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SCIENTIFIC OPINION

Scientific Opinion on the re-evaluation of dodecyl gallate (E 312) as a food additive[1]

EFSA Panel on Food additives and Nutrient Sources added to Food (ANS)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The EFSA ANS Panel was asked to deliver a scientific opinion re-evaluating dodecyl gallate (E 312) as a food additive. The Panel considered that whilst from theoretical considerations dodecyl gallate could be metabolised to dodecyl alcohol and gallic acid, there were insufficient data to demonstrate the rate and extent of dodecyl gallate metabolism *in vivo*. Having reviewed the data on the toxicokinetics (rate and extent of metabolism) of propyl, octyl and dodecyl gallate in a previous EFSA evaluation of propyl gallate, the Panel concluded that the available metabolism data on gallates were insufficient to provide a basis for the read-across of systemic toxicity data on propyl, octyl and dodecyl gallate to be valid. The Panel noted the absence of concern for genotoxicity and the lack of increase of tumours in the long-term study. However, owing to the lack of detailed reports on carcinogenicity and chronic toxicity studies with dodecyl gallate and the absence of a basis for read-across for systemic toxicity from propyl gallate data, the Panel could not reach a definitive conclusion on the presence or absence of a carcinogenic potential of dodecyl gallate. The Panel noted that there was no indication for overt toxicity in the available studies; however, owing to the limitations of these studies, the Panel was unable to identify any NOAEL. Overall, the available database was too limited to either establish an ADI or serve as a basis for a margin of safety approach to be applied with confidence. The Panel concluded that although there was unlikely to be a safety concern from the single use for which usage and analytical data were provided, an adequate assessment of the safety of dodecyl gallate as a food additive would require a sufficient toxicological database in line with its current guidance for submission for food additives evaluations.

KEY WORDS

dodecyl gallate, n-dodecyl 3,4,5-trihydroxybenzoate, lauryl gallate, E 312, CAS No 1166-52-5, food additive, antioxidant.

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SUMMARY

Following a request from the European Commission (EC), the Panel on Food Additives and Nutrient Sources Added to Food (ANS) was asked to re-evaluate of the safety of dodecyl gallate (E 312) when used as a food additive.

The Panel was not provided with a newly submitted dossier and based its evaluation on previous evaluations and additional literature that has become available since then, and data available following EFSA public call for data. The Panel noted that not all original studies on which previous evaluations were based were available to the Panel.

Dodecyl gallate (E 312) is authorised as a food additive in the European Union (EU) in accordance with Annex II and Annex III to Regulation (EC) No 1333/2008, and specific purity criteria have been defined in the Commission Regulation (EU) No 231/2012. The Panel noted that whilst the EC specifications allow for the presence of chlorinated organic compounds these are not identified or specified and considered that identification of possible chlorinated impurities would be needed for possible evaluation of toxicological significance.

In its last evaluation in 1987, the Scientific Committee on Food (SCF) established a group acceptable daily intake (ADI) for propyl, octyl and dodecyl gallate of 0–0.5 mg/kg bw/day. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) last evaluated the three gallates in 1997 and established an ADI of 1.4 mg/kg bw/day for propyl gallate, whilst no ADI for octyl and dodecyl gallate was allocated since relevant data on kinetics and metabolism were not made available.

Little is known about the occurrence of the dodecyl gallate in food and only fragmentary data exist. These data were published in articles which focused on development of analytical methods. The data on manufacturing were very limited and provided no details on side reactions or impurities in chemicals originating from synthesis conditions.

Propyl gallate was extensively hydrolysed to propyl alcohol and gallic acid. Gallic acid was further metabolised to 4-*O*-methyl gallic acid by *O*-methylation, glucuronidated and excreted via urine. Propyl alcohol was incorporated into intermediate metabolism of the individual (EFSA ANS Panel, 2014). The Panel considered that whilst from theoretical considerations dodecyl gallate could be metabolised to dodecyl alcohol and gallic acid, there were insufficient data to demonstrate the rate and extent of dodecyl gallate metabolism *in vivo*. The Panel noted that the available data demonstrated decreased hydrolysis of dodecyl gallate compared with propyl gallate. The Panel therefore concurred with the most recent JECFA evaluation and the Nordic Working group on Food Toxicology and Risk Assessment (TemaNord) that, on the information available, a group ADI for gallates is not scientifically justifiable.

The Panel noted that the available studies on acute toxicity of dodecyl gallate in rats and pigs indicated low acute oral toxicity. There were short-term and subchronic toxicity studies on dodecyl gallate in rats, dogs and pigs, which reported no overt toxic effects of dodecyl gallate. However, the Panel noted that the available studies were poorly reported and was unable to identify a no observed adverse effect level (NOAEL) from these studies.

No data on genotoxicity of dodecyl gallate were available. The Panel considered that for the evaluation of the genotoxic hazard of intact dodecyl gallate, read-across from data on propyl gallate and from *in silico* expert system was scientifically justified. Therefore, based on the available *in vitro* and *in vivo* results on propyl gallate, which provide a limited evidence of genotoxicity in some *in vitro* systems and no evidence in tests *in vivo* with adequate systemic exposure, the Panel concluded that dodecyl gallate was unlikely to raise concern for genotoxicity.

The Panel noted the absence of concern for genotoxicity and the lack of increase of tumours in the long-term study. However, owing to the lack of detailed reports on carcinogenicity and chronic toxicity studies with dodecyl gallate and the absence of a basis for read-across for systemic toxicity

from propyl gallate data, the Panel could not reach a definitive conclusion on the presence or absence of a carcinogenic potential of dodecyl gallate.

Two studies in rats on the reproductive toxicity of dodecyl gallate were available (van Sluis, 1951; van Esch, 1955); however, the Panel noted that these studies were insufficient to conclude on the reproductive and developmental toxicity of dodecyl gallate.

Having reviewed the data on the toxicokinetics (rate and extent of metabolism) of propyl, octyl and dodecyl gallate in the evaluation of propyl gallate (EFSA ANS Panel, 2014), this evaluation and the ongoing evaluation of octyl gallate, the Panel concluded that the available metabolism data on gallates were insufficient to provide a basis for the read-across of systemic toxicity data on propyl, octyl and dodecyl gallate to be valid. Therefore, there was no longer a basis for the present group ADI and the Panel concluded that propyl, octyl and dodecyl gallate should be evaluated separately and the present group ADI should be withdrawn.

The Panel noted that there was no indication for overt toxicity in the available studies; however, owing to the limitations of these studies, the Panel was unable to identify any NOAEL. Overall, the available database was too limited to either establish an ADI or serve as a basis for a margin of safety approach to be applied with confidence.

To assess the potential exposure to dodecyl gallate via food, two exposure assessments were performed by the ANS Panel: a regulatory maximum level exposure assessment resulting in conservative estimates of exposure and a refined exposure assessment resulting in more realistic exposure estimates. For the refined exposure assessment scenario, two exposure estimates were calculated for the brand-loyal scenario and two for the non-brand-loyal scenario.

Using the "*regulatory maximum level exposure assessment scenario*", mean exposure to dodecyl gallate from its use as a food additive in accordance with Annex II to Regulation (EC) No 1333/2008 ranged from 0.01 to 0.17 mg/kg bw/day in five population groups. The high exposure to dodecyl gallate using this scenario ranged from 0.02 to 0.64 mg/kg bw/day.

In the refined exposure assessment, using one reported use level in chewing gum and analytical data in 10 other food categories, the exposure was maximally 0.05 mg/kg bw/day for the *brand-loyal* and *non-brand-loyal* exposure scenarios in all five population groups. Apart from its authorisation according to Annex II to Regulation (EC) No 1333/2008, dodecyl gallate can also be used as a food additive in food flavourings. When this use is also considered, based on analytical data, the refined exposure to dodecyl gallate increased to a maximum of 0.6 mg/kg bw/day for both the *brand-loyal* and *non-brand-loyal* exposure scenarios.

The Panel concluded that although there was unlikely to be a safety concern from the single use for which usage and analytical data were provided, an adequate assessment of the safety of dodecyl gallate as a food additive would require a sufficient toxicological database in line with its current guidance for submission for food additives evaluations (EFSA ANS Panel, 2012).

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives requires that food additives are subject to a safety evaluation by the European Food Safety Authority (EFSA) before they are permitted for use in the European Union. In addition, it is foreseen that food additives must be kept under continuous observation and must be re-evaluated by EFSA.

For this purpose, a programme for the re-evaluation of food additives that were already permitted in the European Union before 20 January 2009 has been set up under the Regulation (EU) No 257/2010[4]. This Regulation also foresees that food additives are re-evaluated whenever necessary in light of changing conditions of use and new scientific information. For efficiency and practical purposes, the re-evaluation should, as far as possible, be conducted by group of food additives according to the main functional class to which they belong.

The order of priorities for the re-evaluation of the currently approved food additives should be set on the basis of the following criteria: the time since the last evaluation of a food additive by the Scientific Committee on Food (SCF) or by EFSA, the availability of new scientific evidence, the extent of use of a food additive in food and the human exposure to the food additive taking also into account the outcome of the Report from the Commission on Dietary Food Additive Intake in the EU[5] of 2001. The report "Food additives in Europe 2000[6]" submitted by the Nordic Council of Ministers to the Commission, provides additional information for the prioritisation of additives for re-evaluation. As colours were among the first additives to be evaluated, these food additives should be re-evaluated with a highest priority.

In 2003, the Commission already requested EFSA to start a systematic re-evaluation of authorised food additives. However, as a result of adoption of Regulation (EU) 257/2010 the 2003 Terms of References are replaced by those below.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Commission asks the European Food Safety Authority to re-evaluate the safety of food additives already permitted in the Union before 2009 and to issue scientific opinions on these additives, taking especially into account the priorities, procedures and deadlines that are enshrined in the Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with the Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives.

[4] OJ L 80, 26.03.2010, p. 19
[5] COM(2001) 542 final.
[6] Food Additives in Europe 2000, Status of safety assessments of food additives presently permitted in the EU, Nordic Council of Ministers, TemaNord 2002:560.

ASSESSMENT

1. Introduction

The present opinion deals with the re-evaluation of the safety of dodecyl gallate (E 312) when used as a food additive.

Dodecyl gallate (E 312) is authorised as a food additive in the European Union (EU) in accordance with Annex II and Annex III to Regulation (EC) No 1333/2008[7] and has been previously evaluated by the Scientific Committee for Food (SCF, 1976, 1989) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 1962, 1974, 1976, 1980, 1987, 1993a, 1993b, 1997).

The Panel on Food Additives and Nutrient Sources Added to Food (ANS) was not provided with a newly submitted dossier and based its evaluation on previous evaluations and reviews and additional literature that has become available since then, and the data available following a public call for data[8,9,10]. The Panel noted that not all original studies on which previous evaluations or reviews were based were available to the Panel. Initial evaluations were on read-across on the basis of presumed toxicokinetic similarities for a group of three gallates (propyl, octyl and dodecyl); however, subsequent work has established that these presumptions were incorrect. In its last evaluation in 1997, JECFA decided that the grouping of propyl, octyl and dodecyl gallates was not scientifically justifiable and evaluated them separately. The Nordic Working group on Food Toxicology and Risk Assessment (TemaNord) also recommended that the three permitted gallates should be evaluated individually (TemaNord, 2002).

The Panel, having considered the data on qualitative and quantitative similarities in the toxicokinetics of propyl, octyl and dodecyl gallate, agreed with the JECFA conclusion (EFSA ANS Panel, 2014). Therefore, the Panel was unable to use read-across between propyl, octyl and dodecyl gallate and in these re-evaluations the Panel has considered the available data on each gallate individually. This opinion describes the available data on dodecyl gallate. No further data were received following an additional call for toxicological data on dodecyl gallate in 2014.[10]

2. Technical data

2.1. Identity of the substance

Dodecyl gallate (E 312) is the dodecyl ester of 3,4,5-trihydroxybenzoic acid. It has the molecular formula $C_{19}H_{30}O_5$. Dodecyl gallate has a molecular weight of 338.45 g/mol, a Chemical Abstracts Service (CAS) Registry Number of 1166-52-5 and the European Inventory of Existing Commercial chemical Substances (EINECS) number is 214-620-6 (Commission Regulation (EU) No 231/2012[11]; JECFA, 2006). It has the chemical name n-dodecyl 3,4,5-trihydroxybenzoate and the structural formula is shown in Figure 1.

[7] Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354, 31.12.2008, p. 16–33.

[8] EFSA call for scientific data on food additives permitted in the EU and belonging to the functional classes of preservatives and antioxidants. November 2009. Available online: http://www.efsa.europa.eu/en/dataclosed/call/ans091123a.pdf

[9] Call for food additives usages level and/or concentration data in food and beverages intended to human consumption. Published: 27 March 2013. Available online: http://www.efsa.europa.eu/en/dataclosed/call/130327.htm

[10] Call for scientific data on selected food additives permitted in the EU. Extended deadline: 1 September 2014 (batch A), 1 November 2014 (batch B) Available online: http://www.efsa.europa.eu/en/dataclosed/call/140324.htm

[11] Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council. OJ L 83, 22.3.2012, p. 1–295.

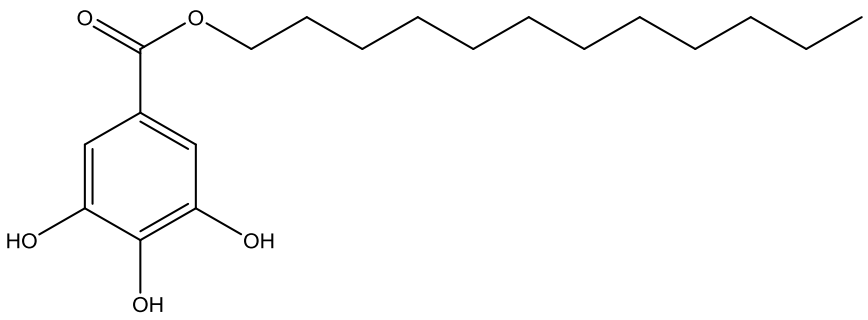

Figure 1: Structural formula of dodecyl gallate

Dodecyl gallate is a white to creamy-white, crystalline odourless solid that is insoluble in water, freely soluble in ethanol and ether. It has a melting point range of 95–98 °C (Commission Regulation (EU) No 231/2012; JECFA, 2006). A C logP of 5.30 was reported for dodecyl gallate (Rosso et al., 2006).

The synonyms include lauryl gallate, gallic acid dodecyl ester, gallic acid lauryl ester, dodecyl 3,4,5-trihydroxybenzoate and progallin LA (SciFinder software[12]).

2.2. Specifications

Specifications for dodecyl gallate are defined in Commission Regulation (EU) No 231/2012 and by JECFA (2006).

Table 1: Specification for dodecyl gallate (E 312) according to Commission Regulation (EU) No 231/2012 and to JECFA (2006)

Purity	**Commission Regulation (EU) No 231/2012**	**JECFA (2006)**
Description	White or creamy-white odourless solid	White to creamy-white crystalline odourless solid
Assay	Content not less than 98 % after drying at 90 °C (six hours)	Not less than 98.5 % on the dried basis
Solubility	Insoluble in water, freely soluble in ethanol and ether	Insoluble in water, freely soluble in ethanol and ether
Melting range	95–98 °C after drying (90 °C, six hours)	95–98 °C after drying
Gallic acid	–	Test summary: sample treated to obtain the gallic acid as a precipitate. The melting point of the gallic acid obtained is about 240 °C
TLC-separation of gallate esters	–	Test summary: TLC is run with a sample solution and a control solution. The major spot of the sample solution corresponds with that for dodecyl gallate in the control solution
Loss on drying	Not more than 0.5 % (90 °C, six hours)	Not more than 0.5 % (90 °C, six hours)
Sulphated ash	Not more than 0.05 %	Not more than 0.05 %
Free acid	Not more than 0.5 % (as gallic acid)	Not more than 0.5 % (as gallic acid)
Chlorinated organic compound	Not more than 100 mg/kg (as chlorine)	Not more than 100 mg/kg (as chlorine)
Specific absorption $E_{1cm}^{1\%}$ in ethanol	$E_{1cm}^{1\%}$ (275 nm) not less than 300 nm and not more than 325 nm	–
Arsenic	Not more than 3 mg/kg	–
Lead	Not more than 2 mg/kg	Not more than 2 mg/kg
Mercury	Not more than 1 mg/kg	–

TLC, thin-layer chromatography.

[12] SciFinder® the choice for chemistry researchTM.

TemaNord (2002) stated that the toxicological significance of the chlorinated impurities should be considered. The Panel noted that whilst the European Commission (EC) specifications allow for the presence of chlorinated organic compounds these are not identified or specified.

The Panel noted that identification of possible chlorinated impurities would be needed for possible evaluation of toxicological significance.

The Panel noted that, according to the EC specifications for dodecyl gallate, impurities of the toxic elements lead, mercury and arsenic are accepted up concentrations of 2, 1 and 3 mg/kg, respectively. Contamination at those levels would have a significant impact on the exposure to these metals, for which the exposures are already close to the health-based guidance values established by the European Food Safety Authority (EFSA) (EFSA CONTAM Panel, 2009, 2010, 2012).

2.3. Manufacturing process

Dodecyl gallate is produced by the esterification of gallic acid with the corresponding alcohol (dodecanol). The esterification is activated by the presence of an anhydrous strong acid (e.g. sulphuric acid or p-toluenesulphonic acid). The water produced is removed via azeotropic distillation with the unreacted alkyl alcohol. The product is isolated and purified by crystallisation. The final product is dried, sieved and packed (Rebafka et al., 1986; Sas et al., 2001).

2.4. Methods of analysis in food

The Panel noted that the Association of Official Analytical Chemists (AOAC, 2000) described official methods for the determination of phenolic antioxidants in oils, fats and butter oil using liquid chromatography. In addition, the International Union of Pure and Applied Chemistry (IUPAC, 1992) described a standard method for the determination of antioxidants in oils, fats and derivatives. The Panel refers to these methods for the analysis of dodecyl gallate.

Rafecas et al. (1998) described a rapid method for the determination of dodecyl gallate and other food grade antioxidants in bakery products (15 samples of doughnuts, biscuits and various types of cake). The method involves direct extraction with acetonitrile–isopropanol (1:1, v/v) and using 2,4,6-trimethylphenol as internal standard. Liquid chromatography with ultraviolet determination at 280 nm was used for the determination of the antioxidants. The linearity of the response showed determination coefficients between 0.9992–0.9999; mean recovery for dodecyl gallate 40.2 % (between 39.8 and 58.2 % depending on method of extraction used); precision of the method showed coefficients of variation of 3.5–5.9 %.

Noguera-Orti et al. (2000) described a rapid high-performance liquid chromatography (HPLC) method for the determination of dodecyl gallate and other synthetic antioxidants (amongst others propyl gallate) in powdered and liquid milk, cream of milk and dietetic supplements. The retention behaviour of the antioxidants on a C18 column, with micellar mobile phases containing sodium dodecyl sulphate (0.05–0.15 M), n-propanol (1–9 %, v/v) and 10 mM phosphate at pH 3, was studied by using mathematical models. Retention was predicted with errors below 3 %. To optimise the mobile phase composition, a procedure which takes into account the position and shape of the peaks was applied. The optimised mobile phase, which contained 0.090 M sodium dodecyl sulphate and 6.6 % n-propanol, allowed the separation of six antioxidants in less than 13 minutes. Calibration curves were linear ($r > 0.9998$) and the limits of detection range from 0.05 to 0.3 ng antioxidant. Repeatabilities for standards containing 5 µg/mL ranged from 0.2 to 1.6 %.

Pinho et al. (2000) used HPLC on a spherisorb C18 (S10ODS2) column, usual operating conditions, and a modification of the extraction procedure as described by AOAC (1990) for oils and fats to quantify the synthetic phenolic antioxidants, including dodecyl gallate, present in liver pâtés. Extensive validation of the extraction procedure used was performed by recovery tests. Over 91 % recoveries of added antioxidants were observed. The precision found was below 3.8 %. Via this method, no synthetic antioxidants were detected in six of the 12 assayed liver pâté brands.

Sin et al. (2006) described an analytical protocol and the estimation of measurement uncertainty, for the determination of dodecyl gallate and other antioxidants in edible oils. The protocol comprises a TLC screening step, quantification by gas chromatography–flame ionisation detection (GC–FID) and HPLC–photodiode array detection (PDA) techniques. Reference material samples of certified sunflower oil, vegetable oil and maize oil were used. Mass spectrometry and a second chromatographic technique were used to unequivocally confirm the analytical results, providing a reliable and validated means for fast turnaround and high sample throughput analysis of dodecyl gallate in edible oils. In total, 286 edible oil- and fat-containing samples for analysis of dodecyl gallate (and a series of other antioxidants) in 11 batches throughout a study period of 12 months were investigated. The linearity for both GC and HPLC was in the range of 10–500 µg/mL, and their corresponding coefficients of correlation were > 0.995. The limit of detection (LOD) (ranging from 2 to 4 µg/g) was estimated as three times the standard deviation of the blanks, and the limit of quantification (LOQ), which was defined as the lowest concentration used in the calibration, was 10 µg/g. The authors stated that the protocol was also found to be applicable to other fat-containing food matrices.

Delgado-Zamarreno et al. (2007) used micellar electrokinetic capillary chromatography (MEKC), with bis-(2-ethylhexyl) sodium sulphosuccinate as the pseudostationary phase, to determine the concentrations of dodecyl gallate and other synthetic antioxidants in edible oils used in oil-based foods. Studies involving solid-phase extraction (on C18 or silica sorbents) and liquid–liquid extraction (solvents: methanol or acetonitrile) were performed to find the best sample treatment before injection into the electrophoretic system. Extractions were carried out on sunflower oil spiked with dodecyl gallate at 1 g/kg. The best methodology for the isolation of antioxidants was liquid–liquid extraction with acetonitrile from edible oil diluted with hexane. The results showed that with this method dodecyl gallate can be analysed in oil-based foods via liquid–liquid extraction in a concentration range between 0.01 and 1 g/kg. A similar method using electrokinetic chromatography for the determination of food grade antioxidants was also described by Darji et al. (2010).

Wang et al. (2012) described a new HPLC methodology for fast quantitative analysis of 10 synthetic antioxidants. In this method, the alternating penalty trilinear decomposition (APTLD) method, as described by Xia et al. (2005), was coupled with HPLC analysis with diode array detection. The method was used to determine dodecyl gallate and nine other phenolic antioxidants (amongst others propyl gallate, octyl gallate) in five kinds of commercial oil samples (tea seed oil, soybean oil, seed oil, blend oil and maize oil). The oil samples were spiked with different concentration levels (10.58–25.37 µg/mL for dodecyl gallate) of the antioxidants and diluted with iso-propanol/n-hexane (4:1, by volume) (1:5). The second-order calibration, with second-order advantage, based on the APTLD algorithm was reported by the authors to be an excellent tool for modelling in cases where overlapping peaks, uncalibrated interferences and baseline drift existed. The authors showed that the methods made the fast determination and resolution of the phenolic antioxidants in oils possible. For the validation of the method, linearity, root mean square error of prediction (RMSEP) and LOD were performed. The data showed that the recovery of dodecyl gallate ranged from 93.8 to 106.1 %, with a LOD of 5.72 µg/mL.

2.5. Reaction and fate in food

Dodecyl gallate is a polyphenolic ester which could be susceptible to ester hydrolysis. No relevant information on the reaction and fate in foods of gallates was found in the literature.

Whilst propyl gallate (E 310) is not stable at high temperatures (degrading at 148 °C) and it is not suitable for frying applications, the longer chain length of dodecyl gallate makes it more lipid soluble, more heat stable and have better carry though (Reische et al., 2008; Saltmarsh, 2013).

2.6. Case of need and use levels

Maximum permitted levels (MPLs) of dodecyl gallate (E 312) have been defined in Annex II to Regulation (EC) No 1333/2008 on food additives.

Currently, dodecyl gallate (E 312) is an authorised food additive in the EU with MPLs ranging from 25 to 400 mg/kg in foods. For certain food categories the MPL is expressed on fat basis. Dodecyl gallate (E 312) is authorised to be used individually or in combination with propyl gallate (E 310), octyl gallate (E 311), tertiary-butylhydroquinone (TBHQ; E 319), butylated hydroxyanisole (BHA; E 320) and butylated hydroxytoluene (BHT; E 321) (Regulation (EC) No 1333/2008).

Table 2 summarises the food categories in which dodecyl gallate (E 312) is permitted and the corresponding MPLs as set by Annex II to Regulation (EC) No 1333/2008.

Table 2: MPLs of dodecyl gallate (E 312) in food categories according to the Annex II to Regulation (EC) No 1333/2008

FCS category number	FCS food category name	E number/group	Restrictions/exceptions	Maximum level (mg/L or mg/kg as appropriate)
01.5	Dehydrated milk as defined by Directive 2001/114/EC	E 310–312, TBHQ and BHA	Only milk powder for vending machines	200 [(a)]
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	E 310–312, TBHQ and BHA	Only fats and oils for the professional manufacture of heat-treated foods; frying oil and frying fat (excluding olive pomace oil) and lard, fish oil, beef, poultry and sheep fat	200 [(a) (b)]
02.2.2	Other fat and oil emulsions, including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	E 310–312, TBHQ and BHA	Only frying fat	200 [(a) (c)]
04.2.5.4	Nut butters and nut spreads	E 310–312, TBHQ and BHA	Only processed nuts	200 [(a) (b)]
04.2.6	Processed potato products	E 310–312, TBHQ and BHA	Only dehydrated potatoes	25 [(a)]
05.3	Chewing gum	E 310–312, TBHQ, BHA and BHT		400 [(a)]
06.3	Breakfast cereals	E 310–312, TBHQ and BHA	Only pre-cooked cereals	200 [(a) (d)]
06.7	Pre-cooked or processed cereals	E 310–312, TBHQ and BHA	Only pre-cooked cereals	200 [(a)]
07.2	Fine bakery wares	E 310–312, TBHQ and BHA	Only cake mixes	200 [(a)]
08.3.1	Non-heat-treated processed meat	E 310–312, TBHQ and BHA	Only dehydrated meat	200 [(a) (d)]
12.2.2	Seasonings and condiments	E 310–312, TBHQ, BHA and BHT		200 [(a) (d)]
12.5	Soups and broths	E 310–312, TBHQ and BHA	Only dehydrated soups and broths	200 [(a) (d)]
12.6	Sauces	E 310–312, TBHQ and BHA		200 [(a) (d)]
15.1	Potato-, cereal-, flour- or starch-based snacks	E 310–312, TBHQ and BHA	Only cereal-based snack foods	200 [(a)]
15.2	Processed nuts	E 310–312, TBHQ and BHA		200 [(a) (d)]

FCS category number	FCS food category name	E number/group	Restrictions/exceptions	Maximum level (mg/L or mg/kg as appropriate)
17.1	Food supplements supplied in a solid form, including capsules and tablets and similar forms, excluding chewable forms	E 310–312, TBHQ, BHA and BHT		400 [(a)]
17.2	Food supplements supplied in a liquid form	E 310–312, TBHQ, BHA and BHT		400 [(a)]
17.3	Food supplements supplied in a syrup-type or chewable form	E 310–312, TBHQ, BHA and BHT		400 [(a)]

(a): The additives may be added individually or in combination.
(b): Expressed on fat basis.
(c): The maximum level is applicable to the sum and the levels are expressed as the free acid.
(d): Maximum limit expressed on fat.
FCS, Food Categorisation System.

The Panel noted that footnotes (b) and (d) to Table 2, as described in the Annex II of the Regulation (EC) No 1333/2008, appear to be identical and one seems to be redundant.

Dodecyl gallate (E 312) is also permitted to be used as a food additive in food flavourings in accordance with to Annex III to Regulation (EC) No 1333/2008 (Part 4). Dodecyl gallate (E 312) may be added to essential oils up to 1 000 mg/kg individually or in combination with propyl gallate (E 310), octyl gallate (E 311), TBHQ (E 319) and BHA (E 320). Furthermore, dodecyl gallate (E 312) may also be added to flavourings other than essential oils up to 100 mg/kg[13] individually or in combination with propyl gallate (E 310) and octyl gallate (E 311).

2.7. Reported use levels or data on analytical levels of dodecyl gallate (E 312) in food

Most food additives in the EU are authorised at a specific MPL. However, a food additive may be used at a lower level than the MPL. Therefore, information on actual use levels is required to perform a more realistic exposure assessment. This is especially true for food additives for which no MPLs are set, but are authorised according to *quantum satis* (QS). For dodecyl gallate (E 312), no food categories are currently authorised at QS (Table 2).

In the framework of Regulation (EC) No 1333/2008 on food additives and of Commission Regulation (EU) No 257/2010[14] regarding the re-evaluation of approved food additives, EFSA issued a public call[15] for occurrence data (analytical data) and a public call[16] for usage level and/or concentration data on dodecyl gallate (E 312). In response to these calls, usage and concentration (analytical data) on dodecyl gallate (E 312) were submitted to EFSA by industry and Member States, respectively.

2.7.1. Summarised data on reported use levels in foods provided by industry

Information on the actual use levels of dodecyl gallate (E 312) was made available to EFSA for only chewing gum (FCS 05.3) by the International Chewing Gum Association (ICGA). The typical and maximum reported usage level was 200 and 300 mg/kg, respectively.

[13] Proportionality rule: when combinations of gallates, TBHQ and BHA are used, the individual levels must be reduced proportionally.
[14] Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives. OJ L 80, 26.3.2010, p. 19.
[15] Call for approved food additives (sorbates, benzoates and gallates) occurrence data in food and beverages intended for human consumption. Published: 1 June 2012. Available online: http://www.efsa.europa.eu/en/dataclosed/call/120601.htm
[16] Call for food additives usage level and/or concentration data in food and beverages intended for human consumption. Published: 27 March 2013. Deadline: 15 September 2013. Available online: http://www.efsa.europa.eu/en/data/call/130327.htm

2.7.2. Summarised data on concentration levels in food submitted by Member States

In total, 959 analytical results were reported to EFSA by four countries: Slovakia (n = 670), Germany (n = 189), Denmark (n = 83) and Ireland (n = 17). These data were mainly for fats and oils (FCS 02.1 and FCS 02.2.2), processed fish and fishery products (FCS 09.2) and sauces (FCS 12.6). Foods were sampled between 2005 and 2013, and majority of them (95 %) were analysed the year that they were collected.

All analytical results on dodecyl gallate (E 312) were left-censored: either not quantified (< LOQ) in 773 samples or not detected (< LOD) in 186 samples. Therefore, it should be noted that the use of middle-bound (MB) LOD/LOQ values (half of LOD or LOQ) in the exposure assessment (section 2.9.2.2), may have resulted in either an overestimation, where dodecyl gallate (E 312) was not present, or underestimation, where the concentration was between the MB and LOQ/LOD value, but the analytical method was not able to detect or quantify it.

Complete information on the methods of analysis (e.g. validation) was not made available to EFSA. All samples were derived from accredited laboratories. The Panel noted that 235 analytical results were reported in food categories in which dodecyl gallate is not authorised for direct addition in accordance with Annex II of Regulation (EC) No 1333/2008, including unprocessed fruit and vegetables (FCS 04.1), noodles (FCS 06.5), processed fish and fishery products (FCS 9.2), fish roe (FCS 9.3), salads and savoury-based sandwich spreads (FCS 12.7) and processed foods (FCS 18). Other authorised uses of dodecyl gallate (E 312) may result in carry-over and its detection in these food categories. It should, however, be noted that dodecyl gallate (E 312) was not detected/not quantified in these food categories.

For 17 analytical results insufficient detail for the description of the food was reported. Therefore, these results were not taken into account in the exposure assessment.

Overall, 942 out of the 959 analytical results reported for dodecyl gallate (E 312) in foods were considered by the Panel in the exposure assessment after discarding the provided analytical results with insufficient description of the food type. In total, for 7 out of 18 food categories, authorised for use of dodecyl gallate (E 312) as a food additive, no analytical data were available, which may have led to an underestimation of the exposure.

Appendix A shows the analytical results of dodecyl gallate (E 312) in foods as reported by Member States.

2.8. Information on existing authorisations and evaluations

Dodecyl gallate (E 312) is authorised as a food additive in the EU in accordance with Annex II and Annex III to Regulation (EC) No 1333/2008 on food additives and specific purity criteria have been defined in the Commission Regulation (EU) No 231/2012.

In 1976, the SCF established a group acceptable daily intake (ADI) of 0–0.2 mg/kg bw/day for gallate, octyl gallate and dodecyl gallate (SCF, 1976). The ADI was based on a no observed effect level (NOEL) of 50 mg/kg bw/day in long-term studies on rats and mice and the application of an uncertainty factor of 250 because of doubts on their effects on reproduction. The SCF last evaluated the three gallates (propyl, octyl, dodecyl) in 1987 and established that a group ADI of 0–0.5 mg/kg bw/day was acceptable (SCF, 1989). The Committee confirmed the previously established no effect level (NEL) of 50 mg/kg bw/day in long-term studies on rats and mice and, in the light of new study data, applied the usual uncertainty factor of 100.

Propyl gallate, octyl gallate and dodecyl gallate were first evaluated by JECFA in 1962 (JECFA, 1962) and since then have been evaluated on numerous occasions (JECFA, 1974, 1976, 1980, 1987, 1993a, b, 1997). For the first evaluation recommendations were made for more data. JECFA last evaluated the three gallates in 1996 and allocated to propyl gallate an ADI of 0–1.4 mg/kg bw/day based on a NOEL of 1 910 mg/kg in the feed (equivalent to 135 mg/kg bw/day) in a 90-day study in

rats and an uncertainty factor of 100 (JECFA, 1997). The temporary ADIs for octyl and dodecyl gallate established by JECFA in 1993 were not extended since the requested data on kinetics and metabolism were not made available.

TemaNord reviewed propyl gallate, octyl gallate and dodecyl gallate and recommended that "*The allocation of the ADI for these compounds should be reconsidered individually.*" (TemaNord, 2002).

Dodecyl gallate (PM Ref. 55200) is included in the Union list of authorised substances that may be intentionally used in the manufacture of plastic layers in plastic materials and articles (Annex I to Commission Regulation (EU) No 10/2011[17]). Dodecyl gallate is permitted as an antioxidant in cosmetic products (European Commission database-CosIng[18]).

2.9. Exposure assessment

2.9.1. Food consumption data used for exposure assessment

2.9.1.1. EFSA Comprehensive European Food Consumption Database

Since 2010, the EFSA Comprehensive European Food Consumption Database (Comprehensive Database) has been populated with national data from national information on food consumption at a detailed level. Competent authorities in the European countries provide EFSA with food consumption data at the level of the individual consumer from the most recent national dietary survey in their country (cf. Guidance of EFSA 'Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment' (EFSA, 2011a)).

The food consumption data included in the Comprehensive Database were collected by different methodologies and thus direct country-to-country comparisons should be interpreted with caution. Depending on the food category and the level of detail used in the exposure calculations, uncertainties can be introduced because of possible subjects' underreporting and/or misreporting of the consumption amounts.

The Panel estimated the chronic exposure to dodecyl gallate (E 312) for the following population groups: toddlers, children, adolescents, adults and the elderly. Calculations were performed using individual body weights. For calculation of chronic exposure, intake statistics were calculated based on individual average consumption over the total survey period. Surveys with only one day per subject were excluded, because they were considered not adequate to assess chronic dietary exposure. High percentile exposure was only calculated for population groups where the sample size was sufficiently large to allow calculation of the 95th percentile of exposure (EFSA, 2011a). Therefore, in the present assessment, high levels of exposure for toddlers from Belgium, Italy and Spain were not included.

Thus, for the present assessment, food consumption data were available from 26 different dietary surveys carried out in 17 European countries, as mentioned in Table 3.

[17] Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. OJ L 12, 15.1.2011, p. 1.
[18] Available online: http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.simple

Table 3: Population groups considered for the exposure estimates of dodecyl gallate (E 312)

Population	Age range	Countries with food consumption surveys covering more than one day
Toddlers	from 12 up to and including 35 months of age	Belgium, Bulgaria, Finland, Germany, the Netherlands, Italy, Spain
Children [(a)]	from 36 months up to and including 9 years of age	Belgium, Bulgaria, the Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Latvia, the Netherlands, Spain, Sweden
Adolescents	from 10 up to and including 17 years of age	Belgium, Cyprus, the Czech Republic, Denmark, France, Germany, Italy, Latvia, Spain, Sweden
Adults	from 18 up to and including 64 years of age	Belgium, the Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, the Netherlands, Spain, Sweden, the UK
The elderly [(a)]	from 65 years of age and older	Belgium, Denmark, Finland, France, Germany, Hungary, Italy

(a): The terms "children" and "the elderly" correspond, respectively, to "other children" and the merge of "elderly" and "very elderly" in the Guidance of EFSA on the 'Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment' (EFSA, 2011b).

Consumption records were codified according to the FoodEx classification system (EFSA, 2011b). Nomenclature from the FoodEx classification system has been linked to the FCS as presented in the Annex II to Regulation (EC) No 1333/2008, part D, to perform exposure estimates.

2.9.1.2. Food categories selected for the exposure assessment of dodecyl gallate (E 312)

The food categories in which the use of dodecyl gallate (E 312) is authorised were selected from the nomenclature of the EFSA Comprehensive Database (FoodEx classification system), at the most detailed level possible (up to FoodEx Level 4) (EFSA, 2011b).

Some food categories or their restrictions/exceptions are not referenced in the EFSA Comprehensive Database and therefore could not be taken into account in the present estimate. This might result in an underestimation of the exposure. The food categories which were not taken into account are described below (in ascending order of the FCS codes):

- 01.5 Dehydrated milk as defined by Council Directive 2001/114/EC[19], only milk powder for vending machines;
- 06.3 Breakfast cereals, only pre-cooked cereals;
- 06.7 Pre-cooked or processed cereals, only pre-cooked cereals;
- 12.5 Soups and broths, only dehydrated soups and broths.

For the following food categories, the restrictions which apply to the use of dodecyl gallate (E 312) could not be taken into account, and therefore the whole food category was considered for the exposure estimations. This results in an overestimation of the exposure:

- 02.1 Fats and oils essentially free from water (excluding anhydrous milkfat), only fats and oils for the professional manufacture of heat-treated foods; frying oil and frying fat (excluding olive pomace oil) and lard, fish oil, beef, poultry and sheep fat;
- 02.2.2 Other fat and oil emulsions, including spreads as defined by Council Regulation (EC) No 1234/2007[20] and liquid emulsions, only frying fat;

[19] Council Directive 2001/114/EC of 20 December 2001 relating to certain partly or wholly dehydrate preserved milk for human consumption. OJ L 15, 17.1.2002, p. 19.
[20] Council Regulation (EC) No 1234/2007 of 22 October 2007 establishing a common organisation of agricultural markets and on specific provisions for certain agricultural products. OJ L 299, 16.11.2007, p. 1.

- 04.2.5.4 Nut butters and nut spreads, only processed nuts;
- 17.1/17.2/17.3 Food supplements, in solid, liquid, syrup-type or chewable form.

Overall, four food categories were not taken into account in the exposure assessment because they or their specific restrictions/exceptions are not referenced in the EFSA Comprehensive Database. Six food categories were included in the exposure assessment without considering the restrictions/exceptions as set in Annex II to Regulation (EC) No 1333/2008. For the remaining food categories, the refinements considering the restrictions/exceptions as set in Annex II to Regulation No 1333/2008 were applied. Overall, 11 food categories were included in the present exposure assessment to dodecyl gallate (E 312) (Appendix B).

2.9.2. Exposure to dodecyl gallate (E 312) from its use as food additive

The exposure to dodecyl gallate (E 312) was calculated by multiplying dodecyl gallate (E 312) concentrations for each food category with their respective consumption amount per kilogram of body weight for each individual in the Comprehensive Database. The exposure per food category was subsequently added to derive an individual total exposure per day. These exposure estimates were averaged over the number of survey days, resulting in an individual average exposure per day for the survey period. This was carried out for all individuals per survey and per population group, resulting in distributions of individual average exposure per survey and population group (Table 3). Based on these distributions, the mean and 95th percentile exposure were calculated per survey for the total population and per population group.

Exposure assessment to dodecyl gallate (E 312) was carried out by the ANS Panel based on: (1) MPLs as set down in the EU legislation (defined as the *regulatory maximum level exposure assessment scenario*); and (2) the reported use levels or analytical data (defined as the *refined exposure assessment scenario*). These two scenarios are discussed in detail below.

2.9.2.1. Regulatory maximum level exposure assessment scenario

The regulatory maximum level exposure assessment scenario is based on the MPLs as set in Annex II to Regulation (EC) No 1333/2008 and listed in Table 2. MPLs expressed for dodecyl gallate (E 312) on fat basis were converted to whole weight based on fat content information obtained from the Comprehensive Database. The MPLs as converted to whole weight and used in this exposure scenario are listed in Appendix B.

A possible additional exposure from the use of dodecyl gallate (E 312) as a food additive in food flavourings in accordance with Annex III to Regulation (EC) No 1333/2008 (Part 4) was not considered in the regulatory maximum level exposure assessment scenario. This may have resulted in underestimation of the overall exposure to dodecyl gallate (E 312).

The exposure estimates derived following this scenario should be considered as the most conservative since it is assumed that the consumer will be continuously (over a lifetime) exposed to dodecyl gallate (E 312) present in food at MPL.

2.9.2.2. Refined exposure assessment scenario

The refined exposure assessment scenario is based on use levels reported by industry and analytical results reported by Member States. This exposure scenario can consider only food categories where the above data were made available to the Panel.

Appendix B summarises the concentration levels of dodecyl gallate (E 312) used in the refined exposure assessment scenarios. Based on the available dataset, the Panel calculated two estimates based on different model populations:

- The brand-loyal consumer scenario: It was assumed that a consumer is exposed long-term to the food additive present at the maximum reported use/analytical level for one food category. This exposure estimate is calculated as follows:
  - Combining food consumption with the maximum of the reported use levels or the maximum of the analytical results for the main contributing food category at the individual level.
  - Using the mean of the typical reported use levels or the mean of analytical results for the remaining food categories.
- The non-brand-loyal consumer scenario: It was assumed that the population is exposed long-term to the food additive present at the mean reported use/analytical levels in food. This exposure estimate is calculated using the mean of the typical reported use levels or the mean of analytical results for all food categories.

In the two refined exposure assessment scenarios, the concentration levels considered by the Panel were extracted from the whole dataset (i.e. reported use levels and analytical results). To consider left-censored analytical data (i.e. analytical results < LOD or < LOQ), the substitution method as recommended in the "Principles and Methods for the Risk Assessment of Chemicals in Food" (WHO, 2009) and the EFSA scientific report "Management of left-censored data in dietary exposure assessment of chemical substances" (EFSA, 2010) was used. In the present opinion, analytical data below LOD or LOQ were assigned half of LOD or LOQ, respectively (MB). Subsequently, per food category, the mean or median, as appropriate, MB concentration was calculated. For the food category 'Chewing gum' (FCS 05.3) the maximum (brand-loyal scenario) or mean typical (non-brand-loyal scenario) reported use level was used.

Two refined estimated exposure scenarios were calculated; considering only the food categories authorised according to Annex II to Regulation (EC) No 1333/2008 and another scenario considering analytical data reported for food categories not authorised according to Annex II to Regulation (EC) No 1333/2008 but for which dodecyl gallate can be present as a food additive in food flavouring (Annex III to Regulation (EC) No 1333/2008).

2.9.2.3. Anticipated exposure to dodecyl gallate (E 312)

Table 4 summarises the estimated exposure to dodecyl gallate (E 312) from its use as a food additive in five population groups (Table 3). Detailed results per population group and survey are presented in Appendix D.

Table 4: Summary of anticipated exposure to dodecyl gallate (E 312) from its use as a food additive in the regulatory maximum level exposure assessment scenario and in the refined exposure scenarios, in five population groups (minimum–maximum across the dietary surveys in mg/kg bw/day)

	Toddlers (12–35 months)	Children (3–9 years)	Adolescents (10–17 years)	Adults (18–64 years)	The elderly (≥ 65 years)
Regulatory maximum level exposure assessment scenario [(a)]					
Mean	0.03–0.16	0.03–0.17	0.01–0.09	0.01–0.09	0.01–0.09
High level	0.16–0.64	0.11–0.56	0.04–0.35	0.05–0.35	0.02–0.35
Refined estimated exposure scenario using reported use levels and analytical data including only the food categories as listed in Table 2					
Brand-loyal scenario					
Mean	0.001–0.005	0.0003–0.01	0.0001–0.009	0.0005–0.005	0.0003–0.002
High level	0.006–0.02	0.002–0.05	0.0008–0.04	0.002–0.02	0.001–0.006
Non-brand-loyal scenario					
Mean	0.0008–0.004	0.0002–0.01	0.0001–0.006	0.0003–0.004	0.0002–0.001
High level	0.006–0.01	0.002–0.04	0.0007–0.03	0.001–0.02	0.0006–0.005
Refined estimated exposure scenario using reported use levels and overall analytical data [(b)]					
Brand-loyal scenario					
Mean	0.04–0.3	0.02–0.1	0.01–0.1	0.002–0.07	0.002–0.07
High level	0.3–0.6	0.05–0.4	0.02–0.2	0.01–0.2	0.01–0.2
Non-brand-loyal scenario					
Mean	0.04–0.3	0.02–0.1	0.01–0.1	0.002–0.07	0.001–0.07
High level	0.3–0.6	0.05–0.4	0.02–0.2	0.01–0.2	0.01–0.2

(a): This scenario included only the food categories as listed in Table 2.
(b): This scenario also included the food categories for which direct addition of dodecyl gallate (E 312) is not authorised according to Annex II to Regulation (EC) No 1333/2008; however, the use of dodecyl gallate (E 312) may result in its presence in these food categories because of carry-over.

The main food categories contributing to the exposure to dodecyl gallate (E 312) are presented in Appendix C (Tables C1 to C5).

In the *regulatory maximum level exposure assessment* scenario (Appendix C, Table C1), fine bakery wares, sauces and, in a limited number of surveys, also other fat and oil emulsions were the main contributors to the total mean exposure to dodecyl gallate (E 312).

In both refined exposure scenarios (Appendix C, Tables C2 to C3) including only the food categories authorised according to Annex II to Regulation (EC) No 1333/2008, sauces and chewing gum were the main contributors to the total mean exposure to dodecyl gallate (E 312) for all age groups. In addition, in the elderly, herbs, spices and seasonings were also important contributors. It should be noted that for chewing gum only the usage level was available and this level was considerably higher than the analytical levels used in the refined exposure assessment scenarios for the other food categories. This very likely influenced the outcome considerably.

When considering also food categories not authorised according to Annex II to Regulation (EC) No 1333/2008, but considered as coming from the authorised use from Annex III (food additive in food flavourings), processed foods were the most important contributor to the total mean exposure to dodecyl gallate (E 312) for all age groups in both refined exposure assessment scenarios.

2.9.3. Uncertainty analysis

Uncertainties in the exposure assessment of dodecyl gallate (E 312) have been discussed above. In accordance with the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2006), the following sources of uncertainties have been considered and summarised in Table 5.

Table 5: Qualitative evaluation of influence of uncertainties on the dietary exposure estimate

Sources of uncertainties	Direction [(a)]
Consumption data: different methodologies/representativeness/underreporting/misreporting/no portion size standard	+/–
Use of data from food consumption survey of a few days to estimate long-term (chronic) exposure	+
Correspondence of reported use levels and analytical data to the food items in the EFSA Comprehensive Food Consumption Database: uncertainties to which types of food the levels refer to	+/–
Food categories selected for the exposure assessment: exclusion of food categories because of missing FoodEx linkage	–
Food categories selected for the exposure assessment: inclusion of food categories without considering the restriction/exception	+
Concentration data: levels considered applicable for all items within the entire food category, exposure calculations based on the maximum or mean levels (reported use from industries or analytical data from mass spectrometry)	+/–
Regulatory maximum level exposure assessment scenario: the food categories authorised according to Annex III to Regulation (EC) No 1333/2008 not considered	–
Regulatory maximum level exposure assessment scenario: the food categories authorised according to Annex II to Regulation (EC) No 1333/2008	+
Concentration data: data not available for certain food category	–
Concentration data: refined exposure scenarios based on analytical data with all results below LOD/LOQ	+/–
Uncertainty in possible national differences in use levels of food categories, concentration data not fully representative of foods on the EU market	+/–

(a): +, uncertainty with potential to cause over-estimation of exposure; –, uncertainty with potential to cause underestimation of exposure.

Overall, the Panel considered that the uncertainties identified would, in general, lead to an overestimate of the real exposure to dodecyl gallate (E 312) as a food additive in European countries for the MPL scenario and when analytical data were used. The data on actual use level would underestimate the exposure if dodecyl gallate were used in permitted categories other than chewing gum, the only permitted use for which actual use level was provided.

2.9.4. Exposure via other sources

According to Commission Regulation (EU) No 10/2011 on dodecyl gallate (PM Ref. 55200), this compound can be used in the manufacture of plastic layers in plastic materials. In the case of food additives permitted also in food contact materials (FCMs) the so-called dual-use rule applies. This means that when migration from the FCMs occurs, the limits and permitted food groups in the food additives legislation must be observed. According to Commission Regulation (EU) No 10/2011, the three gallates have a collective specific migration limit (SML) of 30 mg/kg food. Therefore, the exposure to dodecyl gallate resulting from this source is potentially much higher than from its use as a food additive. The exposure estimates for the gallates as FCMs are based on the assumption that individuals consume 1 kg of food packed in plastics regardless of their age. Using average body weights (EFSA Scientific Committee, 2012) and the assumption of 1 kg of packed foods consumed, exposure to dodecyl gallate would be 2.5, 1.3, 0.6 and 0.4 mg/kg bw/day for toddlers, children, adolescents and adults, respectively.

Furthermore, dodecyl gallate is also permitted as an antioxidant in cosmetic products. According to the Regulation (EC) No 1223/2009[21] on cosmetic products there is no limit.

The exposure via these routes is unknown, and could therefore not be taken into account in this opinion.

[21] Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products. OJ L 342, 22.12.2009, p. 59.

3. Biological and toxicological data

The latest evaluations of propyl, octyl and dodecyl gallates by the SCF was in 1987 (SCF, 1989), and by JECFA in 1996 (JECFA, 1997). The studies on dodecyl gallate reported in these evaluations are summarised below, together with all other relevant and available information.

3.1. Absorption, distribution, metabolism and excretion

3.1.1. *In vitro* studies

The JECFA evaluation (JECFA, 1993b), based on a Netherlands Organisation for Applied Scientific Research (TNO) report from de Bie and van Ommen (1992, as referred to by JECFA, 1993b), described *in vitro* incubations with propyl, octyl and dodecyl gallate performed using homogenates of the liver, mucosa of the small intestine and contents of the caecum/colon as a source of intestinal microflora. The Panel included a detailed summary in its opinion on propyl gallate and noted that the species from which the samples were taken were not stated (EFSA ANS Panel, 2014). However, the Panel noted also that the rate and extent of metabolism of propyl, octyl and dodecyl gallates differed. Therefore, the Panel concluded that the available data on gallates were insufficient for the read-across of systemic toxicity data on propyl, octyl and dodecyl gallate to be valid (EFSA ANS Panel, 2014).

3.1.2. Animal studies

Absorption, distribution, metabolism and excretion (ADME)/toxicokinetic studies on the three gallates were reported in the JECFA evaluations (JECFA, 1993b) and concluded *that* "*Although there are similarities in the metabolism of the different gallates as evidenced by earlier limited data and a newly available in vitro metabolism study, the Committee concluded that there was not enough evidence to allocate a group ADI for the gallates when in vivo pharmacokinetic and metabolic studies were not available*" (JECFA, 1993b). Studies from the JECFA evaluation (1993b) were summarised in the Panel's opinion on propyl gallate (EFSA ANS Panel, 2014) and one on dodecyl gallate is included below.

When adult albino rats were administered by gavage 100 mg dodecyl gallate/rat, the major metabolite in urine was 4-*O*-methyl-gallic acid (no further details) (Booth et al., 1959). Gallic acid in smaller amounts was also identified indicating hydrolysis of the ester followed by 4-*O*-methylation of gallic acid. An intraperitoneal (i.p.) injection of 100 mg gallic acid per rat also resulted in urinary excretion of 4-*O*-methyl gallic acid as well as gallic acid.

3.1.3. Human studies

In a project for the UK Food Standards Agency, Tullberg et al. (2004) compared the kinetics of four chemicals present in human food (BHT, curcumin, gallates and thiabendazole) *in vivo* in rats and humans and in hepatocytes from humans and rats to examine the adequacy of the kinetic uncertainty factors. The plasma concentrations in humans dosed propyl gallate at its ADI (0.5 mg/kg bw/day) were close to the LOQ, whereas more reliable data were obtained at a dose of 10 times the ADI. These data were discussed in the EFSA opinion on propyl gallate (EFSA ANS Panel, 2014). Studies by the same group (Tullberg et al., 2004) with dodecyl gallate administered at its ADI (0.5 mg/kg bw/day) in humans resulted in extremely low plasma concentrations (lower than those obtained for propyl gallate) and generally below the LOQ, which, combined with the low ADI, meant that further human studies *in vivo* were not practicable.

The Panel noted that these differences in plasma concentrations of propyl and dodecyl gallate would be consistent with the differences in rate and extent of metabolism of propyl and dodecyl gallates in other studies which did not support read-across of the toxicity data between different gallates (EFSA ANS Panel, 2014).

3.2. Toxicological data

3.2.1. Acute oral toxicity

The acute oral LD_{50} value for dodecyl gallate in rats was 6 500 mg/kg bw (van Sluis, 1951, as referred to by JECFA, 1993b).

The acute toxicity of dodecyl gallate in rats after i.p. injection produced a LD_{50} value of 100–120 mg dodecyl gallate/kg bw (van Esch and van Genderen, 1954).

In pigs, no sign of toxicity was seen at doses of 2–6 g/kg bw (van Esch, 1955).

The Panel noted that the available studies on acute toxicity that exists in different species for dodecyl gallate indicate low oral acute toxicity.

3.2.2. Short-term and subchronic toxicity

Short-term and subchronic toxicity studies as reported in the JECFA evaluation (JECFA 1993b) are summarised below. No new relevant studies have been identified.

3.2.2.1. Rats

Female weanling albino rats (five animals/group; average 42 g body weight) were given diets containing 2.5 or 5 % dodecyl gallate (equivalent[22] to 3 000 and 6 000 mg dodecyl gallate/kg bw/day) (Allen and DeEds, 1951). All animals fed the low concentration died within 10 days and all animals fed the high concentration died within 7 days. It was reported that the daily intake of feed for both groups was so low that starvation was an obvious major factor in causing death. Autopsy revealed very thin animals with minimal amounts of intra-abdominal fat and swollen abdomens. Histopathological examination of major organs showed no alterations induced by dodecyl gallate at any dose. Five male rats (average 49 g body weight) on a diet containing 0.012 % dodecyl gallate (equivalent[22] to 14.4 mg dodecyl gallate/kg bw/day) for 38 days showed normal food intake and growth. The concentration was then raised to 2.5 % dodecyl gallate (equivalent[22] to 3 000 mg/kg bw/day) which caused a marked decrease in food consumption and the death of three animals by the 52nd day and all animals by the 73rd day. Starvation was mentioned as a causative factor.

Five female rats (age not stated) fed a diet containing 0.006 % dodecyl gallate (equivalent[22] to 60 mg dodecyl gallate/kg bw/day) for 76 days showed no evidence of toxicity (Allen and DeEds, 1951). From day 76, the concentration was raised to 2.5 % (equivalent[22] to 12 500 mg dodecyl gallate/kg bw/day). Three animals were dead by day 111; no cause was specified. The remaining two animals survived for the total feeding period of 254 days without affecting food intake.

From weanling, groups of female albino rats (five animals/group) received 0, 0.012, 0.025, 0.05, 0.1, 0.25, 0.5 or 1.0 % dodecyl gallate in the diet (equivalent[22] to 0, 11, 22.5, 45, 90, 225, 450 or 900 mg/kg bw/day, respectively) for 254 days and groups of male rats (five animals/group) received 0, 0.05 or 1.0 % dodecyl gallate in the diet (equivalent[22] to 0, 45 or 900 mg dodecyl gallate/kg bw/day, respectively) for 225 days (Allen and DeEds, 1951). There was no significant effect on female body weight gain, whereas males in the 1 % dose group (equivalent to 900 mg/kg bw/day dodecyl gallate) showed significant growth retardation.

Dodecyl gallate incorporated in the diet at 0.2 % (equivalent[22] to 180 mg/kg bw/day for three months), did not induce damage in tissues or organs in rats. Slight hypochromic anaemia was observed (van Esch, 1955).

Rats fed a diet containing 7 % fat and 0.2 % dodecyl gallate for 70 days showed no changes to body weight (no further details were available) (Tollenaar, 1957, as referred to by JECFA, 1993b).

[22] Calculated by the Panel according to EFSA Scientific Committee (2012).

Male white rats were administered dodecyl gallate daily by gavage at doses equivalent to 10, 50 or 250 mg/kg bw/day for 150 days (Mikhailova et al., 1985; only the abstract is available in English). At the high dose, numerous deaths occurred. Both the 50 and 250 mg/kg bw/day doses caused changes in serum lipids and enzymes, reduction in weight of the spleen and pathological changes in the liver, kidney and spleen. The authors considered 10 mg/kg bw/day as the no observed adverse effect level (NOAEL).

3.2.2.2. Pigs

Diets containing 0.2 % dodecyl gallate (equivalent[23] to 80 mg/kg bw/day) were fed to pigs for three months without demonstrable ill effect; no anaemia was observed (van Esch, 1955).

The Panel noted that the short-term and subchronic toxicity studies were poorly reported and the Panel was unable to identify a NOAEL from these studies.

3.2.3. Genotoxicity

Although no data on the genotoxicity of dodecyl gallate were available to JECFA (JECFA, 1993b), it was overall concluded "*that it was unlikely that either octyl gallate or dodecyl gallate is genotoxic*" (JECFA, 1993b).

No DNA damage was observed in a SOS-chromotest in *Escherichia coli*, with or without metabolic activation for dodecyl gallate (Potenberg et al., 1988).

However, the Panel noted that:

- compared with propyl gallate, dodecyl gallate does not bear additional functional groups which could trigger reactivity towards DNA or other genotoxic events;
- the only structural difference between propyl and dodecyl gallate concerns the ring substituent, a saturated aliphatic chain, which is not expected to play a role in genotoxicity;
- both propyl and dodecyl gallate are predicted to be non-genotoxic and non-carcinogenic by the *in silico* expert system Toxtree[24].

On this basis, the Panel concluded that for the evaluation of the genotoxic hazard of intact dodecyl gallate, read-across from data on propyl gallate and from the *in silico* expert system was scientifically justified. Therefore, based on the available *in vitro* and *in vivo* results for propyl gallate, which provide a limited evidence of genotoxicity in some *in vitro* systems and no evidence in tests *in vivo* with adequate systemic exposure, the Panel concluded that dodecyl gallate was unlikely to raise concern for genotoxicity.

3.2.4. Chronic toxicity and carcinogenicity

Dodecyl gallate was fed to rats during their lifespan (van Esch, 1955). The butter fat in the diet (modified Sherman diet) was replaced with lard containing 0.035, 0.2 and 0.5 % dodecyl gallate. According to the authors, the dose of dodecyl gallate was equal to 28, 160 or 400 mg/kg bw/day. The authors stated that no increase in tumour incidence was observed. The Panel noted that the extent of tissue examination was not stated. The description of the study available to the Panel was limited (e.g. number of animals not described, no description of the organs examined), which impairs its use for the risk assessment.

In its last evaluation, the SCF indicated that for dodecyl gallate only one long-term study was available. Although this study was not referenced, it is believed to be the study of van Esch (1955)

[23] Calculated by the Panel according to JECFA (2000).
[24] Version 2.6.0 (July 2013). Available online: https://eurl-ecvam.jrc.ec.europa.eu/laboratories-research/predictive_toxicology/qsar_tools/toxtree

reported above. The SCF (1989) reported that no toxicity or increase in tumour incidence was noted with 5 000 mg/kg feed and therefore judged that 5 000 mg/kg feed, equivalent to 250 mg/kg bw/day, could be considered the NEL (no further details were available) (SCF 1989).

Owing to the lack of detailed reporting on carcinogenicity and chronic toxicity studies with dodecyl gallate and the absence of a basis for read-across for systemic toxicity from propyl gallate data, the Panel could not reach a definitive conclusion on the presence or absence of a carcinogenic potential for dodecyl gallate

3.2.5. Reproductive and developmental toxicity

In its last evaluation, the SCF (1989) stated that "*reproduction and teratogenicity studies were carried out with propyl- and octyl gallate. From these studies it was concluded that gallates are not teratogenic. On the contrary, gallates protected rabbits against the teratogenic potential of hydroxyurea. In the reproduction studies, 2500 mg/kg feed produced a few minor effects but 1000 mg/kg feed was without effect*" (no further details were available) (SCF, 1989).

3.2.5.1. Rats

Young rats (12 animals/sex/group) were fed diets containing 7 % fat and 0 or 0.2 % (160 mg/kg bw/day) dodecyl gallate without giving rise to toxic effects. Animals were paired after six months. Litters (F_1 generation) were kept on their diets and mated to generate the F_2 generation (no details given). Compared with controls, reproduction rates were normal and no abnormal development in growth or weight increase was noticed (van Sluis, 1951, as referred to by JECFA, 1993b).

Dodecyl gallate was fed to rats for three generations (van Esch, 1955). The butter fat in the diet (modified Sherman diet) was replaced by lard containing 0.035 or 0.5 % dodecyl gallate. According to the authors, the dose of dodecyl gallate was equal to 28 or 400 mg/kg bw/day. The 0.5 % (400 mg/kg bw/day) group dams and offspring displayed significant retardation of growth. According to the authors, no effects on reproductive performance or other indices of reproduction and no abnormalities were observed at autopsy. The description of the study available to the Panel was limited (e.g. number of animals not described, no reproductive data presented), which impairs its use for the risk assessment.

The Panel noted that the studies of van Sluis (1951) and van Esch (1955) were insufficient to conclude on the reproductive and developmental toxicity of dodecyl gallate.

3.2.6. Allergenicity, hypersensitivity and intolerance

In its latest evaluation in 1987, without identifying any particular study, the SCF stated that "*Gallates may cause skin sensitisation and subsequent exacerbation of the resulting contact dermatitis occurs in some such sensitized individuals after ingestion of gallates.*" (SCF, 1989).

Dodecyl gallate at a dose of 15 mg is a moderate contact sensitiser in guinea pigs (Hausen and Beyer, 1992). Sensitisation was carried out using 15 mg of the pure gallate in Freund's complete adjuvant, by intradermal injections on days 1, 5 and 9. The animals were challenged on day 20. All gallates tested (dodecyl, octyl and propyl) were moderate to strong contact sensitisers, with dodecyl being the strongest. A correlation between side chain length and mean response was observed, giving a maximum of sensitisation at a length of 12 carbon atoms.

3.2.6.1. Observations in humans

Patch tests with dodecyl gallate at 0.2 % (w/v) showed a weak positive response in one sensitised individual. Other individuals have suffered recurring episodes of dermatitis, presumably caused by gallates in food products (Brun, 1970).

One case of hand dermatitis caused by dodecyl gallate was reported in a 23-year-old supermarket cheese counter assistant, who developed painful, itchy hand dermatitis consisting of *dermatitis sicca* on the fingertips and crusts, fissures and exudation on the fingers and backs of the hands (Raccagni et al., 1997). The condition was resistant to topical treatment with corticosteroids. Patch tests were conducted and the patient exhibited a strong, positive reaction to a 0.1 % solution of dodecyl gallate. Her skin condition improved through time off from work and no relapses were observed.

In a case series, Garcia-Melgares et al. (2007) reported that, compared with octyl and propyl gallates, fewer cases of sensitisation to dodecyl gallate (13.04 % of all cases) were detected. According to the authors, this was because dodecyl gallate is not as widely used for industrial purposes as the other two gallates.

One case was reported of a woman (beauty therapist) with skin rashes on the face and neck, and a positive patch test to dodecyl gallate. According to the authors, oral symptoms (swollen tongue) substantially improved when foods (margarine, edible oil) thought to contain gallates were avoided (Gamboni et al., 2013).

Overall, most reported allergic disorders to dodecyl gallate are contact dermatitis, including cheilitis after use of lipsticks, but the frequency appears to be low. Previous exposure and orally induced tolerance, may explained the low rates of allergic contact dermatitis to gallates (Kahn et al., 1974). Only very rare reactions have been reported after oral intake of gallates (Van der Meeren, 1987). Therefore, the use of dodecyl gallate as a food additive does not seem to raise concern as regards allergenicity, hypersensitivity and intolerance.

4. Discussion

The Panel was not provided with a newly submitted dossier and based its evaluation on previous evaluations, additional literature that has become available since then and the data available following a public call for data. The Panel noted that not all original studies on which previous evaluations were based were available to the Panel.

Dodecyl gallate (E 312) is authorised as a food additive in the EU in accordance with Annex II and Annex III to Regulation (EC) No 1333/2008 and specific purity criteria have been defined in the Commission Regulation (EU) No 231/2012. The Panel noted that whilst the EC specifications allow for the presence of chlorinated organic compounds these are not identified or specified and considered that identification of possible chlorinated impurities would be needed for possible evaluation of toxicological significance. The Panel considered that the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EC specification for dodecyl gallate (E 312) should be revised in order to ascertain that dodecyl gallate (E 312) as a food additive will not be a significant source of exposure to those toxic elements in food.

Initial evaluations were based on a read-across approach on the basis of presumed toxicokinetic similarities for a group of three gallates (propyl, octyl and dodecyl). In its last evaluation in 1987 (SCF, 1989), the SCF established a group ADI for propyl, octyl and dodecyl gallate of 0–0.5 mg/kg bw/day. JECFA last evaluated the three gallates at the 46th meeting in 1997 and decided that the grouping of propyl, octyl and dodecyl gallates was not scientifically justifiable and evaluated them separately. In its last evaluation, JECFA established an ADI of 1.4 mg/kg bw/day for propyl gallate based on a 90-day study, but ADIs could not be established for octyl and dodecyl gallate since relevant data on kinetics and metabolism were not made available (JECFA, 1997). Therefore, a new monograph was not prepared in 1997, the last monograph was published in 1993 (JECFA, 1993b).

Little is known about the occurrence of the dodecyl gallate in food and only fragmentary data exist. These data were published in articles which focused on development of analytical methods. The data on manufacturing were very limited and provided no details on side reactions or impurities in chemicals originating from synthesis conditions.

Propyl gallate is extensively hydrolysed to propyl alcohol and gallic acid. Gallic acid was further metabolised to 4-*O*-methyl gallic acid by *O*-methylation, glucuronidated and excreted via urine. Propyl alcohol was incorporated into intermediate metabolism of the individual (EFSA ANS Panel, 2014). The Panel considered that whilst from theoretical considerations dodecyl gallate could be metabolised to dodecyl alcohol and gallic acid, there were insufficient data to demonstrate the rate and extent of dodecyl gallate metabolism *in vivo*. The Panel noted that the available data demonstrated decreased hydrolysis of dodecyl gallate compared with propyl gallate. The Panel therefore concurred with the most recent JECFA evaluation and TemaNord that, on the information available, a group ADI for gallates is not scientifically justifiable.

The Panel noted that the available studies on acute toxicity of dodecyl gallate in rats and pigs indicated low acute oral toxicity.

There were short-term and subchronic toxicity studies on dodecyl gallate in rats, dogs and pigs, which reported no overt toxic effects of dodecyl gallate. However, the Panel noted that the available studies were poorly reported and was unable to identify a NOAEL from these studies.

No data on genotoxicity of dodecyl gallate were available. However, the Panel noted that:

- compared with propyl gallate, dodecyl gallate does not bear additional functional groups which could trigger reactivity towards DNA or other genotoxic events;
- the only structural difference between propyl and dodecyl gallate concerns the ring substituent, a saturated aliphatic chain, which is not expected to play a role in genotoxicity;
- both propyl and dodecyl gallate are predicted to be non-genotoxic and non-carcinogenic by the *in silico* expert system *Toxtree*.

On this basis, the Panel concluded that for the evaluation of the genotoxic hazard of intact dodecyl gallate, read-across from data on propyl gallate and from the *in silico* expert system was scientifically justified. Therefore, based on the available *in vitro* and *in vivo* results for propyl gallate, which provide a limited evidence of genotoxicity in some *in vitro* systems and no evidence in tests *in vivo* with adequate systemic exposure, the Panel concluded that dodecyl gallate was unlikely to raise concern for genotoxicity.

The Panel noted the absence of concern for genotoxicity and the lack of increase of tumours in the long-term study. However, owing to the lack of detailed reports on carcinogenicity and chronic toxicity studies with dodecyl gallate and the absence of a basis for read-across for systemic toxicity from propyl gallate data, the Panel could not reach a definitive conclusion on the presence or absence of a carcinogenic potential of dodecyl gallate.

Two studies in rats on the reproductive toxicity of dodecyl gallate were available (van Sluis, 1951; van Esch, 1955); however, the Panel noted that these studies were insufficient to conclude on the reproductive and developmental toxicity of dodecyl gallate.

The SCF established a group ADI for propyl gallate, together with octyl and dodecyl gallate of 0–0.5 mg/kg bw/day (SCF, 1989). This group ADI was based on a read-across approach using presumed toxicokinetic similarities (metabolism to gallic acid and the corresponding alcohol) for a group of the three gallates (propyl, octyl and dodecyl). However, having reviewed the data on the toxicokinetics (rate and extent of metabolism) of propyl, octyl and dodecyl gallate in the evaluation of propyl gallate (EFSA ANS Panel, 2014), this evaluation and the ongoing evaluation of octyl gallate, the Panel concluded that the available metabolism data on gallates were insufficient to provide a basis for the read-across of systemic toxicity data on propyl, octyl and dodecyl gallate to be valid. Therefore, there was no longer a basis for the present group ADI and the Panel concluded that propyl, octyl and dodecyl gallate should be evaluated separately and the present group ADI should be withdrawn. The Panel noted that JECFA had reached a similar conclusion in 1997.

The Panel noted that there was no indication of overt toxicity in the available studies; however, owing to the limitations of these studies, the Panel was unable to identify any NOAEL. Overall, the available database was too limited to either establish an ADI or serve as a basis for a margin of safety approach.

Exposure assessments of food additives under re-evaluation are carried out by the ANS Panel based on (1) MPLs set down in the EU legislation (defined as the *regulatory maximum level exposure assessment scenario*) and (2) usage or analytical data (defined as the *refined exposure assessment scenario*). The Panel considers that the refined exposure assessment approach results in more realistic long-term exposure estimates because of the underlying assumptions and the occurrence data used.

These two exposure assessments were performed for dodecyl gallate. For the refined exposure assessment scenario, two exposure estimates were calculated for the *brand-loyal scenario* and two for the *non-brand-loyal scenario*.

Using the "*regulatory maximum level exposure assessment scenario*", mean exposure to dodecyl gallate from its use as a food additive ranged from 0.01 to 0.17 mg/kg bw/day in five population groups. The high exposure to dodecyl gallate using this scenario ranged from 0.02 to 0.64 mg/kg bw/day (Table 4).

Considering only food categories in Annex II to Regulation (EC) No 1333/2008, the refined exposure to dodecyl gallate, using one reported use level in chewing gum and analytical data in 10 other food categories, was maximally 0.05 mg/kg bw/day for the *brand-loyal* and *non-brand-loyal* exposure scenarios in all five population groups (Table 4). When the overall reported analytical data were considered, the refined exposure to dodecyl gallate increased to a maximum of 0.6 mg/kg bw/day for the *brand-loyal* and *non-brand-loyal* exposure scenarios (Table 4).

The Panel noted that reported uses of dodecyl gallate were very limited and that analytical data in food were below LOQ or LOD. Whilst it was not possible from the toxicological data to establish an ADI or a margin of safety, if the single use reported was correct then the estimated exposures from this use and use level would unlikely be of safety concern. The Panel noted that these reported uses were much more limited than the permitted uses and that with the data available it was not possible to evaluate the risk from the permitted uses.

CONCLUSIONS

The Panel concluded in its evaluation of propyl gallate that there was no longer a basis for the present group ADI and that propyl, octyl and dodecyl gallates should be evaluated separately and the present group ADI should be withdrawn. The Panel noted that JECFA had reached a similar conclusion in 1997. The Panel considered that whilst read-across was valid for genotoxicity data, the available data were insufficient for the read-across to be valid for systemic toxicity because of the differences in metabolism, lack of evidence for a common mode of action or similar dose responses in biological or toxicological effects of gallates.

No substantial new toxicological data have emerged since the last JECFA monograph (JECFA, 1993b) and evaluation (JECFA, 1997), nor following a specific call for data. The Panel concluded that there was a lack of adequate toxicological data on dodecyl gallate.

The Panel concluded that an ADI for dodecyl gallate cannot be established and the toxicity data were also too limited for a margin of safety approach to be applied with confidence.

The Panel concluded that although there was unlikely to be a safety concern from the single use for which usage and analytical data were provided, an adequate assessment of the safety of dodecyl gallate as a food additive would require a sufficient toxicological database in line with its current guidance for submission for food additives evaluations (EFSA ANS Panel, 2012).

The Panel also concluded that the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EC specification for dodecyl gallate (E 312) should be revised in order to ascertain that dodecyl gallate (E 312) as a food additive will not be a significant source of exposure to those toxic elements in food.

DOCUMENTATION PROVIDED TO EFSA

1. Pre-evaluation document prepared by the Danish technological research service institution (DHI), Denmark, November 2011.

2. Van Esch G and van Genderen H, 1955. The toxicity of the antioxidants propyl-, octyl-, and dodecylgallate. Voeding, 16, 683–6. Submitted to EFSA by the FDA, November 2011.

3. International Chewing Gum Association (ICGA). Data on use levels of dodecyl gallate (E 312) in foods in response to the EFSA call for food additives usage level and/or concentration data in food and beverages intended for human consumption (2013). Submitted on September 2013.

4. Analytical data provided by Members States in response to the EFSA call for food additives usage level and/or concentration data in food and beverages intended for human consumption (November, 2013).

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APPENDICES

Appendix A. Summary of analytical results (middle bound mg/kg or mg/L as appropriate) of dodecyl gallate (E 312) provided by Member States

FCS category no	FCS food category	MPL	n	%LC	Range		All data				
					LOD	LOQ	Min	Median	Mean	P95 [a]	Max
2.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	200 [b] [c]	476	100	0.1–5.0	0.2–15.0	0.09	0.5	0.78	2.5	5.0
2.2.2	Other fat and oil emulsions, including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	200 [b] [d]	69	100	0.3–10.0	1.0–20.0	0.5	5.0	4.9	5.0	5.0
4.1	Unprocessed fruit and vegetables [e] [f]	200	1	100	5.0	10.0	2.5	2.5	2.5	–	2.5
4.2.6	Processed potato products	25 [b]	48	100	5.0–5.0	10.0–10.0	2.5	2.5	2.6	–	5.0
6.5	Noodles [e]	200	3	100	1.7–1.7	5.0–5.0	2.5	2.5	2.5	–	2.5
8.3.1	Non-heat-treated processed meat	200 [b] [g]	3	100	0.3–0.5	1.0–2.0	0.5	1.0	0.8	–	1.0
9.2	Processed fish and fishery products [e]	200	222	100	0.1–0.5	0.2–2.0	0.09	0.5	0.6	1.0	1.0
9.3	Fish roe [e]	200	3	100	0.3–0.5	1.0–2.0	0.5	0.5	0.7	–	1.0
12.2.2	Seasonings and condiments	200 [b] [g]	3	100	1.7–1.7	5.0–5.0	2.5	2.5	2.5	–	2.5
12.5	Soups and broths	200 [b] [g]	9	100	1.0–1.7	5.0–10.0	2.5	5.0	4.7	–	5.0
12.6	Sauces	200 [b] [g]	80	100	0.3–10.0	1.0–20.0	0.5	5.0	4.3	5.0	5.0
12.7	Salads and savoury-based sandwich spreads [e]	200	1	100	5.0	10.0	2.5	2.5	2.5	–	2.5
15.1	Potato-, cereal-, flour- or starch-based snacks	200 [b]	16	100	1.7–5.0	5.0–10.0	2.5	2.5	2.5	–	2.5
17.1/17.2/17.3	Food supplements	400 [b]	3	100	5.0–5.0	10.0–15.0	2.5	2.5	2.5	–	2.5
18	Processed food [e]	200	5	100	0.3–10.7	1.0–51.9	0.5	5.4	3.8	–	5.4

(a): The 95th percentile obtained on occurrence data with fewer than 60 analytical results may not be statistically robust (EFSA, 2011a) and therefore are not reported in the table.
(b): The additives may be added individually or in combination.
(c): Expressed on fat basis.
(d): The maximum level is applicable to the sum and the levels are expressed as the free acid.
(e): The presence of dodecyl gallate in this food category may be because of carry-over.
(f): Only potatoes.
(g): Maximum limit expressed on fat.
%LC, percentage of left-censored data; Max, maximum; Min, minimum; n, number of data; P95, 95th percentile.

Appendix B. Concentration levels of dodecyl gallate (E 312) used in the MPL and refined exposure scenarios (mg/kg or mL/kg as appropriate)

FCS category no	FCS food category	MPL	MPL scenario [a]	Concentration levels used in the refined exposure assessment		Data source/comments
				Mean	Maximum	
1.5	Dehydrated milk as defined by Directive 2001/114/EC	200 [b]	–	–	–	Not taken into account (no corresponding FoodEx code)
2.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	200 [b] [c]	149.8	0.8	5.0	Analytical data
2.2.2	Other fat and oil emulsions, including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	200 [b] [d]	200	5.0	5.0	Analytical data
4.1	Processed fruit and vegetables [e] (only potatoes)	200	–	2.5	2.5	Analytical data
4.2.5.4	Nut butters and nut spreads	200 [b] [c]	97	–	–	No data available
4.2.6	Processed potato products	25 [b]	25	2.6	5.0	Analytical data
5.3	Chewing gum	400 [b]	400	200	300	Only one usage level available; no analytical data available
6.3	Breakfast cereals	200 [b] [f]	–	–	–	Not taken into account (no corresponding FoodEx code)
6.5	Noodles [e]	200	–	2.5	2.5	Analytical data
6.7	Pre-cooked or processed cereals	200 [b]	–	–	–	Not taken into account (no corresponding FoodEx code)
7.2	Fine bakery wares	200 [b]	200	–	–	No data available
8.3.1	Non-heat-treated processed meat	200 [b] [f]	51	1.0	1.0	Analytical data
9.2	Processed fish and fishery products [e]	200	–	0.6	1.0	Analytical data
9.3	Fish roe [e]	200	–	0.7	1.0	Analytical data
12.2.2	Seasonings and condiments	200 [b] [f]	10.4	2.5	2.5	Analytical data
12.5	Soups and broths	200 [b] [f]	–	–	–	Not taken into account (no corresponding FoodEx code)
12.6	Sauces	200 [b] [f]	37	5.0	5.0	Analytical data
12.7	Salads and savoury-based sandwich spreads [e]	200	–	2.5	2.5	Analytical data
15.1	Potato-, cereal-, flour- or starch-based snacks	200 [b]	200	2.5	2.5	Analytical data

FCS category no	FCS food category	MPL	MPL scenario [a]	Concentration levels used in the refined exposure assessment		Data source/comments
				Mean	Maximum	
15.2	Processed nuts	200 [b] [f]	97	–	–	No data available
17.1/17.2/17.3	Food supplements	400 [b]	400	2.5	2.5	Analytical data
18	Processed food [e]	200	–	5.4	5.4	Analytical data

(a): MPLs expressed on fat basis converted for exposure assessment to whole weight based on information on fat content reported in the Comprehensive Database.
(b): The additives may be added individually or in combination.
(c): Expressed on fat basis.
(d): The maximum level is applicable to the sum and the levels are expressed as the free acid.
(e): The presence of dodecyl gallate in this food category may be because of carry-over.
(f): Maximum limit expressed on fat.

Appendix C. Main food categories contributing to exposure to dodecyl gallate (E 312)

Table C1: Main food categories contributing to exposure to dodecyl gallate (E 312) using MPLs (> 5 % to the total mean exposure) and number of surveys in which each food category is contributing

FCS category number	Foods	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys) [(a)]				
2.1	Fats and oils essentially free from water	5.2 (1)	5.8–16.6 (2)	9.9–22.8 (2)	11.1–40.7 (3)	17.6–45.1 (2)
2.2.2	Other fat and oil emulsions, including spreads	60.5 (1)	5.1–64.5 (3)	–	51.7 (1)	52.9 (1)
4.2	Processed fruit and vegetables	10.0 (1)	5.9–8.7 (2)	9.3–12.1 (2)	7.8 (1)	10.3 (1)
5.3	Chewing gum	11.2 (1)	5.4–23.3 (5)	17.1–41.6 (2)	5.7–39.2 (3)	15.7 (1)
7.2	Fine bakery wares	21.6–81.3 (6)	8.8–94.6 (13)	19.0–87.3 (10)	30.6–70.3 (12)	37.4–82.2 (4)
12.6	Sauces	7.0–66.0 (5)	10.1–68.7 (12)	6.7–49.5 (11)	7.9–51.3 (14)	6.1–46.0 (6)
15.1	Potato-, cereal-, flour- or starch-based snacks	5.6–46.6 (6)	5.8–43.8 (6)	5.7–52.4 (11)	5.2–18.0 (12)	5.1–18.3 (2)
15.2	Processed nuts	21.7 (1)	5.8–15.3 (6)	5.6–32.4 (8)	5.1–32.1 (13)	5.1–28.5 (5)
17	Food supplements	–	6.0–8.8 (2)	–	5.9–19.5 (4)	9.3–30.9 (2)

(a): The total number of surveys may be greater than the total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific population.

Table C2: Main food categories contributing to exposure to dodecyl gallate (E 312) from its use as a food additive using the brand-loyal refined exposure scenario (> 5 % to the total mean exposure) and number of surveys in which each food category is a contributor

FCS category number	Foods	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys) [(a)]				
2.1	Fats and oils essentially free from water	7.0–20.3 (2)	6.5–15.9 (2)	6.1–11.9 (2)	6.6–44.6 (4)	48.7 (1)
2.2.2	Other fat and oil emulsions, including spreads	11.6 (1)	7.2–12.4 (2)	–	14.0 (1)	30.8 (1)
4.2	Processed fruit and vegetables	13.5 (1)	15.8–41.9 (2)	27.8–29.1 (2)	5.1–27.7 (2)	17.4–38.6 (2)
5.3	Chewing gum	6.1–64.7 (3)	10.8–77.1 (10)	9.1–89.8 (10)	5.7–88.1 (12)	28.3–64.5 (2)
12.2.2	Herbs, spices, seasonings	27.8–43.9 (2)	23.4–27.0 (2)	23.7 (1)	6.1–34.3 (3)	13.5–65.5 (2)
12.6	Sauces	6.7–98.8 (6)	8.1–94.7 (15)	9.3–96.7 (12)	11.0–96.0 (15)	18.3–97.8 (7)
15.1	Potato-, cereal-, flour- or starch-based snacks	12.2–63.0 (3)	28.2–49.0 (2)	15.2–23.8 (2)	6.9–12.7 (4)	7.9 (1)

(a): The total number of surveys may be greater than the total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific population.

Table C3: Main food categories contributing to exposure to dodecyl gallate (E 312) from its use as a food additive using the non-brand-loyal exposure scenario (> 5 % to the total mean exposure) and number of surveys in which each food category is a contributor

FCS category number	Foods	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys) [a]				
2.1	Fats and oils essentially free from water	–	–	–	5.2–12.9 (2)	14.6 (1)
2.2.2	Other fat and oil emulsions, including spreads	15.8 (1)	8.2–16.5 (2)	–	18.2 (1)	37.0 (1)
4.2	Processed fruit and vegetables	11.0 (1)	11.1–32.8 (2)	20.3–22.9 (2)	21.0 (1)	13.4–28.0 (2)
5.3	Chewing gum	18.3–59.5 (2)	9.2–71.4 (10)	7.2–86.6 (10)	5.2–84.9 (10)	23.0–59.4 (2)
12.2.2	Herbs, spices, seasonings	29.5–55.6 (2)	5.0–31.5 (3)	30.3 (1)	6.0–41.8 (4)	6.3–68.2 (3)
12.6	Sauces	8.7–98.6 (6)	8.2–95.4 (15)	12.1–96.3 (12)	14.1–95.5 (15)	20.4–97.5 (7)
15.1	Potato-, cereal-, flour- or starch-based snacks	13.9–67.0 (3)	6.1–57.1 (3)	6.9–26.3 (3)	9.4–15.4 (4)	14.3 (1)
17	Food supplements	–	–	–	–	5.5 (1)

(a): The total number of surveys may be greater than the total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific population.

Table C4: Main food categories contributing to exposure to dodecyl gallate (E 312) from its use as a food additive and as a food additive in food flavourings using the brand-loyal refined exposure scenario (> 5 % to the total mean exposure) and number of surveys in which each food category is a contributor

FCS category number	Foods	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys) [a]				
2.1	Fats and oils essentially free from water	–	–	–	11.3 (1)	11.0 (1)
4.2	Processed fruit and vegetables	6.3–42.7 (5)	5.4–32.0 (12)	5.8–43.0 (9)	5.2–30.8 (10)	8.4–30.4 (5)
5.3	Chewing gum	–	5.9–7.8 (2)	7.5–7.6 (2)	5.1 (1)	–
12.6	Sauces	13.0 (1)	8.3–16.1 (4)	6.4–19.5 (4)	5.0–15.6 (6)	8.4–9.4 (3)
12.7	Salads and savoury-based sandwich spreads	–	8.3–11.2 (2)	11.4 (1)	15.5 (1)	–
18	Processed foods	43.4–98.3 (7)	44.6–98.5 (15)	43.5–97.6 (12)	42.9–98.9 (15)	59.3–95.0 (7)

(a): The total number of surveys may be greater than the total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific population.

Table C5: Main food categories contributing to exposure to dodecyl gallate (E 312) from its use as a food additive and as a food additive in food flavourings using the non-brand-loyal exposure scenario (> 5 % to the total mean exposure) and number of surveys in which each food category is a contributor

FCS category number	Foods	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys) [(a)]				
4.2	Processed fruit and vegetables	6.4–43.5 (5)	5.4–32.4 (12)	5.9–43.1 (9)	5.2–31.1 (10)	8.4–30.8 (5)
5.3	Chewing gum	–	5.4–5.7 (2)	6.1–6.5 (2)	–	–
12.6	Sauces	11.4 (1)	7.2–14.2 (4)	5.7–17.3 (4)	5.8–13.7 (5)	7.3–8.2 (3)
12.7	Salads and savoury-based sandwich spreads	–	8.4–11.4 (2)	11.6 (1)	15.7 (1)	–
18	Processed foods	44.2–98.3 (7)	45.3–98.6 (15)	44.3–97.7 (12)	43.5–99.0 (15)	60.2–95.1 (7)

(a): The total number of surveys may be greater than the total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific population.

Appendix D. Summary of total estimated exposure of dodecyl gallate (E 312) from its use as a food additive for the MPL scenario and refined exposure scenarios per population group and survey: mean and high level (mg/kg bw/day)

	Number of subjects	MPL scenario		Refined scenario in accordance with Annex II				Refined scenario in accordance with Annexes II and III			
				Brand-loyal scenario		Non-brand-loyal scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level
Toddlers											
Belgium (Regional_Flanders)	36	0.05		0.005	–	0.004	–	0.04	–	0.04	
Bulgaria (NUTRICHILD)	428	0.16	0.64	0.001	0.006	0.001	0.006	0.1	0.4	0.1	0.4
Germany (DONALD_2006_2008)	261	0.06	0.32	0.001	0.008	0.001	0.01	0.2	0.4	0.2	0.4
Spain (enKid)	17	0.04		0.001	–	0.001	–	0.1	–	0.1	
Finland (DIPP_2003_2006)	497	0.03	0.16	0.004	0.02	0.003	0.01	0.3	0.6	0.3	0.6
Italy (INRAN_SCAI_2005_06)	36	0.12		0.001	–	0.0008	–	0.1	–	0.1	
The Netherlands (VCP_kids)	322	0.06	0.31	0.004	0.013	0.003	0.01	0.1	0.3	0.1	0.3
Children											
Belgium (Regional_Flanders)	625	0.03	0.12	0.003	0.01	0.003	0.01	0.04	0.1	0.03	0.1
Bulgaria (NUTRICHILD)	433	0.13	0.56	0.001	0.01	0.001	0.01	0.1	0.4	0.1	0.4
The Czech Republic (SISP04)	389	0.06	0.35	0.004	0.01	0.003	0.01	0.1	0.2	0.1	0.2
Germany (DONALD_2006_2008)	660	0.08	0.34	0.004	0.02	0.003	0.01	0.1	0.2	0.1	0.2
Denmark (Danish_Dietary_Survey)	490	0.04	0.11	0.01	0.04	0.01	0.03	0.1	0.2	0.1	0.2
Spain (enKid)	156	0.04	0.17	0.01	0.04	0.01	0.03	0.1	0.2	0.1	0.2
Spain (NUT_INK05)	399	0.10	0.43	0.01	0.02	0.004	0.01	0.1	0.2	0.1	0.2
Finland (DIPP_2003_2006)	933	0.11	0.28	0.01	0.05	0.01	0.04	0.1	0.3	0.1	0.3
Finland (STRIP)	250	0.16	0.50	0.01	0.02	0.01	0.02	0.04	0.1	0.1	0.1
France (INCA2)	482	0.17	0.48	0.01	0.02	0.01	0.01	0.1	0.2	0.1	0.2
Greece (Regional_Crete)	839	0.04	0.29	0.0003	0.002	0.0002	0.002	0.02	0.05	0.02	0.05
Italy (INRAN_SCAI_2005_06)	193	0.17	0.56	0.001	0.004	0.001	0.004	0.1	0.2	0.1	0.2
Latvia (EFSA_TEST)	189	0.07	0.36	0.003	0.01	0.003	0.01	0.02	0.1	0.02	0.1
The Netherlands (VCP_kids)	957	0.07	0.34	0.01	0.02	0.01	0.02	0.1	0.2	0.1	0.2
Sweden (NFA)	1473	0.10	0.30	0.01	0.02	0.01	0.02	0.1	0.1	0.1	0.1
Adolescents											
Belgium (Diet_National_2004)	584	0.05	0.18	0.004	0.01	0.003	0.01	0.02	0.1	0.02	0.1
Cyprus (Childhealth)	303	0.01	0.04	0.0001	0.001	0.0001	0.0007	0.01	0.0	0.01	0.02
The Czech Republic (SISP04)	298	0.06	0.29	0.003	0.009	0.002	0.007	0.1	0.2	0.1	0.2

	Number of subjects	MPL scenario		Refined scenario in accordance with Annex II				Refined scenario in accordance with Annexes II and III			
				Brand-loyal scenario		Non-brand-loyal scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level
Germany (National_Nutrition_Survey_II)	1011	0.09	0.35	0.004	0.01	0.003	0.01	0.02	0.1	0.02	0.1
Denmark (Danish_Dietary_Survey)	479	0.02	0.08	0.009	0.04	0.006	0.03	0.1	0.2	0.1	0.2
Spain (AESAN_FIAB)	86	0.04	0.14	0.001	0.006	0.001	0.006	0.02	0.1	0.1	0.1
Spain (enKid)	209	0.04	0.16	0.007	0.03	0.005	0.02	0.1	0.2	0.1	0.2
Spain (NUT_INK05)	651	0.07	0.28	0.004	0.02	0.003	0.01	0.1	0.2	0.1	0.2
France (INCA2)	973	0.08	0.26	0.005	0.02	0.003	0.01	0.04	0.1	0.04	0.1
Italy (INRAN_SCAI_2005_06)	247	0.07	0.27	0.001	0.006	0.001	0.004	0.03	0.1	0.03	0.1
Latvia (EFSA_TEST)	470	0.04	0.23	0.002	0.009	0.002	0.01	0.02	0.1	0.02	0.1
Sweden (NFA)	1018	0.06	0.22	0.005	0.02	0.004	0.01	0.04	0.1	0.04	0.1
Adults											
Belgium (Diet_National_2004)	1304	0.03	0.13	0.003	0.009	0.002	0.02	0.02	0.1	0.01	0.1
The Czech Republic (SISP04)	1666	0.04	0.19	0.001	0.003	0.001	0.003	0.07	0.1	0.07	0.1
Germany (National_Nutrition_Survey_II)	10419	0.09	0.35	0.003	0.009	0.002	0.02	0.02	0.1	0.02	0.1
Denmark (Danish_Dietary_Survey)	2822	0.01	0.05	0.004	0.02	0.003	0.02	0.07	0.2	0.07	0.2
Spain (AESAN)	410	0.03	0.16	0.0005	0.002	0.0004	0.002	0.04	0.1	0.04	0.1
Spain (AESAN_FIAB)	981	0.03	0.16	0.001	0.002	0.0004	0.002	0.05	0.1	0.05	0.1
Finland (FINDIET_2007)	1575	0.04	0.13	0.003	0.017	0.003	0.01	0.07	0.2	0.07	0.2
France (INCA2)	2276	0.05	0.17	0.003	0.007	0.002	0.02	0.04	0.1	0.04	0.1
The United Kingdom (NDNS)	1724	0.06	0.19	0.003	0.007	0.002	0.02	0.05	0.1	0.05	0.1
Hungary (National_Repr_Surv)	1074	0.02	0.08	0.001	0.002	0.0003	0.001	0.002	0.01	0.002	0.01
Ireland (NSIFCS)	958	0.05	0.15	0.002	0.004	0.001	0.003	0.03	0.1	0.03	0.1
Italy (INRAN_SCAI_2005_06)	2313	0.03	0.14	0.001	0.003	0.001	0.002	0.02	0.1	0.02	0.1
Latvia (EFSA_TEST)	1306	0.03	0.13	0.001	0.006	0.001	0.02	0.01	0.04	0.01	0.04
The Netherlands (DNFCS_2003)	750	0.05	0.18	0.005	0.015	0.004	0.01	0.04	0.1	0.04	0.1
Sweden (Riksmaten_1997_98)	1210	0.04	0.11	0.002	0.005	0.001	0.005	0.05	0.1	0.05	0.1
Elderly and very elderly											
Belgium (Diet_National_2004)	1230	0.02	0.10	0.001	0.006	0.001	0.005	0.01	0.1	0.01	0.1
Germany (National_Nutrition_Survey_II)	2496	0.09	0.35	0.002	0.006	0.001	0.005	0.02	0.1	0.02	0.1
Denmark (Danish_Dietary_Survey)	329	0.01	0.02	0.001	0.002	0.001	0.001	0.06	0.2	0.06	0.2

	Number of subjects	MPL scenario		Refined scenario in accordance with Annex II				Refined scenario in accordance with Annexes II and III			
				Brand-loyal scenario		Non-brand-loyal scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level
Finland (FINDIET_2007)	463	0.03	0.12	0.001	0.004	0.001	0.004	0.07	0.2	0.07	0.2
France (INCA2)	348	0.04	0.12	0.002	0.005	0.001	0.004	0.04	0.1	0.04	0.1
Hungary (National_Repr_Surv)	286	0.02	0.06	0.0004	0.001	0.0002	0.0006	0.002	0.01	0.001	0.01
Italy (INRAN_SCAI_2005_06)	518	0.02	0.14	0.0003	0.001	0.0003	0.001	0.02	0.1	0.02	0.1

ABBREVIATIONS

ADI	acceptable daily intake
ADME	Absorption, Distribution, Metabolism and Excretion
ANS	Food Additives and Nutrient Sources Added to Food
AOAC	Association of Official Analytical Chemists
APTLD	alternating penalty trilinear decomposition
BHA	butylated hydroxyanisole
BHT	butylated hydroxytoluene
bw	body weight
CAS	Chemical Abstracts Service
C logP	Calculated logarithm of its partition coefficient between n-octanol and water $\log(c_{octanol}/c_{water})$
DNA	Deoxyribonucleic acid
EC	European Commission
EINECS	European Inventory of Existing Commercial chemical Substances
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FCM	food contact material
FCS	Food Categorisation System
GC-FID	gas chromatography–flame ionisation detection
HPLC	high-performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
ICGA	International Chewing Gum Association
i.p.	intraperitoneal
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD_{50}	lethal dose for 50 % of animals
LOD	limit of detection
LOQ	limit of quantification
MB	middle bound
MEKC	micellar electrokinetic chromatography
MPL	maximum permitted level
NEL	no effect level
NOAEL	no observed adverse effect level
NOEL	no observed effect level
PDA	photodiode array detection
QS	*quantum satis*
RMSEP	root mean square error of prediction
SCF	Scientific Committee on Food Additives
SML	specific migration limit
TBHQ	tertiary-butylated hydroquinone
TemaNord	Nordic Working Group on Food Toxicology and Risk Assessment
TLC	thin-layer chromatography
TNO	Netherlands Organisation for Applied Scientific Research
UK	United Kingdom
WHO	The World Health Organization
v/v	volume/volume ratio
w/v	weight/volume ratio