotoxic <i>in vivo</i>.</p> <p><u>Conclusion</u></p> <p>Based on the above mentioned data the substance is classified: SCF_list: 7 Restriction: not applicable Remark for Commission: none.</p>

Identification of substance/ compound	Assessment
	<p data-bbox="533 316 1346 347">Needed data or information: Analytical proof of the residual content</p> <p data-bbox="533 384 674 416"><u>References</u></p> <ul data-bbox="533 437 2002 576" style="list-style-type: none"> <li data-bbox="533 437 1093 469">- Unpublished data submitted by the petitioner. <li data-bbox="533 475 2002 576">- Scientific Committee on Food, 1999. Opinion on an additional list of monomers and additives for Food Contact Materials (expressed on (17 June 1999 at 117th SCF meeting); see internet address: http://europa.eu.int/comm/food/fs/sc/scf/out37_en.pdf. <p data-bbox="533 612 1509 644">(Opinion expressed by the SCF on 24 September 2002, 134th meeting of the SCF)</p>

Identification of substance/ compound	Assessment
<p><u>PM/REF_n.:</u> 22330/50</p> <p><u>Name of the substance:</u> Mixture of (80%) 2,4-diamino-3, 5-diethyltoluene and (20%) 2,6-diamino-3,5-diethyltoluene</p> <p><u>CAS number:</u> 68479-98-1</p>	<p style="text-align: right;">SDS CS/PM/3887 REV. II /22330 March 2002</p> <p><u>General information</u></p> <p>According to petitioner, the mixture of (80%) 2,4-diamino-3, 5-diethyltoluene and (20%) 2,6-diamino-3, 5-diethyltolueneylol-methacrylamide (DETDA) is used as a chain extender for thermo-setting plastics used as a coating or a sealing layer on plastics and as a chain extender and curing agent for polyurethane and epoxy resins. Petitioner further indicates that DETDA is an existing chemical listed in EINECS, Annex I. It is presently not used in other food applications, but has been used for several years in the construction industry as sealing material.</p> <p><u>Previous evaluations (by SCF)</u></p> <p>New substance not previously evaluated by the SCF</p> <p><u>Evaluation</u></p> <p>Worst-case migration was calculated from a polyurethane elastomer model containing 2.6 mass % of DETDA. Because DETDA was anticipated to be reactive in olive oil, the residual content of the test substance (sum of both isomers) was determined. A value of 0.33 mg/kg polymer was found. The worst-case migration for 100% loss of the substance was calculated to be 5.0-µg/kg food simulant.</p> <p>Two batches of 3,5-diethyltoluenediamine (mixture of 2,4 and 2,6 diamine, purity > 95%) were tested with different results in gene mutation assays in bacteria; one test was negative (no toxic or mutagenic effects were observed either in the absence or presence of metabolic activation). A second test was positive (only in the presence of metabolic activation, the test material induced reproducible and dose-related increases in revertant colonies in <i>Salmonella</i> strains TA1538, TA98 and TA100).</p> <p>In a forward mutation test in mouse lymphoma cells another (third) batch (purity 98.4%) of the test substance produced positive results. Weak but reproducible and dose-related increases in mutation frequency were observed in all the experiments in the presence of metabolic activation. No significant increase in mutant frequency was observed in the absence of metabolic activation. The same batch, given by the oral route at the maximum tolerated dose (500-mg/kg b.w.) was negative in a mouse bone marrow micronucleus test. However, in this experiment there is lack of evidence of target cells</p>

Identification of substance/ compound	Assessment
	<p>exposure and thus absence of genotoxicity cannot be proven. Considering the genotoxic profile of the structurally related carcinogen, 2,4-toluenediamine, a rat liver UDS is requested.</p> <p><u>Conclusion</u></p> <p>Based on the above mentioned data the substance is classified: SCF_list: 7 Restriction: Remark for Commission: none.</p> <p>Needed data or information:</p> <ul style="list-style-type: none"> - an <i>in vivo/in vitro</i> rat liver UDS on a representative batch - an explanation for the contradictory results observed in the Ames test, <p><u>References</u></p> <ul style="list-style-type: none"> - Unpublished data submitted by the petitioner. <p>(Opinion expressed by the SCF on 24 September 2002, 134th meeting of the SCF)</p>

Identification of substance/ compound	Assessment
<p>PM/REF_n.: 26230</p> <p>Name of the substance: N-vinylpyrrolidone</p> <p>CAS number: 88-12-0</p>	<p style="text-align: right;">SDS CS/PM/3155 REV. II/ 262300 August 2001</p> <p><u>General information</u></p> <p>According to petitioner N-vinylpyrrolidone (NVP) is used as a co-monomer in the production of thickening agents in adhesives for food packaging purposes (to glue edges of cardboard boxes)</p> <p><u>Previous evaluations (by SCF)</u></p> <p>In 2001 the substance, when present as a residue of the polymers poly-vinylpyrrolidone and poly-vinyl-polypyrrolidone (PVP and PVPP) used as a food additives, was evaluated by the SCF (SCF, May 2001). The Committee concluded that intakes of PVP and PVPP from food additives do not give cause for concern provided the limit of NVP residues in PVP and PVPP is 10 mg/kg PVP/PVPP. In the light of this SCF opinion, the Committee re-evaluated the substance, as a food contact material on the basis of of adequate migration data and on the basis of a gene mutation assay in bacteria, a chromosomal aberration assay in cultured mammalian cells, a gene mutation assay in cultured mammalian cells, a micronucleus assay, an UDS assay in rat hepatocytes, a cell transformation assay in Balb/3T3 cells, and a 2-year inhalation study in rat.</p> <p><u>Evaluation</u></p> <p>The petition concerns a very specific application of NVP as co-polymer of thickening agents used in adhesives for gluing edges of paperboard boxes. Under these conditions, calculated migration was very low. This is related to the extremely low mass/dm² of NVP. However, if NVP is used for purposes other than the one requested in the petition, worse case contamination and migration might be higher since NVP is of low molecular weight and migration might be much higher. Furthermore, since the substance is soluble both in aqueous and organic media, it is likely to migrate into any type of foods.</p> <p>A gene mutation assay in bacteria, a chromosomal aberration test in cultured mammalian cells, a micronucleus assay and a UDS assay in rat hepatocytes all gave negative results. In a gene mutation assay in cultured mammalian cells (L5178 TK+/- cell line) a small increase of mutant frequency was observed but this increase was lower than the usual cut-off value of the negative control for this test. In a cell transformation assay Balb/3T3 cells, NVP did not induce a significant increase in</p>

Identification of substance/ compound	Assessment
	<p>transformed foci over the applied concentration range (0.01 nl/ml to 0.5 nl/ml). However, this study was considered difficult to interpret due to the large discrepancy (3-fold) between the value of the previous negative control of the cell line and the value of the negative control recorded during the study. Based on the above data NVP was considered to be not genotoxic. The inhalation of NVP vapour caused liver toxicity and the development of neoplastic liver lesions in rats at all dose groups (5-20 ppm). The observed effects were dose dependent. A NOAEL could not be deduced since all tested doses induced adverse effects.</p> <p>Since after inhalation exposure, both local and liver (systemic) tumours were induced, potential carcinogenicity by the oral route cannot be excluded.</p> <p>More detail on the toxicity of NVP is given in the previous SCF opinion (SCF, May 2001).</p> <p><u>Conclusion</u></p> <p>Based on the above mentioned data the substance is classified: SCF_list: 4A Restriction: n.d. by an agreed sensitive method. Remark for Commission: only to be used in adhesives for paper and board and QMA < 10 µg/6dm²</p> <p><u>Needed data or information:</u> None.</p> <p><u>References</u></p> <ul style="list-style-type: none"> - Unpublished data submitted by the petitioner. - Opinion of the Scientific Committee on Food on the Safety of n-vinyl-2-pyrrolidone residues in poly-vinylpyrrolidone and poly-vinyl-polypyrrolidone (insoluble poly-vinylpyrrolidone) when used as food additives. Adopted by the SCF on 30 May 2001 (http://europa.eu.int/comm/food/fs/sc/scf/out87_en.pdf). <p>(Opinion expressed by the SCF on 24 September 2002, 134th meeting of the SCF)</p>

Identification of substance/ compound	Assessment
<p>PM/REF_n.: 45450</p> <p>Name of the substance: p-cresol-dicyclopentadiene/isobutylene, copolymer</p> <p>CAS number: 68610-51-5</p>	<p style="text-align: right;">SDS CS/PM/2802 REV.V/45450 July 2001</p> <p><u>General information</u></p> <p>According to petitioner, p-cresol-dicyclopentadiene/isobutylene, copolymer is a polymeric additive used as stabiliser for ABS polymers used in liners for refrigerators and freezers. Minor uses, such as spouts for coffee machines and as thermos bottle lids, where there will be short-term contact above 70°C, are also possible.</p> <p><u>Previous evaluations (by SCF)</u></p> <p>The substance was evaluated in 1997 (SCF, 1997) on the basis of migration data, two gene mutation assays in bacteria, a chromosomal aberration assay in cultured mammalian cells and a gene mutation assay in cultured mammalian cells. Acute toxicity data, a 28-day oral rat study and a 90 days oral rat study were also provided. The Committee remarked that despite the indication of possible bioaccumulation (i.e. log Po/w >4) it found the substance acceptable for the use in ABS for liners in freezers or very short contact.</p> <p>The petitioner sent additional information and the substance was re-evaluated by the SCF in 1998 (SCF, 1998). It classified it in List 3 with a restriction of 0.05 mg/kg of food. The Committee remarked that the applicant did not demonstrate the absence of potential for bioaccumulation. Although the substance is insoluble in water and the log Po/w >6 (no reliable figure), it is unlikely that this substance accumulates, but no direct proof is given. It was concluded that due to its restricted use, the exposure will be minimal and therefore the question of potential bioaccumulation is not considered relevant.</p> <p><u>Evaluation</u></p> <p>Specific migration of the substance was determined in 3% acetic acid, 15% ethanol and 50% ethanol (as alternative for olive oil). ABS sheets, containing 0% and 1% of the test substance were tested by total immersion for 2 h at 70°C followed 10 days at 40°C. In 3% acetic acid and in 15% ethanol no migration was found (detection limit of analytical method: 9.3 µg/kg food). In 50% ethanol migration of the substance was found to be 0.088 µg/kg food.</p> <p>In two gene mutation assays in bacteria, the test substance did not induce gene-mutations in any of the five <i>Salmonella</i> strains and in the <i>E coli</i> strains. Further, in a chromosomal aberration assay in cultured mammalian cells no increase in the</p>

Identification of substance/ compound	Assessment
	<p>number of cells with chromosomal aberration was observed. The substance also tested negative in gene mutation assay in cultured mammalian cells. It is concluded that the copolymer is non-genotoxic.</p> <p>In a 28-day and a 90-day oral rat study increases in prothrombin time (PT) and activated partial thrombosplatin time (APTT) were observed. The PT and APTT changes are not attributable to liver dysfunction but are a consequence of inadequate absorption or utilisation of vitamin K under the influence of high intestinal load of the antioxidant. Vitamin K is required for the hepatic synthesis of factors II, VII, IX, and X. In an ADME study it is shown that the majority of the test substance is not absorbed, but passes through the GI-tract to be excreted in the faeces. Overall, the effects of the test substance were limited to clotting disturbances most likely caused by nutritional interference. It appears significant that even at the very high doses of p-cresol-dicyclopentadiene/isobutylene, copolymer (doses ranged from 0 to 50000 mg/kg equivalent to 0 to 2500 mg/kg b.w.) used in the 28-day study, no particular target organ toxicity occurred. Only non-specific signs of systemic intolerance prevailed which, in principle, were reversible upon discontinuation of the treatment.</p> <p><u>Conclusion</u> Based on the above mentioned data the substance is classified: SCF_list: 3 Restriction: 5 mg/kg of food. Based on the reduced core set of toxicological data according to the migration level. Remark for Commission: none</p> <p>Needed data or information: None.</p> <p><u>References:</u></p> <ul style="list-style-type: none"> - Unpublished data submitted by the petitioner. - Scientific Committee on Food, 1997. Additional list of monomers and additives evaluated by the WG "Food Contact Materials" of the SCF during the 69th-70th Meetings (adopted during the SCF meeting of 12 and 13 June 1997) see internet address http://europa.eu.int/comm/food/fs/sc/oldcomm7/out12_en.html - Scientific Committee on Food, 1998. Opinion on an additional list of monomers and additives for Food Contact Materials (expressed on 18 September 1998 at 113th SCF meeting); see internet address: http://europa.eu.int/comm/food/fs/sc/scf/out16_en.html <p>(Opinion expressed by the SCF on 24 September 2002, 134th meeting of the SCF)</p>

Identification of substance/ compound	Assessment
<p><u>PM/REF_n.:</u> 94400</p> <p><u>Name of the substance:</u> Triethyleneglycol bis [3-(3-tert-butyl-4-hydroxy-5-methylphenyl) propionate</p> <p><u>CAS number:</u> 36443-68-2</p>	<p style="text-align: right;">SDS CS/PM/2643 REV. IV/ 13323 Nov 2001</p> <p><u>General information</u> Triethyleneglycol bis [3-(3-tert-butyl-4-hydroxy-5-methylphenyl) propionate is an antioxidant for plastics destined for packaging of foodstuffs.</p> <p><u>Previous evaluations (by SCF)</u> The substance was evaluated in 1989 (SCF, 1989) on the basis of adequate migration data, a 90-day oral study in rat, a 2-year oral study in rat, a 90-day oral study in dog and on teratogenicity and mutagenicity studies. The substance was classified in SCF_List 2 and a TDI of 0.05 mg/kg b.w. was derived on the basis of a NOAEL of 5 mg/kg b.w. derived from the 2-year oral study in rat.</p> <p>Additional data were provided by the petitioner i.e. acute toxicity data, skin/eye irritation data in rabbit, a dermal study in pig, a 90-day oral study in rat, an ADME study in rat, a gene mutation assay in bacteria, a chromosomal aberration assay in cultured mammalian cells, a cell transformation assay, a special investigation on the thyroid hormone status in rat, a 4-week oral study in monkey plus investigations of liver parameters, serum thyroid hormones and serum thyroid stimulating hormone (TSH), a 2-6 week oral study in rat plus investigations on morphological/biochemical parameters and investigations of the thyroid hormone status and an hydrolysis study in rat .</p> <p><u>Evaluation</u> The Committee in 1989 concluded that, based on the available data from oral studies in rat over a 2 to 6 weeks period, the observed induction of neoplasm in the thyroid arises through a non-genotoxic mode of action. Studies on the effects on the thyroid indicate that the growth-promoting effect of Irganox 245 on the thyroid is most probably mediated by the elevated serum TSH levels caused by an increased release from the pituitary gland in response to decreased serum T3 levels (thyroid-pituitary feed back mechanism). In a 28-day monkey study liver weight change and histopathological changes in the liver were observed. Additional examination of liver enzymes and thyroid function revealed, however, that in this species Irganox 245 is only a weak inducer of liver xenobiotic-metabolising enzymes and has no effect on the thyroid. In a 2-generation reproduction study with rats body weight changes were observed. In a teratogenicity study with rats no</p>

Identification of substance/ compound	Assessment
	<p>irreversible effects were observed. From an ADME study it is shown that the substance was efficiently eliminated from the body. The mean recovery, after 168 hours, is about 95.56%. After 168 hours, 35% of the radioactivity administered was excreted via urine and excretion via the faeces accounted for 55%. The maximum levels of radioactivity (Cmax) in plasma and blood were reached 1 hour after administration (reflecting a rapid absorption of the test substance).</p> <p>For the effect on the thyroid-pituitary system, the overall NOAEL is 5 mg/kg b.w. The sub acute study in monkeys indicates that primates are less sensitive to this effect, which is in agreement with what is known on the interspecies differences for this effect between humans and rodents. It is also known that humans are less sensitive to hepatic peroxisome proliferation than rodents. Thus the critical effects for Irganox 245 in rats does not provide an appropriate basis for deriving a TDI and therefore a NOAEL in another species is used.</p> <p>In a sub acute (4-week) study with monkeys the LOAEL for liver hypertrophy (NOAEL not determined) was 200 mg/kg b.w.. In a 90-day dog study the NOAEL was 30 mg/kg b.w. (LOAEL is 100 mg/kg b.w. for changes in blood parameters).</p> <p>For calculating the TDI the NOAEL of 30 mg/kg b.w. from the 90-day dog study is used. Making use of an uncertainty factor of 200 (10 for intraspecies and 10 for interspecies and 2 for the fact that no kinetic data are available on dogs and given the short-term exposure (90 days) a TDI of 0.15 mg/kg b.w. is derived.</p> <p><u>Conclusion</u> Based on the above mentioned data the substance is classified: SCF_list: 2, TDI = 0.15 mg/kg b.w.</p> <p>Remark for Commission: none.</p> <p><u>Needed data or information:</u> None.</p> <p><u>References:</u></p> <ul style="list-style-type: none"> - Unpublished data submitted by the petitioner. - Scientific Committee for Food, 1989. In "Compilation of the evaluations of the Scientific Committee for Food on certain monomers and additives used in the manufacture of plastic materials intended to come into contact with foodstuffs until the 21 March 1997". 42nd Series of Reports of the Scientific Committee for Food. Office of Official Publications of the

Identification of substance/ compound	Assessment
	European Communities, Luxembourg, 2000 (Opinion expressed by the SCF on 24 September 2002, 134th meeting of the SCF)

Previous opinions adopted by the SCF in the area of Food Contact Materials (status up to August 2002)

1) Evaluations of individual substances

The 42nd Series of Reports of the SCF (Compilation of the evaluations of the Scientific Committee for Food on certain monomers and additives used in the manufacture of plastics materials intended to come into contact with foodstuffs expressed until 21st March 1997, 2000) contains the compilation of the SCF opinions on Food Contact Materials for the period 1974 (the beginning of the existence of the Committee) to May 1997.

Following this compilation, the Committee has evaluated or re-evaluated a number of substances. All these opinions have been published on the Internet (at the webpages of the Committee, in the Europa server, www.europa.eu.int):

- Opinion on the 17th additional list of monomers and additives for food contact materials (expressed on 27 February 2002)
- Opinion on the 16th additional list of monomers and additives for food contact materials (expressed on 13th December 2001)
- Opinion on the 15th additional list of monomers and additives for food contact materials (expressed on 13th December 2001)
- Statement on a recent report on primary aromatic amines in food and packaging samples in a Danish magazine (expressed on 26 September 2001)
- Opinion on the 14th additional list of monomers and additives for food contact materials (expressed on 30th May 2001)
- Opinion on the 13th additional list of monomers and additives for food contact materials (expressed on 30th May 2001)
- Opinion on the 12th additional list of monomers and additives for food contact materials (expressed on 28th February 2001)
- Opinion on the 11th additional list of monomers and additives for food contact materials (expressed on 19 October 2000)
- Opinion on the 10th additional list of monomers and additives for food contact materials (expressed on 22 June 2000)
- Opinion on the 9th additional list of monomers and additives for food contact materials (expressed on 22 June 2000)
- Opinion on an additional list of monomers and additives intended to be used for food contact materials (10 compounds) (expressed on 2 December 1999)
- Statement on the use of Novolac glycidyl ethers (NOGE) as additives in food contact materials. Minutes of the 119th meeting of the SCF (1st/2nd December 1999)
- Statements on a recent survey on Bisphenol A diglycidyl ether (BADGE) and Bisphenol F diglycidyl ether (BFDGE) in canned food. Minutes of the 119th meeting of the SCF (1st/2nd December 1999)
- Opinion on an additional list of monomers and additives intended to be used for food contact materials (9 compounds) (expressed on 23 September 1999)
- Opinion on an additional list of monomers and additives intended to be used for food contact materials (11 compounds) (expressed on 17 June 1999)

- Opinion on an additional list of monomers and additives intended to be used for food contact materials (6 compounds) (expressed on 24 March 1999)
- Opinion on Bisphenol A diglycidyl ether (expressed on 24 March 1999)
- Opinion on an additional list of monomers and additives intended to be used for food contact materials (23 compounds) (expressed on 10 December 98)
- Opinion on an additional list of monomers and additives intended to be used for food contact materials (13 compounds) (expressed on 17 September 1998)
- Opinion on an additional list of monomers and additives intended to be used for food contact materials (37 compounds) (expressed on 19 March 1998)
- Additional list of monomers and additives evaluated by the WG "Food Contact Materials" of the SCF during the 69th-70th meetings. (16 compounds) (adopted during the SCF meeting of 12 and 13 June 1997). Also appearing in the Forty-third series of Reports of the Scientific Committee for Food, ISBN 92-828-5887-1)

2) Guidelines

The Committee has adopted also "**Guidelines of the Scientific Committee on Food for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation**". These guidelines have been modified for the last time on 13 December 2001. (Document SCF/CS/PLEN/GEN/100 Final).

APPENDIX 1

DEFINITION OF THE SCF LISTS

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.

LIST 4 (for monomers)

Section 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.

Section 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.

Section 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.

Section 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.

APPENDIX 2

Extract of the "Guidelines of the Scientific Committee on Food for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation"

These guidelines establish the general requirements of data to be submitted. As a general principle, the greater the exposure through migration, the more toxicological information will be required. In case of high migration (i.e. 5 - 60 mg/kg/food) an extensive data set is needed to establish the safety. In case of migration between 0.05 – 5 mg/kg food a reduced data set may suffice. If the data are appropriate, a restriction of 5 mg/kg of food is attributed to the substance. In case of low migration (i.e. <0.05 mg/kg food) only a limited data set is needed. If the data are appropriate, also in this case a restriction of 0.05 mg/kg of food is attributed to the substance. The full text of the guidelines provides a more detailed explanation. The guidelines are available at the web pages of the Committee.