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Re-evaluation of lecithins (E 322) as a food additive

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Abstract

The present opinion deals with the re-evaluation of lecithins (E 322) when used as a food additive. Lecithins (E 322) is an authorised food additive in the EU according to Annex II and Annex III to Regulation (EC) No 1333/2008 on food additives, and have been previously evaluated by JECFA in 1973 and by the SCF in 1982. Among lecithins, phosphatidylcholine is hydrolysed in choline in the cytidine-5-diphosphate-choline pathway in all cells of the body. Following the conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010, the Panel concluded that there was no need for a numerical ADI for lecithins (E 322) and that there was no safety concern for the general population from more than 1 year of age at the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive. The Panel further concluded that there is no safety concern for the exposure to the choline from lecithins (E 322) as a food additive at use and use levels reported by industry. For infants (from 12 weeks up to 11 months of age), the Panel concluded that there was no safety concern at the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive and for the choline from lecithins (E 322) as a food additive at use and use levels reported by industry. For infants and young children consuming foods for special medical purposes, the Panel concluded that there was no safety concern with respect to the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive and for exposure to choline resulting from these uses of lecithins (E 322).

Keywords: Lecithins, E 322, CAS No 8002-43-5 (lecithins), CAS No 85711-58-6 (hydrolysed lecithins), phosphatidylcholine, choline

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Summary

The present opinion deals with the re-evaluation of lecithins (E 322) when used as a food additive.

Lecithins are mixtures or fractions of phosphatides obtained by physical procedures from animal or vegetable foodstuffs. Lecithins (E 322) is an authorised food additive in the European Union (EU) according to Annex II and Annex III to Regulation (EC) No 1333/2008 on food additives, and have been previously evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1973 (JECFA, 1974a,b) and by the Scientific Committee on Food (SCF) in 1982 (SCF, 1982).

The Panel noted that the composition of the preparations used in the various studies was different. However, because all the constituents were qualitatively similar, the Panel considered the studies relevant for the risk assessment of lecithins (E 322).

Among lecithins, phosphatidylcholine is hydrolysed in choline in the cytidine-5-diphosphate-choline pathway in all cells of the body. The content of choline that can theoretically be released from phosphatidylcholine containing two linoleate groups is 13.2%. For choline, the EFSA NDA Panel (2016) prepared a scientific opinion on dietary reference values (DRVs) in 2016 in which it was concluded that average requirements (ARs) and population reference intakes (PRIs) for choline could not be derived for adults, infants (aged 7–11 months) and children, and therefore defined adequate intakes (AIs) for total choline (free and bound). For infants during the first 6 months of life, the amount of total choline provided in human milk was considered adequate.

Following oral administration, phosphatidylcholine is absorbed intact or as lysophosphatidylcholine or choline after intestinal hydrolysis. In humans, dietary lecithins are hydrolysed by phospholipases to liberate choline which is rapidly absorbed and appears in plasma predominantly as free choline.

The acute toxicity of lecithins (E 322) in mice, rats and rabbits is low.

Subchronic toxicity studies in rats and dogs did not report any adverse effect, even at the highest doses tested (3,750 mg essential phospholipid (EPL)/kg body weight (bw) per day, 1,000 mg soya phosphatidylinositol or EPL/kg bw per day in rats and dogs, respectively, and 5,460 mg lecithins/kg bw per day in rats).

The Panel considered the available genotoxicity data on lecithins (E 322) to be sufficient to conclude that there is no concern with respect to genotoxicity.

Chronic toxicity studies in rats did not report any adverse effects, even at the highest dose tested (3,750 mg EPL/kg bw per day). No carcinogenic effects were reported in rats, even at the highest dose tested (1,470 and 2,280 mg soya lecithin/kg bw per day in males and females, respectively) for 2 years.

The Panel considered that no adverse effects were observed in the developmental toxicity studies performed in mice, rat and rabbits up to the highest dose tested. However, the Panel noted that no reproductive toxicity studies were available. Several neurodevelopmental toxicity studies were conducted with lecithin. The Panel concluded that the relevance of the studies is limited but, at concentrations of 5% soya lecithin and higher in the diet during the gestation, lactation and the post-weaning period, there were indications for alterations in the development of the brain.

The Panel noted that, in Annex II of Regulation (EC) No 1333/2008, the use levels of lecithins (E 322) in food for infants under the age of 12 weeks are included in categories 13.1.1, 13.1.5.1 and 13.1.5.2. The Panel considered that these uses would require a specific risk assessment; therefore, the current re-evaluation of lecithins (E 322) as a food additive is not considered to be applicable for infants under the age of 12 weeks. Concerning uses of lecithins in food for infants and young children, the Panel concurs with the SCF (1998) and SCF (2003).The Panel noted that it is prudent to keep the number of additives used in foods for infants and young children to the minimum necessary.

The Panel considered that the refined exposure assessment approach resulted in more realistic long-term exposure estimates compared to the *maximum level exposure assessment scenario*. From the *refined estimated exposure scenario*, in the *brand-loyal scenario*, mean exposure to lecithins (E 322) ranged from 7 mg/kg bw per day in adolescents to 82 mg/kg bw per day in children. The 95th percentile ranged from 15 mg/kg bw per day in adolescents to 187 mg/kg bw per day in children. In the *non-brand-loyal scenario*, mean exposure ranged from 3 mg/kg bw per day in adults/elderly to 22 mg/kg bw per day in toddlers. The 95th percentile ranged from 6 mg/kg bw per day in adults/elderly to 62 mg/kg bw per day in infants.

The Panel considered that dietary intakes of lecithins (E 322) from the regular diet could be estimated in average ranging from 4 to 71 mg/kg bw per day across all population age groups.

Lecithins (E 322) is used in a wide range of foods, and it is therefore not expected that brand-loyalty will result in higher exposure in general population, except in specific populations consuming foods for special medical purposes and in infants and young children consuming infant and/or

follow-on formulae. The Panel therefore selected the brand-loyal refined scenario as the most relevant exposure scenario for this additive in these specific situations when justified.

I. General population

a) Above 1 year of age

Following the conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010 (EFSA, 2014), and given that:

- adequate exposure data were available and the highest relevant exposure estimate calculated in the refined exposure assessment scenario based on the reported data from food industry was for toddlers (12–35 months) up to 175 mg lecithins/kg bw per day at the 95th percentile (brand-loyal scenario),
- exposure via natural occurrence as reported by JECFA provided a daily mean intake of several grams of lecithin (approximately 1–5 g corresponding to 14–71 mg/kg bw for a 70-kg adult population),
- lecithins are natural constituents of all cells in the human body and also are natural components of the diet,
- toxicity database for lecithins was overall sufficient but not adequate regarding the endpoint of neurobehavioural developmental effects,
- there was no concern with respect to genotoxicity,
- no adverse effects were reported in chronic and carcinogenicity study in rats at the highest dose tested of 3,750 mg lecithins/kg bw per day,

the Panel concluded that there was no need for a numerical acceptable daily intake (ADI) for lecithins (E 322) and that there was no safety concern for the general population from more than 1 year of age at the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive.

Moreover, taking into consideration that:

- hydrolysed lecithins and choline are produced in the gut as a result of normal digestion of lecithins. Choline is rapidly absorbed and appears in plasma predominantly as free choline,
- choline is a precursor of the neurotransmitter acetylcholine,
- the content of choline, that can theoretically be released from phosphatidylcholine containing two linoleate groups, is up to 13.2%, and the measured content of choline from commercial lecithins (E 322) up to 3.4%,
- 13.2% release would result in exposure up to 23 mg choline/kg bw per day at the 95th percentile intake of lecithins in toddlers (brand loyal scenario),
- total choline intake considering regular diet (estimated in average ranging from 4 to 18 mg/kg bw per day) across all population age groups and choline intake resulting from lecithins (E 322) used as a food additive are below the upper intake level (UL) for choline defined by the IOM (1998),

the Panel concluded that there is no safety concern for the exposure to the choline from lecithins (E 322) as a food additive at use and use levels reported by industry.

b) Infants (from 12 weeks up to 11 months of age)

Taking further into consideration that:

- adequate exposure estimates calculated in the refined exposure assessment scenario based on the reported data from food industry for infants (12 weeks to 11 months) was up to 163 mg/kg bw per day at the 95th percentile (brand-loyal scenario),
- 13.2% release would result in exposure up to 22 mg choline/kg bw per day at the 95th percentile dietary exposure of lecithins (E 322) in infants (brand loyal scenario),
- total choline intake considering regular diet in the same population group (estimated in average ranging from 9 to 16 mg/kg bw per day), and choline intake resulting from lecithins used as a food additive were in the same order as the adequate intake levels (AI) (EFSA NDA, 2016),

the Panel concluded that there was no safety concern at the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive and for the choline from lecithins (E 322) as a food additive at use and use levels reported by industry.

II. Infants and young children consuming foods for special medical purposes

Taking further into consideration that:

- with respect to the exposure estimates calculated based on the reported data from food industry for infants (12 weeks to 11 months) and young children, the highest exposure was 232 mg lecithins/kg bw per day for toddlers (12–35 months) at the 95th percentile (brand-loyal scenario),
- 13.2% release would result in exposure up to 31 mg choline/kg bw per day at the 95th percentile dietary exposure of lecithins (E 322) in toddlers (brand loyal scenario),
- total choline intake considering regular diet in the same population group (estimated on average as ranging from 13–18 mg/kg bw per day), and choline intake resulting from lecithins used as a food additive, are in the same order as the adequate intake levels (AI) (EFSA NDA, 2016),

the Panel concluded that there was no safety concern with respect to the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive and for exposure to choline resulting from these uses of lecithins (E 322).

The Panel recommended that the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EU specification for lecithins (E 322) should be revised in order to ensure that lecithins (E 322) as a food additive will not be a significant source of exposure to those toxic elements in food. The Panel recommended that the limit for cadmium should be included in the specifications.

The Panel noted some case reports of hypersensitivity reactions associated with soya and egg lecithins (see Section 3.5.7). The Panel agree with the opinion from EFSA NDA Panel (2014) that this hypersensitivity is due to the residual proteins in lecithins (E 322) and therefore their content should be reduced as much as possible.

Regarding the results of the inadequate neurobehavioural studies, to clarify the relevance of the data, a study with lecithins (E 322) in compliance with the current OECD TG 426 would be warranted.

In case the food additive lecithins (E 322) is used in infant formulae and follow-on formulae supplemented with choline or choline salts (see Section 1.2), the Panel recommended that the intake of choline from all sources including the use of the food additive lecithins (E 322) via infant formulae (category 13.1.1), follow-on formulae (category 13.1.2) or other food should be in the order of the AIs defined by the EFSA NDA Panel (2016).

The Panel noted discrepancies between the data reported from industry and the Mintel database, where lecithins (E 322) is labelled in more products than in food categories for which data were reported from industry. Therefore, the Panel recommended collection of data of usage and use levels of lecithins (E 322) in order to perform a more realistic exposure assessment. Moreover, there are several authorised uses that are not supported by data submitted by industry nor by the Mintel database.

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1. Introduction

The present opinion deals with the re-evaluation of lecithins (E 322) when used as a food additive.

1.1. Background and Terms of Reference as provided by the European Commission

1.1.1. 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[1]. 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[2] of 2001. The report 'Food additives in Europe 2000'[3] 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.

1.1.2. 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.

1.1.3. Interpretation of Terms of Reference

The Panel on Food Additives and Nutrient Sources added to Food (ANS) described its risk assessment paradigm in its Guidance for submission for food additive evaluations in 2012 (EFSA ANS Panel, 2012). This Guidance states that, in carrying out its risk assessments, the Panel sought to define a health-based guidance value, such as an acceptable daily intake (ADI) (IPCS, 2004), applicable to the general population. According to the definition above, the ADI as established for the general population does not apply to infants below 12 weeks of age (JECFA, 1978; SCF, 1998). In this context, the re-evaluation of the use of food additives, such as thickening agents and certain emulsifiers, in food for infants below 12 weeks represents a special case for which specific recommendations were given by the Joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) (JECFA, 1972, 1978) and by the SCF (SCF, 1996, 1998). The Panel endorsed these recommendations.

[1] 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, pp. 19–27.

[2] COM(2001) 542 final.

[3] Food Additives in Europe 2000, Status of safety assessments of food additives presently permitted in the EU, Nordic Council of Ministers, TemaNord 2002, p. 560.

In the current EU legislation (Regulation (EC) No 1333/2008[1]) use levels of additives in food for infants under the age of 12 weeks in categories 13.1.1 and 13.1.5.1 (Annex II) and uses of food additives in nutrient preparations for use in food for infants under the age of 12 weeks and maximum levels for the carry-over from these uses (Annex III, Part 5, section B) are included. The Panel considers that these uses would require a specific risk assessment in line with the recommendations given by JECFA and SCF and endorsed by the Panel in its current Guidance for submission for food additives evaluations (EFSA ANS Panel, 2012). Therefore a risk assessment as for the general population is not considered to be applicable for infants under the age of 12 weeks and will be performed separately.

This re-evaluation refers exclusively to the uses of lecithins (E 322) as a food additive in food, including food supplements, and does not include a safety assessment of other uses of lecithins.

1.2. Information on existing evaluations and authorisations

Lecithins

Lecithins (E 322) is an authorised food additive in the European Union (EU) according to Annex II and Annex III to Regulation (EC) No 1333/2008 on food additives and specific purity criteria on lecithins (E 322) have been defined in the Commission Regulation (EU) No 231/2012.

In the EU, lecithins (E 322) has been evaluated by the SCF in 1981 (SCF, 1982), who discussed hydrolysed lecithins and their comparability to lecithins stating that, in the final conclusion, 'hydrolysed lecithin is produced in the gut as a result of normal digestion. There appears to be no specific toxicological effect in rats due to feeding of hydrolysed lecithins. This substance can therefore be regarded metabolically and toxicologically as an alternative to lecithin'.

Referring to older neurobehavioural studies, the SCF considered in 1997 that 'the issue of lecithins and choline in infant formulae should be considered further. However, in the context of carry-over levels of only 0.5 mg/kg, the use of lecithins in nutrient preparations for infant formulae is acceptable and not likely to be of concern' (SCF, 1997). The SCF further outlined, in 1997, 'In an earlier report (SCF, 1983) the Committee considered lecithins as acceptable technological additives at levels up to 5 g/L. However, the Directive on Additives Other Than Colours and Sweeteners[4] lists the maximum level as 1 g/L. This reduction in the maximum level was agreed during the negotiations on the draft Directive in response to a report (UK Ministry of Agriculture Fisheries and Food, 1992) which recommended that the maximum level of lecithins in infant formulae should be restricted to that of human milk (1 g/L). This recommendation was based on studies which claimed neurobehavioural effects in the offspring of rats fed high doses of lecithin. Although these studies were of poor quality, the report noted that large increases in plasma choline could affect neurotransmission in the brain and that particular caution was needed in the infant since the brain was still actively developing'.

Lecithins (E 322) was evaluated by JECFA in 1974 (JECFA, 1974a,b). For lecithin (JECFA, 1974a), JECFA did not specify a numerical ADI (ADI 'not limited').

In 2014, the EFSA Panel on Dietetic Products, Nutrition and Allergies (EFSA NDA Panel, 2014) prepared a scientific opinion on the evaluation of allergenic foods and food ingredients for labelling purposes where the allergenicity of egg and soya lecithins were considered. The possibility of residual allergenicity in food products manufactured using egg lecithin has been reported in a double-blind placebo-controlled food challenge (DBPCFC). Heat denaturation and other food-processing treatments do not reliably reduce the allergenicity of egg. Minimum eliciting doses (MEDs) of ingested egg proteins reported to trigger objective reactions in clinical studies range from few micrograms to milligrams.

The prevalence of clinically confirmed soya allergy in unselected populations in Europe appears to be low, although available studies are scarce. The sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) protein pattern of the standard soya lecithin is very similar to that of soya flour. The lowest MED reported in soya-allergic patients undergoing DBPCFC was 0.2 mg of soya protein, although the majority of patients only reacted to higher doses (EFSA NDA Panel, 2014).

Soybeans and eggs and products thereof (including lecithins) are listed in the Annex II of the Regulation 1169/2011 as substances or products causing allergies or intolerances which indication as allergens is mandatory food information.

[4] European Parliament and Council Directive N.95/2/EC on 20 February 1995 on Food Additives Other Than Colours and Sweeteners, OJ L 61, 18.3.1995, p. 1.

Lecithins are currently authorised in the EU as feed additives (as emulsifying agents) for an unlimited period for all species or categories of animals (Commission Directive of 12 April 1991 amending the Annexes to Council Directive 70/524/EEC concerning additives in feedingstuffs (91/248/EEC)).[5]

In 2016, the EFSA Panel on Additives and Products or Substances used in Animal Feed (EFSA FEEDAP Panel, 2016) prepared a scientific opinion on safety and efficacy of lecithins for all animal species. The FEEDAP Panel considered that lecithins are safe for all target species, and that setting a maximum content for lecithins is not considered necessary.

According to the information provided by the European Medicines Agency (EMA), lecithins are used as an excipient in a large number of 'centrally authorized medical products' as well as in 'nationally authorized medical products'. The Committee on Herbal Medicinal Products (HMPC) of the EMA published a draft monograph accepting the traditional medicinal use of soya bean lecithin (deoiled, enriched phospholipids from soya bean).

Choline

In humans, dietary lecithins are known to be hydrolysed and liberate choline (see Section 3.5).

The EFSA NDA Panel (2016) prepared a scientific opinion on dietary reference values (DRVs) for choline. In this opinion, the NDA Panel considered dietary choline including choline compounds (e.g. glycerophosphocholine, phosphocholine, phosphatidylcholine, sphingomyelin). The NDA Panel considered that none of the biomarkers of choline intake or status was suitable for deriving DRVs for choline. With respect to choline intake and possible health consequences, the NDA Panel concluded that there is a lack of data on choline intake in infants in the second half year of life and on associations between choline intake and health outcomes in children that could be used to set requirement for choline in these age groups. Overall, the NDA Panel concluded that average requirements (ARs) and population reference intakes (PRIs) for choline could not be derived for adults, infants and children, and therefore defined adequate intakes (AIs):

- For all adults, the Panel set an AI at 400 mg/day based on the average observed choline intake in healthy populations in the EU and in consideration of the amounts of choline needed to replete about 70% of depleted subjects who showed signs of organ dysfunction in a depletion/repletion study.
- Considering that there is no evidence for an insufficient choline intake of fully breast-fed infants during the first 6 months of life, the amount of choline provided in human milk was considered to be adequate. Considering a choline concentration of 145 mg/L (average of two studies on full-term infants) and assuming a mean milk transfer of 0.8 L/day during the first 6 months of lactation in exclusively breastfeeding women, the estimated choline intake of fully breast-fed infants during the first 6 months of life would be 116 mg/day, rounded up to 120 mg/day.
- For all infants aged 7–11 months, the NDA Panel derived an AI of 160 mg/day and, for children aged 1–17 years, AIs range from 140 mg/day (1–3 years) to 400 mg/day (15–17 years).
- For pregnant women, the NDA Panel derived an AI of 480 mg/day, calculated by extrapolation from the AI for non-pregnant women and the mean gestational increase in body weight.

For lactating women, the amount of choline secreted per day in human milk during the first 6 months of exclusive breastfeeding (120 mg/day) was added to the AI for non-lactating women, and an AI of 520 mg/day is set. With regard to excessive intake of choline, the NDA Panel referenced on the setting of tolerable upper intake levels (ULs) for choline by the US Institute of Medicine (IOM, 1998) and noted that no UL was established by IOM for infants (EFSA NDA Panel, 2016).

In 1998, the Food and Nutrition Board of the IOM established ULs for choline (Table 1) (IOM, 1998). The recommendation for adults was based on a single case report of hypotension, several other studies involving cholinergic effects and secondarily, on preventing the fishy body odour due to increased excretion of trimethylamine. For infants, the UL was judged not determinable because of a lack of data concerning adverse effects in this age group and concern about the infant's ability to handle excess amounts. According to IOM, 'the only source of intake of choline for infants should be from food or formula to prevent high levels of intake'. The UL of 3.5 g/day for adults was adjusted for children and adolescents on the basis of relative body weight.

[5] Reg (EC) No 1831/2003. European Union Register of Feed Additives. Edition 254. Appendixes 3e, 4 – 23.03.2017 European Union legislation on feed additives: http://ec.europa.eu/food/safety/animal-feed/feed-additives/index_en.htm

Table 1: Tolerable upper intake level (UL) for choline (IOM, 1998)

Age group	UL (mg/day)
Infants 0–12 months	Not possible to establish; source of intake should be food and formula only
Children 1–8 years	1,000
Children 9–13 years	2,000
Adolescents 14–18 years*	3,000
Adults 19 years and older*	3,500

*: Including pregnancy and lactation.

The IOM noted that individuals with trimethylaminuria, renal or liver disease, depression or Parkinson's disease might be at increased risk of adverse effects with choline intakes at the UL (IOM, 1998).

Choline, choline chloride, choline citrate, choline bitartrate are listed in Annex III of Commission Directive 2006/141/EC on infant formulae and follow-on formulae and amending Directive 1999/21/EC of 22 December 2006 and may be used in the manufacture of infant formulae and follow-on formulae.

2. Data and methodologies

2.1. Data

The ANS Panel was not provided with a newly submitted dossier. EFSA launched public calls for data[6,7,8] and, if relevant, contacted other risk assessment bodies to collect relevant information from interested parties.

The Panel based its assessment on information submitted to EFSA following the public calls for data, information from previous evaluations and additional available literature up to the last Working Group meeting before the adoption of the opinion.[9] Attempts were made at retrieving relevant original study reports on which previous evaluations or reviews were based; however, these were not always were these available to the Panel.

The EFSA Comprehensive European Food Consumption Database (Comprehensive Database)[10] was used to estimate the dietary exposure.

The Mintel's Global New Products Database (GNPD) is an online resource listing food products and compulsory ingredient information that should be included in labelling. This database was used to verify the use of lecithins (E 322) in food products.

2.2. Methodologies

This opinion was formulated following the principles described in the EFSA Guidance on transparency in the scientific aspects of risk assessment (EFSA Scientific Committee, 2009) and following the relevant existing Guidances from the EFSA Scientific Committee.

The ANS Panel assessed the safety of lecithins (E 322) as a food additive in line with the principles laid down in Regulation (EU) 257/2010 and in the relevant guidance documents: Guidance on submission for food additive evaluations by the SCF (2001) and taking into consideration the Guidance for submission for food additive evaluations in 2012 (EFSA ANS Panel, 2012).

When the test substance was administered in the feed or in the drinking water, but doses were not explicitly reported as mg/kg bw per day based on actual feed or water consumption, the daily intake was calculated by the Panel using the relevant default values as indicated in the EFSA Scientific Committee Guidance document (EFSA Scientific Committee, 2012) for studies in rodents or, in the case of other animal species, by JECFA (2000). In these cases, the daily intake is expressed as equivalent. When, in human studies in adults (aged above 18 years), the dose of the test substance administered

[6] Call for scientific data on food additives permitted in the EU and belonging to the functional classes of emulsifiers, stabilisers and gelling agents. Published: 23 May 2010. Available online: http://www.efsa.europa.eu/en/dataclosed/call/ans091123

[7] Call for food additives usage level and/or concentration data in food and beverages intended for human consumption – Extended deadline: 30 September 2014. Available online: http://www.efsa.europa.eu/sites/default/files/consultation/140310.pdf

[8] Call for data on lecithins (E 322) permitted as food additives in the EU – Extended Deadline: 31 December 2015. Available online: http://www.efsa.europa.eu/it/data/call/150608

[9] 23 November 2016.

[10] Available online: http://www.efsa.europa.eu/en/datexfoodcdb/datexfooddb.htm

was reported in mg/person per day, the dose in mg/kg bw per day was calculated by the Panel using a body weight of 70 kg as default for the adult population as described in the EFSA Scientific Committee Guidance document (EFSA Scientific Committee, 2012).

Dietary exposure to lecithins (E 322) from its use as a food additive was estimated combining food consumption data available within the EFSA Comprehensive European Food Consumption Database with the maximum levels according to Annex II to Regulation (EC) No 1333/2008[11] and/or reported use levels and analytical data submitted to EFSA following a call for data. Different scenarios were used to calculate exposure (see Section 3.3.1). Uncertainties on the exposure assessment were identified and discussed.

In the context of this re-evaluation, the Panel followed the conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EC) No 257/2010 (EFSA ANS Panel, 2014).

3. Assessment

3.1. Technical data

3.1.1. Identity of the substance

According to Commission Regulation (EU) No 231/2012[12], the lecithins (E 322) is identified as mixtures or fractions of phosphatides obtained by physical procedures from animal or vegetable foodstuffs. They also include the corresponding hydrolysed products. Although Commission Regulation No 231/2012 includes both types of lecithins (non-hydrolysed and hydrolysed) under the same food additive (E 322), JECFA differentiates between them and treats them as different food additives (INS 322i and INS 322ii) with distinct specifications (see Section 3.1.2).

In the CAS Registry Numbers database, different CAS numbers are listed for specific lecithins.[13] The general CAS number for lecithins is 8002-43-5. The CAS number for hydrolysed lecithins is 85711-58-6. However, depending on the source of the lecithins, different CAS numbers have been assigned. For example, the soya bean lecithins have the CAS number 8030-76-0, and the egg phospholipids have the CAS number 93685-90-6. The European Inventory of Existing Commercial Chemical Substances (EINECS) number for lecithins, described as the complex combination of diglycerides of fatty acids linked to the choline ester of phosphoric acid, is 232-307-2. This is also the EINECS number given in the Commission Regulation No 231/2012, even though, under this number, the EINECS database does not refer to hydrolysed lecithins. For hydrolysed lecithins, the EINECS number is 288-318-8. The EINECS number to soya bean lecithins is 310-129-7 and, for egg yolk, lecithins is 297-639-2.

According to Commission Regulation No 231/2012, lecithins appear as a brown liquid or viscous semiliquid or powder. Hydrolysed lecithins are light brown to brown viscous liquid or paste.

Synonyms for lecithins are phosphatides or phospholipids. For hydrolysed lecithins, the synonyms are lysolecithins or lysophospholipids (Tanno, 2012; SciFinder, 2013).

The main source of lecithins is soya bean oil. Other plant sources include oil from cottonseeds, corn, sunflower seeds and rapeseed, together with animal sources such as egg yolk and bovine brain (Wendel, 1995; Tanno, 2012). The Panel noted that the use of bovine brain has not been confirmed by the industries.

As defined in the ChemIDplus database, lecithins are 'A complex mixture of phospholipids, glycolipids and triglycerides with substantial amounts of phosphatidylcholines, phosphatidylethanolamines and phosphatidylinositols, which are sometimes loosely termed as 1,2-diacyl-3-phosphocholines' (ChemIDplus, 2014).

The structural formulae of the main phospholipids in lecithins (E 322) are given in Figure 1. The fatty acid moiety of phospholipids can differ, such as between stearic, palmitic, oleic and linoleic acids (Wendel, 1995; Merck Index, 2006; Tanno, 2012).

Because the fatty acids in lecithins have variable carbon chain lengths, an exact molecular formula and a molecular weight can only be given for individual components. For example, the molecular formula for the phosphatidylcholine containing two linoleate groups is $C_{44}H_{80}O_8NP$ and the molecular weight is 782.1 g/mol.

[11] Commission 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.
[12] 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, pp. 1–295.
[13] SciFinder, 2013

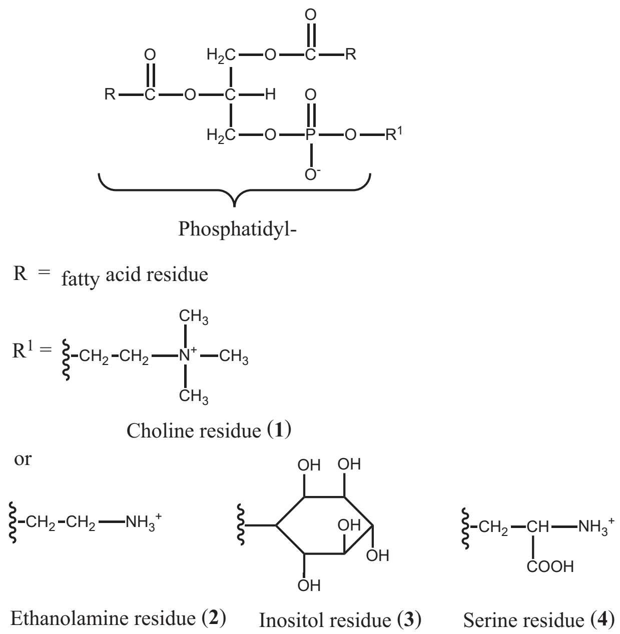

Figure 1: Main structures for phospholipid components in lecithins: phosphatidylcholine (1), phosphatidylethanolamine (2), phosphatidylinositol (3), phosphatidylserine (4). If R^1 = H, the compound is phosphatidic acid

The amount (percentage) of the principal components of lecithins depends on raw material sources (EFEMA, 2013). Food-grade lecithins obtained from soya beans or other sources is a mixture containing about 60% phospholipids and 40% triglycerides, sterols and carbohydrates in various proportions (SCF, 1982).

The phospholipid composition of soya bean lecithin on an oil-free basis is 21% phosphatidylcholine, 22% phosphatidylethanolamine, 19% phosphatidylinositol, 10% phosphatidic acid, 1% phosphatidylserine and 12% glycolipids (Wendel, 1995). Data on phospholipid composition for several batches of soya lecithin (liquid, deoiled, hydrolysed), sunflower lecithin (liquid, deoiled) and rape seed lecithin obtained by ^{31}P nuclear magnetic resonance spectroscopy (^{31}P-NMR) provided by the interested party (Document provided to EFSA n.18) are summarised in Table 2.

Table 2: Summarised data on phospholipid composition of soya lecithin (liquid, de-oiled, hydrolysed), sunflower lecithin (liquid, deoiled) and rape seed lecithin from the European Lecithin Manufacturers Association (ELMA) (Document provided to EFSA n.18)

	Phosphatidyl choline (%)	Phosphatidyl inositol (%)	Phosphatidyl ethanolamine (%)	Phosphatidic acid (%)
Soya lecithin liquid	12.69–16.7	6.47–11.84	6.45–13.57	2.28–5.96
Soya lecithin de-oiled	16.83–22.23	14.66–17.27	10.00–13.67	5.28–8.57
Soya lecithin hydrolysed*	7.66–8.81	6.16–9.15	3.54–5.51	2.09–2.69
Sunflower lecithin liquid	14.34–17.23	12.30–14.92	4.85–6.82	1.32–3.21
Sunflower lecithin de-oiled	24.97–27.57	15.12–21.17	9.91–10.50	2.56–2.80
Rape seed lecithin	16.74–18.18	10.45–12.30	6.46–8.03	2.44–3.59

*: In this product phospholipids are partially hydrolysed. Reported content of liso phosphatidyl choline is 3.85–4.56%, lyso phosphatidyl inositol is 0.88–1.36%, lyso phosphatidyl ethanolamine is 1.67–2.31% and lyso phosphatidic acid is 1.19–1.34%

The content of choline that can theoretically be released from phosphatidylcholine containing two linoleate groups is 13.2% and from lyso phospatidyl choline containing one linoleate group is 20.2%.

Based on the data provided by ELMA (Document provided to EFSA n.18), the calculated content of choline that can theoretically be released from commercial lecithins is given in Table 3.

Table 3: Calculated content of choline that can theoretically be released from commercial lecithins based on the data provided by ELMA (Document provided to EFSA n.18)

	Phosphatidylcholine content (%)	Calculated content of choline, that can theoretically be released from lecithin (%)
Soya lecithin liquid	12.69–16.7	1.67–2.20
Soya lecithin de-oiled	16.83–22.23	2.22–2.93
Soya lecithin hydrolysed	11.51–13.37*	1.51–1.84
Sunflower lecithin liquid	14.34–17.23	1.89–2.27
Sunflower lecithin deoiled	25.57	3.38
Rape seed lecithin	16.74	2.21

*: Total content of phosphatidylcholine and lyso phospatidylcholine.

Wendel (1995) reported that the fatty acid composition of oil-free soya bean lecithins was:

- 18.4% palmitic acid; $CH_3(CH_2)_{14}COOH$,
- 4.0% stearic acid: $CH_3(CH_2)_{16}COOH$,
- 10.7% oleic acid: $CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$),
- 58.0% linoleic acid: ($CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$),
- 6.8% linolenic acid: ($CH_3(CH_2CH{=}CH)_3(CH_2)_7CO_2H$),
- 2.1% others.

Hydrolysed lecithins (lysolecithins) are the products of partial hydrolysis of food-grade lecithins, where the fatty acid in the 2-position of the phospholipids is enzymatically removed. They contain about 51% phospholipids, 18% total free fatty acids, 1% moisture and 24% triglycerides, sterols, commercial pancreatin (enzyme, inactivated) and carbohydrates in various proportions (SCF, 1982).

Refined lecithins with high levels of phospholipids (> 95%), prepared by acetone and alcohol fractionation (see Section 3.1.3), are soft, yellow-brown powders (EFEMA, 2013). The density of commercial crude lecithin is 0.97 g/mL (liquid) and 0.5 g/mL (granule) (Wendel, 1995).

According to JECFA, both lecithin and partially hydrolysed lecithin 'are only partially soluble in water, but readily hydrate to form emulsions; the oil-free phosphatides are soluble in fatty acids, but are practically insoluble in fixed oils' (JECFA, 2007a,b). However, the hydrolysed lecithin (lysolecithin) has an increased solubility in water and greater emulsifying activity for formation of oil-in-water emulsions (Tanno, 2012). The solubilities of soya bean lecithin and some of its individual ingredients are given in Table 4.

Table 4: Solubilities of soya bean lecithins and of various phospholipids (Wendel, 1995; Tanno, 2012)

	Water	Hexane	Alcohol	Acetone
Soya bean lecithins	Insoluble/dispersible	Soluble	Soluble	Insoluble
Phosphatidylcholine	Soluble/dispersible	Soluble	Readily soluble	Sparingly soluble
Phosphatidylethanolamine	Readily soluble/dispersible	Soluble	Soluble	Insoluble
Phosphatidylinositol	Readily soluble/dispersible	Soluble	Insoluble	Insoluble
Lysophospholipids	Soluble	Partially soluble	Soluble	Soluble

The Panel noted that several studies have been conducted with a substance named essential phospholipid (EPL), although, in some studies, the composition of the EPL used was not indicated. The Panel noted that, when given, the composition of the EPL consisted of 75% phosphatidylcholine (fatty acids content as follows: 65% linoleic acid, 5% linolenic acid, 10% oleic acid, 15% palmitic acid and 5% stearic acid). The remaining 25% consisted of 5% phosphatidylethanolamine (kephalins) and 20% accompanying lipids from the soya bean.

No information on the particle size of lecithin powder was provided to the Panel. The FEEDAP Scientific opinion on safety and efficacy of lecithins for all animal species (EFSA FEEDAP Panel, 2016) contains the following information on particle size of lecithin powder: 'Three batches of the de-oiled lecithin powder with different physical characteristics were analysed for particle size distribution (by laser diffraction), showing variable results. The coarser powders had < 0.3% of the particles with a diameter ≤ 200 μm; the finest powder had < 13.9% and < 1.6% of the particles with diameters < 100 μm and 50 μm, respectively'.

3.1.2. Specifications

The specifications for lecithins (E 322) as defined in the Commission Regulation (EU) No 231/2012 and by JECFA (2007a,b) are listed in Table 5.

Table 5: Specifications for lecithins (E 322) according to Commission Regulation (EU) No 231/2012 and JECFA (2007a,b)

	Commission Regulation (EU) No 231/2012	JECFA (2007a)	JECFA (2007b)
	Lecithins (E 322)	**Lecithin (INS 322i)**	**Lecithin, Partially Hydrolysed (INS 322ii)**
Definition	Lecithins are mixtures or fractions of phosphatides obtained by physical procedures from animal or vegetable foodstuffs; they also include hydrolysed products obtained through the use of harmless and appropriate enzymes. The final product must not show any signs of residual enzyme activity. The lecithins may be slightly bleached in aqueous medium by means of hydrogen peroxide. This oxidation must not chemically modify the lecithin phosphatides	Usually prepared from oil-bearing seeds used for food, especially soybeans; may also be prepared from animal sources; a complex mixture of acetone-insoluble phosphatides which consists chiefly of phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol, combined with various amounts of other substances such as triglycerides, fatty acids, and carbohydrates; refined grades may contain any of these components in varying proportions and combinations depending on the type of fractionation used; its oil-free forms, the preponderance of triglycerides and fatty acids is removed and the product contains 90% or more of phosphatides representing all or certain fractions of the total phosphatide complex	Prepared by partial hydrolysis of lecithin by the use of a suitable lipase. When the desired degree of hydrolysis is attained, the product is heated in order to inactivate the residual enzyme
Assay	Lecithins: not less than 60.0% of substances insoluble in acetone Hydrolysed lecithins: not less than 56.0% of substances insoluble in acetone	Not less than 60% of acetone-insoluble matter (phosphatides)	Not less than 56% of acetone-insoluble matter (phosphatides)
Description	Lecithins: brown liquid or viscous semiliquid or powder Hydrolysed lecithins: light brown to brown viscous liquid or paste	Consistency of both natural grades and refined grades may vary from plastic to fluid, depending upon free fatty acid and oil content, and upon the presence or absence of other diluents; from light yellow to brown, depending on the source, on crop variations, and on whether it is bleached or unbleached; odourless or has a characteristic, slight nut-like odour. Edible diluents, such as cocoa butter and vegetable oils, often replace soybean oil to improve functional and flavour characteristics	Consistency may vary from plastic to fluid, depending upon free fatty acid and oil content, and upon the presence or absence of other diluents. Its colour varies from light yellow to brown, depending on the source, on crop variations, and on whether it is bleached or unbleached; odourless or has a characteristic, slight nutlike odour. Edible diluents, such as cocoa butter and vegetable oils, often replace soybean oil to improve functional and flavour characteristics
Identification			
Tests for choline, for phosphorus and fatty acids	Passes test	Test for phosphorus: Ignite 1 g of the sample with 2 g of anhydrous sodium carbonate. Cool and dissolve the residue in 5 mL of water and 5 mL of nitric acid. Add 5 mL of ammonium molybdate TS and heat to boiling. A yellow precipitate is obtained Test for choline: To 0.5 g of the sample, add 5 mL of diluted hydrochloric acid (1 + 1), heat in a water bath for 2 h, and filter. Use this solution as the test	Test for phosphorus: Ignite 1 g of the sample with 2 g of anhydrous sodium carbonate. Cool and dissolve the residue in 5 mL of water and 5 mL of nitric acid. Add 5 mL of ammonium molybdate TS and heat to boiling. A yellow precipitate is obtained Test for choline: To 0.5 g of the sample, add 5 mL of diluted hydrochloric acid (1 + 1), heat in a water bath for 2 h, and filter. Use this solution as the test

	Commission Regulation (EU) No 231/2012	JECFA (2007a)	JECFA (2007b)
	Lecithins (E 322)	**Lecithin (INS 322i)**	**Lecithin, Partially Hydrolysed (INS 322ii)**
		solution. Perform *Paper Chromatography* with 10 μL of the test solution, using choline chloride solution (1 + 200) as the control solution and *n*-butanol–water–acetic acid mixture (4:2:1) as the developing solvent. A red–orange spot corresponding to the spot obtained from the control solution is observed. For the filter paper, use a No. 2 filter paper for chromatography. Stop the development when the developing solvent rises about 25 cm, air-dry, spray with Dragendorff TS to develop a colour, and observe in daylight Test for fatty acids: Reflux 1 g of the sample for 1 h with 25 mL of 0.5 N ethanolic potassium hydroxide. When cooled to 0°, a precipitate of potassium soap is obtained	solution. Perform *Paper Chromatography* with 10 μL of the test solution, using choline chloride solution (1 + 200) as the control solution and *n*-butanol–water–acetic acid mixture (4:2:1) as the developing solvent. A red–orange spot corresponding to the spot obtained from the control solution is observed. For the filter paper, use a No. 2 filter paper for chromatography. Stop the development when the developing solvent rises about 25 cm, air-dry, spray with Dragendorff TS to develop a colour, and observe in daylight Test for fatty acids: Reflux 1 g of the sample for 1 h with 25 mL of 0.5 N ethanolic potassium hydroxide. When cooled to 0°, a precipitate of potassium soap is obtained
Test for hydrolysed lecithin	To a 800-mL beaker, add 500 mL of water (30–35°C). Then slowly add 50 mL of the sample with constant stirring. Hydrolysed lecithin will form a homogeneous emulsion. Non-hydrolysed lecithin will form a distinct mass of about 50 g	To a 800-mL beaker, add 500 mL of water (30–35°C). Then, slowly add 50 mL of the sample with constant stirring. Hydrolysed lecithin will form a homogeneous emulsion. Non-hydrolysed lecithin will form a distinct mass of about 50 g	To a 800-mL beaker, add 500 mL of water (30–35°C). Then, slowly add 50 mL of the sample with constant stirring. Hydrolysed lecithin will form a homogeneous emulsion. Non-hydrolysed lecithin will form a distinct mass of about 50 g
Solubility	–	Only partially soluble in water; readily hydrates to form emulsions; oil-free phosphatides are soluble in fatty acids, but are practically insoluble in fixed oils	Only partially soluble in water, but readily hydrates to form emulsions; the oil-free phosphatides are soluble in fatty acids, but are practically insoluble in fixed oils
Purity			
Loss on drying	Not more than 2.0% (105°C, 1 h)	Not more than 2% (105°C, 1 h)	Not more than 2% (105°C, 1 h)
Toluene-insoluble Matter	Not more than 0.3%	Not more than 0.3%	Not more than 0.3%
Acid value	Lecithins: not more than 35 mg of potassium hydroxide per gram Hydrolysed lecithins: not more than 45 mg of potassium hydroxide per gram	Not more than 36	Not more than 45
Peroxide value	Equal to or less than 10	Not more than 10	Not more than 10
Arsenic	Not more than 3 mg/kg	–	–
Lead	Not more than 2 mg/kg	Not more than 2 mg/kg	Not more than 2 mg/kg
Mercury	Not more than 1 mg/kg	–	–

According to the information from the interested party (Document provided to EFSA n.18), phospholipids can be modified by enzymes in a wide variety of ways. Phospholipases A and B split off fatty acids, whereas phospholipases C and D attack at the glycerophosphate bond. Specifications for five commercial lipases with a different level of details, developed by recombinant DNA techniques, were submitted (Document provided to EFSA n.18). Concerning the residual enzymatic activity, according to Association of Manufacturers and Formulators of Enzyme Products (AMFEP) it is stated that: 'Depending on production process enzyme activity can be excluded, in our case by drying at 70°C for 24 h and further with a low moisture content of 0.4–0.5%'. As an indicator of residual enzymatic activity, it is also possible to use acid value. If it is stable, there is no enzyme activity (Document provided to EFSA n.18).

The Panel noted that according to the Commission Regulation (EU) No 231/2012 the final product must not show any signs of residual enzyme activity.

Food Chemicals Codex (2010-2011)also contains specifications for hydroxylated lecithins. The Panel noted that the EU specification for E 322 states that 'The lecithins may be slightly bleached in aqueous medium by means of hydrogen peroxide. This oxidation must not chemically modify the lecithin phosphatides'.

In a study of five batches of non-hydrolysed lecithins from 2007 to 2009, provided by industry, measurements of Enterobacteriaceae (negative/1 g), salmonellae (negative/25 g), heavy metals (lead $<$ 0.1 mg/kg, mercury $<$ 0.005 mg/kg and arsenic $<$ 0.1 mg/kg), residual solvents (hexane $<$ 1 mg/kg, ethanol $\leq$ 3.8 mg/kg, acetone $\leq$ 2.5 mg/kg), pesticides (not detectable, limit of detection (LOD): 0.01–10 mg/kg), aflatoxins ($<$ 0.2 mg/kg), polycyclic aromatic hydrocarbons (benzo(a)anthracene $\leq$ 4.4 μg/kg, chrysene $\leq$ 7.8 μg/kg, benzo(b)fluoranthene $<$ 0.5 μg/kg, benzo(a)pyrene $\leq$ 1.4 μg/kg), polychlorinated biphenyls (not detectable, LOD not indicated) and dioxins (sum of dioxins $\leq$ 0.75 pg TEQ (WHO)/g fat and sum of dioxins and dioxin precursors like PCBs $\leq$ 1.5 pg TEQ (WHO)/g fat) were performed (Document provided to EFSA n.3).

Data on protein content in lecithins provided by ELMA (Document provided to EFSA n.18), as well as literature data, are rather variable due to number of different extraction systems and specific assays have been utilised. Many of these methods have not been validated and, in addition, interferences from residual lipids may confound the chemical assay results. Results for protein content are in the range 115–27,000 mg/kg for crude soya lecithins, 232–1338 mg/kg for in fluid soya lecithin, 65–480 mg/kg for in deoiled soya lecithin and 49 mg/kg for in egg lecithins (Document provided to EFSA n.18; Porras et al., 1985; Müller et al., 1998; Gu et al., 2001; Paschke et al., 2001; Martin-Hernandez et al., 2005).

The Panel noted that there is no specification for the presence of residual proteins from the source material used in the manufacturing of the food additive.

According to EFSA NDA Panel (2014), the lowest MED reported in soya-allergic patients undergoing DBPCFC was 0.2 mg of soya protein, although the majority of patients only reacted to higher doses. MEDs of ingested egg proteins reported to trigger objective reactions in clinical studies range from few micrograms to milligrams. The Panel also noted some case reports of hypersensitivity reactions associated with egg and soya lecithins (see Section 3.5.7). The Panel agree with the opinion from EFSA NDA Panel (2014) that this hypersensitivity is due to the residual proteins in lecithins (E 322) and therefore their content should be reduced as much as possible.

The Panel noted that, according to the EU specifications for lecithins (E 322), impurities of the toxic elements arsenic, lead and mercury are accepted up concentrations of 3, 2 and 1 mg/kg, respectively. Contamination at those levels could have a significant impact on the exposure to these metals, for which the intake is already close to the health-based guidance values established by the EFSA (EFSA CONTAM Panel, 2009a,b, 2010, 2012). The Panel noted that limit for cadmium should be included in the specifications.

According to data provided by industry, concentrations of toxic elements: lead, mercury and arsenic were below the LOD of 0.1, 0.005 and 0.1 mg/kg, respectively (Document provided to EFSA n.3), and between 1 and 2.5 order of magnitude below the limits set in the EU specifications.

3.1.3. Manufacturing process

The commercial production of lecithins used as food additives is based mainly on soya bean oil; other sources, such as cottonseed, corn, sunflower, rapeseed, egg and bovine brain, are of minor importance (Wendel, 1995; Tanno, 2012).

The first step for the production of lecithins from soya bean is the compression of the seeds to obtain the crude soya bean oil. To this crude oil, water is added to hydrate the phosphatides and the water–oil mixture is then heated at 70°C for 30–60 min. Afterwards, the oil-insoluble lecithin fraction (a wet gum known as lecithin hydrate) is separated by centrifugation. The gum is then transferred to a holding tank to allow addition of bleaching agents, if required. Hydrogen peroxide and benzoyl peroxide are used to bleach the lecithin. Bleaching may be carried out either using a 0.3–1.5% hydrogen peroxide solution instead of water for the degumming process, or by the addition of peroxide to the holding tank. Lecithins are separated from the triglycerides by a molecular membrane degumming process (Tanno, 2012). The Panel noted that according to the Commission Regulation (EU) No 231/2012, only hydrogen peroxide may be used as a bleaching agent in the manufacturing of lecithins (E 322).

Crude lecithin generally has high viscosity and is a brown fluid. The composition of crude lecithin can be changed by fractionation with solvents. Most of the triglycerides and fatty acids can be separated from crude lecithin by acetone fractionation to give oil-free lecithin powders. Lecithins can be enriched by alcohol extraction. Phosphatidylcholine is concentrated by extraction with alcohol. This fraction has increased emulsifying activity for the formation of oil-in-water emulsions. The alcohol-insoluble fraction is rich in the hydrophobic phosphatidylinositol and therefore favours the formation of water-in-oil emulsions. Phosphatidylethanolamine is evenly divided between the alcohol soluble and insoluble fractions. High-grade lecithins are also made by removing the hexane-insoluble material by filtration (Tanno, 2012).

There are many parameters which characterise the physical properties of lecithins such as acetone insoluble matter, acid value, moisture content, hexane-insoluble matter, colour, consistency and clarity (Tanno, 2012).

The partly hydrolysed lecithins are industrially produced by the action of the enzyme phospholipase A2, which selectively hydrolyses the fatty acid in the 2-position of the phospholipid (Tanno, 2012). Any enzymatic activity in the final product is inactivated by heating (TemaNord, 2002).

3.1.4. Methods of analysis in food

Because lecithin compounds (including phosphatidylcholine, phosphatidylethanolamine and phosphatidylinositol) are too polar to be subjected to direct gas chromatographic analysis, liquid chromatographic methods are usually used for their analysis (Tanno, 2012).

The procedures described by Helmerich and Koehler (2003) are only appropriate for the analysis of technical mixtures. These authors determined phospholipids in eight commercial lecithins and three flour improvers by thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC) and ^{31}P-NMR. Most components could be quantified by TLC. The highest selectivity was provided by ^{31}P-NMR, whereas HPLC was the method with the lowest selectivity. The best sensitivity was observed for HPLC and TLC with detection limits of 20–170 mg/L.

A method for the determination of the total phosphorous content in lecithins is described in AOAC (1980). After extraction of the sample, the amount of phosphorous is determined as P_2O_5.

3.1.5. Stability of the substance, and reaction and fate in food

Information about the stability of lecithins has been provided by industry (Document provided to EFSA n.3). Packed samples of three batches of fluid lecithins were stored under recommended storage conditions (10–35°C, 60% relative humidity), and tested against EU specifications for assay, description, toluene-insoluble matter, acid value and peroxide value at regular time points up to 36 months. All batches were observed to be stable as the measured values were matching the specifications. Additionally, the same samples were tested for aerobic bacteria (< 10 cfu/g) and *Salmonella* (negative in 25 g).

Long-term storage of lecithins at high temperatures in the presence of air leads to oxidation of the unsaturated fatty acids, resulting in an off-flavour and black colouration (Tanno, 2012).

3.2. Authorised uses and use levels

Maximum levels of lecithins (E 322) have been defined in Annex II to Regulation (EC) No 1333/2008[14] on food additives, as amended. In this document, these levels are named maximum permitted levels (MPLs).

Currently, lecithins (E 322) is an authorised food additive in the EU at *quantum satis* (QS) in most foods apart from fats and oils essentially free from water, infant and follow-on formulae, processed cereal-based foods and baby foods for infants and young children, and other foods for young children. Lecithins (E 322) is included in the Group I of food additives authorised at QS.

Table 6 summarises foods that are permitted to contain lecithins (E 322) and the corresponding MPLs as set by Annex II to Regulation (EC) No 1333/2008.

[14] 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, pp. 16–33.

Table 6: MPLs of lecithins (E 322) in foods according to the Annex II to Regulation (EC) No 1333/2008

Food category number	Food category name	E-number/ group	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)
01.3	Unflavoured fermented milk products, heat-treated after fermentation	Group I		QS
01.4	Flavoured fermented milk products including heat-treated products	Group I		QS
01.5	Dehydrated milk as defined by Directive 2001/114/EC	E 322		QS
01.6.3	Other creams	Group I		QS
01.7.1	Unripened cheese excluding products falling in category 16	Group I	Except mozzarella	QS
01.7.5	Processed cheese	Group I		QS
01.7.6	Cheese products (excluding products falling in category 16)	Group I		QS
01.8	Dairy analogues, including beverage whiteners	Group I		QS
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	E 322	Except virgin oils and olive oils	30,000
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	Group I		QS
02.3	Vegetable oil pan spray	Group I		QS
03	Edible ices	Group I		QS
04.2.1	Dried fruit and vegetables	Group I		QS
04.2.2	Fruit and vegetables in vinegar, oil, or brine	Group I		QS
04.2.4.1	Fruit and vegetable preparations excluding compote	Group I		QS
04.2.5.4	Nut butters and nut spreads	Group I		QS
04.2.6	Processed potato products	Group I		QS
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	Group I		QS
05.2	Other confectionery including breath refreshening microsweets	Group I		QS
05.3	Chewing gum	Group I		QS
05.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4	Group I		QS
06.2.2	Starches	Group I		QS
06.3	Breakfast cereals	Group I		QS
06.4.1	Fresh pasta	E 322		QS

Food category number	Food category name	E-number/ group	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)
06.4.2	Dry pasta	E 322	Only gluten-free and/or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC	QS
06.4.3	Fresh precooked pasta	E 322		QS
06.4.4	Potato gnocchi	Group I	Except fresh refrigerated potato gnocchi	QS
06.4.5	Fillings of stuffed pasta (ravioli and similar)	Group I		QS
06.5	Noodles	Group I		QS
06.6	Batters	Group I		QS
06.7	Precooked or processed cereals	Group I		QS
07.1	Bread and rolls	Group I	Except products in 7.1.1 and 7.1.2	QS
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt	E 322		QS
07.1.2	Pain courant francais; *Friss búzakenyér, fehér és félbarna kenyerek*	E 322		QS
07.2	Fine bakery wares	Group I		QS
08.3.1	Non-heat-treated meat products	Group I		QS
08.3.2	Heat-treated meat products	Group I	Except *foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben*	QS
08.3.3	Casings and coatings and decorations for meat	Group I		QS
09.2	Processed fish and fishery products including molluscs and crustaceans	Group I		QS
09.3	Fish roe	Group I	Only processed fish roe	QS
10.2	Processed eggs and egg products	Group I		QS
11.2	Other sugars and syrups	Group I		QS
12.1.2	Salt substitutes	Group I		QS
12.2.2	Seasonings and condiments	Group I		QS
12.3	Vinegars	Group I		QS
12.4	Mustard	Group I		QS
12.5	Soups and broths	Group I		QS
12.6	Sauces	Group I		QS
12.7	Salads and savoury based sandwich spreads	Group I		QS
12.8	Yeast and yeast products	Group I		QS
12.9	Protein products, excluding products covered in category 1.8	Group I		QS
13.1.1	Infant formulae as defined by Directive 2006/141/EC	E 322	[(a)]	1,000

Food category number	Food category name	E-number/ group	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)
13.1.2	Follow-on formulae as defined by Directive 2006/ 141/EC	E 322	[(a)]	1,000
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/ 125/EC	E 322	Only biscuits and rusks, cereal-based foods, baby foods	10,000
13.1.4	Other foods for young children	E 322	[(a)]	10,000
13.1.5.1[(b)]	Dietary foods for infants for special medical purposes and special formulae for infants	E 322	[(a)]	1,000
13.1.5.2[(c)]	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC	E 322	[(a)]	1,000
13.1.5.2[(d)]	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC	E 322	Only biscuits and rusks, cereal-based foods, baby foods	10,000
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	Group I		QS
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	Group I		QS
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) No 41/2009	Group I	Including dry pasta	QS
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	Group I	Only vegetable juices	QS
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	Group I	Only vegetable nectars	QS
14.1.4	Flavoured drinks	Group I		QS
14.1.5.2	Other	Group I	Excluding unflavoured leaf tea; including flavoured instant coffee	QS
14.2.3	Cider and perry	Group I		QS
14.2.4	Fruit wine and made wine	Group I		QS
14.2.5	Mead	Group I		QS
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Group I	Except whisky or whiskey	QS
14.2.7.1	Aromatised wines	Group I		QS
14.2.7.2	Aromatised wine-based drinks	Group I		QS

Food category number	Food category name	E-number/ group	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)
14.2.7.3	Aromatised wine-product cocktails	Group I		QS
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15% of alcohol	Group I		QS
15.1	Potato-, cereal-, flour- or starch-based snacks	Group I		QS
15.2	Processed nuts	Group I		QS
16	Desserts excluding products covered in 1, 3 and 4	Group I		QS
17.1[(e)]	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	Group I		QS
17.2[(e)]	Food supplements supplied in a liquid form	Group I		QS
17.3[(e)]	Food supplements supplied in a syrup-type or chewable form	Group I		QS
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	Group I		QS

MPL, maximum permitted level.
(a): If more than one of the substances E 322, E 471, E 472c and E 473 are added to a foodstuff, the maximum level established for that foodstuff for each of those substances is lowered with that relative part as is present of the other substances together in that foodstuff.
(b): The additives of categories 13.1.1 and 13.1.2 are applicable.
(c): The additive of categories 13.1.2 is applicable.
(d): The additive of category 13.1.3 is applicable.
(e): Food Classification System (FCS) 17 refers to food supplements as defined in Directive 2002/46/EC of the European Parliament and of the Council excluding food supplements for infants and young children.

According to Annex III, parts 1, 2, 3, 4 and part 5, section A of Regulation (EC) No 1333/2008, lecithins (E 322) is also authorised as a carrier in food additives such as colours, fat-soluble antioxidants and glazing agents for fruit at QS, as a food additive other than carriers in food additives in all food additive preparations at QS, and as a food additive including carrier for all food enzymes, all food flavourings and all nutrients, except nutrient intended to be used in foodstuffs for infants and young children at QS.

In addition, according to Annex III, part 5, section B of Regulation (EC) No 1333/2008, lecithins (E 322) can be added in all nutrients intended to be used in foodstuff for infants and young children listed in point 13.1 of Annex II to Regulation (EC) No 1333/2008 (Table 4) for uses in nutrient preparations under the condition that the maximum level in foods mentioned in point 13.1 of Part E of Annex II is not exceeded.

3.3. Exposure data

3.3.1. Reported use levels on lecithins (E 322)

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 for performing a more realistic exposure assessment, especially for those food additives for which no MPL is set and which are authorised according to QS.

In the framework of Regulation (EC) No 1333/2008 on food additives and of Commission Regulation (EU) No 257/2010 regarding the re-evaluation of approved food additives, EFSA issued public calls[15,16] for occurrence data (usage level and/or concentration data) on lecithins (E 322). In response to this public call, updated information on the actual use levels of lecithins (E 322) in foods was made available to EFSA by industry. No analytical data on the concentration of lecithins (E 322) in foods were made available by the Member States.

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

Industry provided EFSA with data on use levels (n = 563) of lecithins (E 322) in foods for 33 out of the 79 food categories in which lecithins (E 322) is authorised.

Updated information on the actual use levels of lecithins (E 322) in foods was made available to EFSA by FoodDrinkEurope (FDE, Document provided to EFSA n.20), BABBI Confectionary Industry (Document provided to EFSA n.25), Specialised Nutrition Europe (SNE, Document provided to EFSA n.27), CHEPLAPHARM Arzneimittel GmbH (Document provided to EFSA n.21), Stollwerck (Document provided to EFSA n.22), the International Chewing Gum Association (ICGA, Document provided to EFSA n.24), the Association of the European Self-Medication Industry (AESPG, Document provided to EFSA n.19), Rudolf Wild GmbH & Co. KG (Document provided to EFSA n.26), the European Lecithin Manufacturers Association (ELMA, Document provided to EFSA n.23) and Nathura (Document provided to EFSA n.28).

The Panel noted that data from ELMA (Document provided to EFSA n.23) and Rudolf Wild (Document provided to EFSA n.26), food additive producers, are not representing food industries using lecithins in their food products, although producers that recommended usage levels to users of lecithins which might, ultimately, use different levels. The data provided by these producers were therefore used in the current exposure assessment only for the regulatory scenario to estimate QS levels when no usage data were reported by industries for food categories with QS levels.

Appendix A displays all data on the use levels of lecithins (E 322) in foods as reported by industry (food industry and lecithins producers).

3.3.2. Summarised data extracted from the Mintel Global New Products Database

The Mintel GNPD is an online database that monitors products introductions in consumer packaged goods markets worldwide. It contains information of over 2 million food and beverage products of which more than 900,000 are or have been available in the European food market. Mintel started covering European Union's food markets in 1996, currently having 20 out of its 28 member countries and Norway present in the Mintel GNPD.[17]

For the purpose of this Scientific Opinion, the Mintel GNPD[18] was used for checking the labelling of products containing lecithin (E 322) within the EU food products because the Mintel GNPD shows the compulsory ingredient information presented in the labelling of products.

According to Mintel, lecithins (E 322) is labelled on more than 52,300 products published in the Mintel GNPD database between 2011 and 2016.

Appendix B presents the percentage of the food products labelled with lecithins (E 322) between 2011 and 2016, out of the total number of food products per food subcategory according to the Mintel food classification.

3.3.3. Food consumption data used for exposure assessment

3.3.3.1. EFSA Comprehensive European Food Consumption Database

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

15 Available online: http://www.efsa.europa.eu/en/dataclosed/call/ans091123
16 Available online: http://www.efsa.europa.eu/sites/default/files/consultation/140310.pdf
17 Missing Bulgaria, Cyprus, Estonia, Latvia, Lithuania, Luxembourg, Malta and Slovenia.
18 Mintel Global New Products Database. Available online: http://www.gnpd.com/sinatra/home/. Accessed on 1 November 2016.

Assessment' (EFSA, 2011a). New consumption surveys recently[19] added in the Comprehensive database were also taken into account in this assessment.[10]

The food consumption data gathered by EFSA 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 for exposure calculations, uncertainties could be introduced owing to possible subjects' under-reporting and/or misreporting of the consumption amounts. Nevertheless, the EFSA Comprehensive Database represents the best available source of food consumption data across Europe at present.

Food consumption data from the following population groups: infants, toddlers, children, adolescents, adults and the elderly were used for the exposure assessment. For the present assessment, food consumption data were available from 33 different dietary surveys carried out in 19 European countries (Table 7).

Consumption records were codified according to the FoodEx classification system (EFSA, 2011b).

Table 7: Population groups considered for the exposure estimates of lecithins (E 322)

Population	Age range	Countries with food consumption surveys covering more than 1 day
Infants	From 12 weeks on up to and including 11 months of age	Bulgaria, Denmark, Finland, Germany, Italy, UK
Toddlers	From 12 months up to and including 35 months of age	Belgium, Bulgaria, Denmark, Finland, Germany, Italy, Netherlands, Spain, UK
Children[(a)]	From 36 months up to and including 9 years of age	Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Latvia, Netherlands, Spain, Sweden, UK
Adolescents	From 10 years up to and including 17 years of age	Austria, Belgium, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Italy, Latvia, Spain, Sweden, UK
Adults	From 18 years up to and including 64 years of age	Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Netherlands, Romania, Spain, Sweden, UK
The elderly[(a)]	From 65 years of age and older	Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Romania, Sweden, UK

(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, 2011a).

Nomenclature from the FoodEx classification system has been linked to the Food Classification System (FCS) as presented in Annex II of Regulation (EC) No 1333/2008, part D, to perform exposure estimates. In practice, FoodEx food codes were matched to the FCS food categories.

3.3.3.2. Food categories selected for the exposure assessment of lecithins (E 322)

The food categories in which the use of lecithins (E 322) 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 could therefore not be taken into account in the present estimate. This may have resulted in an underestimation of the exposure. This was the case for six categories (Appendix C). The food categories which were not taken into account are described below (in ascending order of the FCS codes):

- 02.3 Vegetable oil pan spray;
- 06.6 Batters;
- 06.7 Pre-cooked or processed cereals;
- 08.3.3 Casings and coatings and decorations for meat;
- 12.1.2 Salt substitutes;
- 14.1.3 Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products, only vegetable nectars.

[19] Available online: http://www.efsa.europa.eu/en/press/news/150428.htm

For the following food categories, the differences between subgroups could not be taken into account, and therefore the whole category was considered in the exposure assessment:

- 08.3 Processed meat
  - 08.3.1 Non-heat treated processed meat;
  - 08.3.2 Heat-treated processed meat.
- 17.1/17.2/17.3 Food supplements, in solid, liquid, syrup-type or chewable form. According to Regulation (EC) No 1333/2008, the food supplement category (FC 17) excludes 'food supplements for infants and young children'. However, in the EFSA Comprehensive database, food supplements are consumed by infants and young children with no information provided on the food supplement type. In the exposure assessment, it was therefore assumed that the food supplements consumed in these population groups were the same as those consumed in the older population groups for which concentration data were supplied, resulting in an overestimation of the exposure to lecithins (E 322) in these two population groups.

For the refined scenario, six additional food categories were not taken into account in the exposure assessment because no concentration data were provided to EFSA (Appendix C). For the remaining food categories, the refinements considering the restrictions/exceptions as set in Annex II to Regulation No 1333/2008 were applied.

Overall, for the maximum level exposure scenario, 35 food categories were included, whereas, for the refined scenarios, 29 food categories were included in the present exposure assessment (Appendix C).

3.4. Exposure estimate

3.4.1. Exposure to lecithins (E 322) from its use as a food additive

The Panel estimated chronic exposure for the following population groups: infants, toddlers, children, adolescents, adults and the elderly. Dietary exposure to lecithins (E 322) was calculated by multiplying lecithins (E 322) concentrations for each food category (Appendix C) by their respective consumption amount per kg 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. Dietary surveys with only 1 day per subject were excluded because they are considered as not adequate to assess repeated exposure.

This was carried out for all individuals per survey and per population group, resulting in distributions of individual exposure per survey and population group (Table 7). On the basis of these distributions, the mean and 95th percentile of exposure were calculated per survey and per population group. The 95th percentile of exposure was only calculated for those population groups where the sample size was sufficiently large to allow this calculation (EFSA, 2011a). Therefore, in the present assessment, The 95th percentile of exposure for infants from Italy and for toddlers from Belgium, Italy and Spain were not included.

Two exposure scenarios were defined and carried out by the ANS Panel regarding the concentration data of lecithins (E 322) used: (1) maximum levels of data provided to EFSA (defined as *the maximum level exposure assessment scenario*) and (2) the reported use levels (defined as the *refined exposure assessment scenario*). These two scenarios are discussed in detail below.

Because lecithins (E 322) is also authorised in food categories 13.1.5.1 and 13.1.5.2, a refined estimated exposure assessment scenario taking into account these two food categories was performed to estimate the exposure of infants and toddlers who may eat and drink these foods for special medical purposes (FSMP).

Considering that these specific foods are not reported in the EFSA Comprehensive data set, but that foods for infants and young children in good health are, the Panel assumed that the consumption patterns of infants and toddlers who need to eat the FSMP are the same as the ones of infants and toddlers from the general population. Thus, the consumption of FSMP under the food category 13.1.5 was assumed to be the same amount as the formulae and food products of food categories 13.1.1, 13.1.2, 13.1.3 and 13.1.4., e.g. the consumption of 'specific' infant formulae was assumed to be the same amount than the infant formulae of the FC 13.1.1.

Concerning the uses of lecithins (E 322) as carriers, there might be food categories where lecithins (E 322) is used according to annex III and not to annex II. These food categories can only be addressed by analytical data or limits set in the Regulation (EC) No 1333/2008 that were not available to the Panel. Therefore, a possible additional exposure from the use of lecithins (E 322) as a food additive in Annex III to Regulation (EC) No 1333/2008 was not considered in any of the exposure assessment scenario.

3.4.1.1. 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 6. Because lecithins (E 322) is authorised according to QS in almost all food categories, a 'maximum level exposure assessment' scenario was estimated based on the maximum reported use levels provided by industry, as described in the EFSA Conceptual framework (EFSA ANS Panel, 2014). The maximum levels used in this exposure scenario are listed in Appendix C.

The Panel considers the exposure estimates derived following this scenario as the most conservative because it is assumed that the population group will be exposed to lecithins (E 322) present in food at the MPL use levels over a longer period of time.

3.4.1.2. Refined exposure assessment scenario

In this opinion, the refined exposure assessment scenario is based on use levels reported by industry. This exposure scenario can consider only food categories for which the above data were available to the Panel.

Appendix C summarises the concentration levels of lecithins (E 322) used in the refined exposure assessment scenario. Based on the available data set, the Panel calculated two refined exposure estimates based on different model populations:

- The brand-loyal consumer scenario: It was assumed that a consumer is exposed long-term to lecithins (E 322) present at the maximum reported use level for one food category. This exposure estimate is calculated as follows:
  - Combining food consumption with the maximum of the reported use levels for the main contributing food category at the individual level.
  - Using the mean of the typical reported use levels for the remaining food categories.
- The non-brand-loyal consumer scenario: It was assumed that a consumer is exposed long-term to lecithins (E 322) present at the mean reported use in food. This exposure estimate is calculated using the mean of the typical reported use levels for all food categories.

In addition to these, as mentioned before, for the scenario taking into account the FSMP, considering that it is very specific diet, it is assumed that consumers are brand-loyal and only the results of the brand-loyal scenario are presented.

3.4.1.3. Dietary exposure to lecithins (E 322)

Table 8 summarises the estimated exposure to lecithins (E 322) from their use as food additives in six population groups (Table 7) according to the different exposure scenarios. Detailed results per population group and survey are presented in Appendix D.

Table 8: Summary of dietary exposure to lecithins (E 322) from their use as food additives in the maximum level exposure assessment scenario and in the refined exposure scenarios, in six population groups (minimum–maximum across the dietary surveys in mg/kg bw per day)

	Infants (12 weeks–11 months)	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						
Mean	50–178	69–365	71–314	32–177	70–118	72–116
95th percentile	109–368	130–520	119–576	59–324	134–237	132–199
Refined estimated exposure assessment scenario						
Brand-loyal scenario						
Mean	18–56	16–78	16–82	7–45	9–34	11–30
95th percentile	49–163	39–175	31–187	15–108	20–84	21–74

	Infants (12 weeks–11 months)	Toddlers (12–35 months)	Children (3–9 years)	Adolescents (10–17 years)	Adults (18–64 years)	The elderly (≥ 65 years)
Non-brand-loyal scenario						
Mean	15–21	11–22	7–21	4–12	3–9	3–8
95th percentile	39–62	23–41	14–39	8–27	6–19	6–16

Considering the general population, from the *regulatory maximum level exposure assessment scenario*, mean exposure to lecithins (E 322) from its use as a food additive ranged from 32 mg/kg bw per day in adolescents to 365 mg/kg bw per day in toddlers. The 95th percentile of exposure to lecithins (E 322) ranged from 59 mg/kg bw per day in adolescents to 576 mg/kg bw per day in children. From the *refined estimated exposure scenario* considering concentration levels not exceeding the MPLs for food categories listed under Annex II to Regulation No 1333/2008, in the *brand-loyal scenario*, mean exposure to lecithins (E 322) from its use as a food additive ranged from 7 mg/kg bw per day in adolescents to 82 mg/kg bw per day in children. The 95th percentile exposure to lecithins (E 322) ranged from 15 mg/kg bw per day in the adolescents to 187 mg/kg bw per day in children. In the *non-brand-loyal scenario*, mean exposure to lecithins (E 322) from its use as a food additive ranged from 3 mg/kg bw per day in adults/elderly to 22 mg/kg bw per day in toddlers. The 95th percentile of exposure to lecithins (E 322) ranged from 6 mg/kg bw per day in the adults/elderly to 62 mg/kg bw per day in infants.

From the refined estimated exposure scenario taking into account the foods for special medical purposes, in the *brand-loyal scenario*, mean exposure to lecithins (E 322) from its use as a food additive ranged from 24 mg/kg bw per day in toddlers to 85 mg/kg bw per day in infants. The 95th percentile of exposure to lecithins (E 322) ranged from 66 mg/kg bw per day to 232 mg/kg bw per day in toddlers (not presented in Table 8).

3.4.1.4. Main food categories contributing to exposure for the general population (i.e. not taking into account FCS 13.1.5)

Main food categories contributing to exposure to lecithins (E 322) using the maximum level exposure assessment scenario and the refined exposure assessment scenario (Tables 9–11)

Table 9: Main food categories contributing to exposure to lecithins (E 322) using maximum usage levels (> 5% to the total mean exposure) and number of surveys in which each food is contributing

FCS category number	FCS food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys)[(a)]					
01.5	Dehydrated milk as defined by Directive 2001/114/EC	6.5 (1)	–	28.7 (1)	–	–	–
01.6	Cream and cream powder	8.8 (1)	8.7 (1)	9.5 (1)	6.1 (1)	5.8 (1)	–
01.7.1	Unripened cheese excluding products falling in category 16	21.4 (1)	7.5–12.6 (2)	–	–	7.2 (1)	–
01.8	Dairy analogues, including beverage whiteners	10.3 (1)	7.6 (1)	–	–	–	–
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	–	–	6.3–10.8 (3)	7–11.3 (2)	7.2–20.6 (3)	12.5–17.4 (2)
02.2.2	Other fat and oil emulsions mainly of type water-in-oil	5.5–23.5 (2)	9.5–19.4 (2)	13.5 (1)	14.3 (1)	–	5.3 (1)
03	Edible ices	–	–	8.6 (1)	–	–	–

FCS category number	FCS food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys)[(a)]					
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC	5.6 (1)	6.3–10.6 (2)	5.2–14.6 (9)	5.1–17.8 (7)	5.3 (1)	–
05.2	Other confectionery including breath refreshening microsweets	–	–	–	7 (1)	–	–
06.3	Breakfast cereals	6 (1)	10.3 (1)	–	–	–	6.2 (1)
07.1	Bread and rolls	24.8–66.5 (4)	34.4–74.4 (9)	26.1–71.5 (17)	37.1–70.3 (16)	36.7–72.8 (17)	34.6–75.6 (14)
07.2	Fine bakery wares	9.6–24.7 (3)	5.7–34.2 (10)	14.6–38.8 (16)	13.7–35.8 (15)	5.3–28.6 (16)	6.5–36.4 (13)
08.3	Processed meat	7.9 (1)	5–11.1 (5)	5.6–12.6 (6)	5.5–11.8 (8)	5.2–7.6 (8)	5.4–6.5 (4)
12.5	Soups and broths	29.7 (1)	13.8 (1)	11.4–19.3 (2)	5.6–15.4 (3)	5.1–16.3 (7)	6.6–18.6 (7)
12.6	Sauces	–	–	5.2 (1)	5.2–5.8 (3)	5.5–5.6 (3)	5.4 (1)
13.1.1	Foods for infants and young children	12.4–56.6 (6)	5.8–15 (4)	–	–	–	–
13.3	Dietary foods for weight control diets	–	–	–	–	9.8 (1)	–
16	Desserts excluding products covered in categories 1, 3 and 4	–	5.2–7.6 (3)	5.2–6.2 (3)	–	–	–

FCS: Food Classification System.
(a): The total number of surveys may be greater than the total number of countries as listed in Table 7 because some countries submitted more than one survey for a specific population.

Table 10: Main food categories contributing to exposure lecithins (E 322) using the brand-loyal refined exposure scenario (> 5% to the total mean exposure) and number of surveys in which each food category is contributing

Food Classification System (FCS) category number	FCS food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys)[(a)]					
01.8	Dairy analogues, including beverage whiteners	–	5.4 (1)	–	–	–	–
02.2.2	Other fat and oil emulsions mainly of type water-in-oil	–	–	17 (1)	17.1 (1)	–	–
03	Edible ices	–	5.8 (1)	30.4 (1)	11 (1)	–	–
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC	–	6.1–12.1 (3)	5.7–21.9 (9)	5.3–25.4 (8)	8.4 (1)	–
05.2	Other confectionery including breath refreshening microsweets	–	–	8.2 (1)	16.5 (1)	–	–
05.3	Chewing gum	–	–	–	10.6 (1)	–	–
07.1	Bread and rolls	6.2–36.3 (4)	7.5–74.8 (9)	6.5–70.9 (15)	6–67.3 (16)	7–71.9 (17)	6–75.4 (14)
07.2	Fine bakery wares	20.2–37.4 (3)	8.2–80.7 (10)	7.5–90.2 (17)	7.4–83.5 (16)	9.8–74.3 (17)	13.2–78.1 (14)
12.5	Soups and broths	15.9 (1)	–	6.9 (1)	6.3 (1)	6.1–8 (2)	6.6–11.6 (2)
12.6	Sauces	–	5.1 (1)	5.3–10.7 (2)	8.8–10.4 (3)	5.2–10.5 (6)	5.6–6.3 (2)
13.1	Foods for infants and young children	50.6–93.9 (6)	8.3–65.8 (3)	–	–	–	–

Food Classification System (FCS) category number	FCS food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys)[(a)]					
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual	–	–	–	7.2 (1)	6.5–28.8 (5)	16 (1)
14.1.5.2	Coffee, tea, herbal and fruit infusions, chicory; tea, herbal and fruit infusions and chicory extracts; tea, plant, fruit and cereal preparations for infusions, as well as mixes and instant mixes of these products	–	–	–	–	–	5.2–6.6 (2)
16	Desserts excluding products covered in categories 1, 3 and 4	5.3–10.8 (2)	5–20.9 (6)	9–16.1 (3)	5.8 (1)	5.5–7.1 (3)	10.2 (1)

(a): The total number of surveys may be greater than the total number of countries as listed in Table 7 because some countries submitted more than one survey for a specific population.

Table 11: Main food categories contributing to exposure to lecithins (E 322) using the non-brand-loyal refined exposure scenario (> 5% to the total mean exposure) and number of surveys in which each food category is contributing

Food Classification System (FCS) category number	FCS food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys)[(a)]					
01.8	Dairy analogues, including beverage whiteners	–	5.9 (1)	5.7 (1)	–	–	–
02.2.2	Fat and oil emulsions mainly of type water-in-oil	–	5.4–8.1 (3)	5.3–21.8 (6)	5–19.1 (4)	6.1–10.2 (5)	7.9–13.2 (6)
03	Edible ices	–	–	6–13.7 (2)	5.2–6.1 (2)	–	–
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC	5.6 (1)	7.8–27.6 (7)	5.2–35.2 (18)	7.6–35.7 (17)	5.1–23 (16)	5.5–15.8 (7)
05.2	Other confectionery including breath refreshening microsweets	–	–	5.3 (1)	6.6 (1)	–	–
05.3	Chewing gum	–	–	5.6 (1)	11.2 (1)	–	–
07.1	Bread and rolls	6.1–16 (3)	11.5–44.1 (9)	9.1–36.7 (17)	13.2–34.4 (16)	12–51.5 (17)	13.8–50.9 (14)
07.2	Fine bakery wares	7.4–19.4 (3)	10.5–58.5 (9)	8.1–70.8 (17)	6.9–56.6 (16)	10.7–51.9 (17)	13.4–53.1 (14)
12.5	Soups and broths	–	7.6 (1)	5.6–9.1 (2)	7.7 (1)	5.9–9.7 (2)	5.3–10.2 (4)
12.6	Sauces	–	6.1–6.3 (3)	5.2–8.3 (7)	5.9–11.3 (9)	5.2–12 (10)	5–8.4 (8)
13.1	Foods for infants and young children	66.5–95 (6)	5.3–79.8 (7)	–	–	–	–
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	–	–	–	7.4 (1)	6.8–28.2 (5)	16.3 (1)

Food Classification System (FCS) category number	FCS food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys)[(a)]					
14.1.5.2	Coffee, tea, herbal and fruit infusions, chicory; tea, herbal and fruit infusions and chicory extracts; tea, plant, fruit and cereal preparations for infusions, as well as mixes and instant mixes of these products	9 (1)	5.3–10.3 (2)	6.7–8.4 (2)	5.9–8.9 (3)	5.2–13.3 (6)	6.5–22.5 (7)
16	Desserts excluding products covered in categories 1, 3 and 4	–	5.5–7.6 (2)	5.4–5.9 (2)	–	–	–

(a): The total number of surveys may be greater than the total number of countries as listed in Table 7 because some countries submitted more than one survey for a specific population.

3.4.1.5. Uncertainty analysis

Uncertainties in the exposure assessment of lecithins (E 322) have been discussed above. In accordance with the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2007), the following sources of uncertainties have been considered and summarised in Table 12.

Table 12: Qualitative evaluation of influence of uncertainties on the dietary exposure estimate

Sources of uncertainties	Direction[(a)]
Consumption data: different methodologies/representativeness/under-reporting/misreporting/no portion size standard	+/–
Use of data from food consumption survey of a few days to estimate long-term (chronic) exposure for high percentiles (95th percentile)	+
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 due to missing FoodEx linkage (n = 6 out of 79 food categories)	–
Food categories included in the exposure assessment: data not available for certain food categories which were excluded from the exposure estimates (n = 48 only for the refined scenarios out of 79 food categories)	–
Concentration data: • levels considered applicable for all items within the entire food category	 +
Maximum level exposure assessment scenario: • food categories which may contain lecithins (E 322) due to carry-over not considered • food categories authorised at MPL according to Annex II to Regulation (EC) No 1333/2008	 – +
Refined exposure assessment scenarios: • food categories which may contain lecithins (E 322) due to carry-over not considered • exposure calculations based on the maximum or mean levels (reported use from industries)	 – +/–
Uncertainty in possible national differences in use levels of food categories	+/–

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

Overall, the Panel considered that the uncertainties identified would, in general, result in an overestimation of the exposure to lecithins (E 322) as a food additive in European countries for the maximum level exposure scenario and for the refined scenario, if it is considered that the food additive may not be used in food categories for which no usage data have been provided, and considering that usage of lecithins (E 322) according to Annex III to Regulation No 1333/2008 was not taken into account.

Lecithins (E 322) is authorised as a Group I food additive in 79 food categories (Table 2). EFSA was provided with reported use levels for only 33 food categories out of the 79 in which it is authorised. The Panel calculated that, out of the foods authorised to contain lecithins (E 322) according to Annex II to Regulation (EC) No 1333/2008, 33–95% of the amount of food consumed (by weight) per population group was reported to potentially contain lecithins as a food additive. Based on this, the Panel noted that the information from the Mintel GNPD supported the observation that, due to its Group I authorisation, lecithins may not be used in all food categories in which it is authorised. Furthermore, the Panel noted that information from the Mintel's GNPD (Appendix B) indicated that approximately 65% of the food products in which lecithins (E 322) was labelled, were included in the current exposure estimates.

3.4.2. Exposure via the regular diet

According to JECFA (WHO, 1974), the average diet provides a daily intake of several grams of lecithin (approximately 1–5 g corresponding to 14–71 mg/kg bw for a 70-kg adult population).

In the human diet, according to Zeisel (1981), most choline is consumed in the form of lecithin which is highly present in common consumed foods such as liver (850 mg per 100 g), eggs (394 mg per 100 g), soya beans (1,480 mg per 100 g), peanuts (1,113 mg per 100 g) and wheat germ (2,820 mg per 100 g).

In a recent opinion, the EFSA NDA Panel (NDA, April 2016) provided dietary intakes estimates of total choline from the regular diet of the European population group. The choline content of exhaustive food products was calculated as the sum of free choline and choline derived from the choline products from glycerolphosphatocholine, phosphocholine, phosphatidylcholine and sphingomyelin. Phospholipid lecithin (phosphatidylcholine) is known as being the ultimate source of most dietary choline (Zeisel, 1981).

Nutrient intake calculations were performed only on subjects with at least two reporting days. Choline intake from dietary supplements was not assessed. Total choline intake mean estimates ranged from 75 to 127 mg/day in infants < 1 years old (corresponding to 9–16 mg/kg bw per day using the EFSA default body weight), 151 to 210 mg/day in children aged from 1 to < 3 years (corresponding to 13–18 mg/kg bw per day), 177–304 mg/day in children aged from 3 to < 10 years (corresponding to 8–13 mg/kg bw per day) and 244–373 mg/day in children aged from 10 to < 18 years (corresponding to 4–6 mg/kg bw per day). Total choline intake mean estimates ranged from 269 to 468 mg/day in adults aged from 18 to ≥ 75 years (corresponding to 4–7 mg/kg bw per day).

Overall, the Panel considered that dietary intakes of total choline from regular diet could be estimated in average ranging from 4 to 18 mg/kg bw per day across all population age groups.

Moreover, the Panel noted that mean dietary intakes of lecithins from the regular diet are in the range of the mean estimated exposure from the use of the food additive itself (Table 8, non-brand loyal consumer scenario).

3.4.3. Exposure via other sources

Exposure to lecithins due to the following uses was not considered in this opinion.

Lecithins as an ingredient in food supplements and other foods

Lecithin is an ingredient of preparations promoted as tonics and dietary supplements in a wide range of disorders (Radimer et al., 2000; Martindale, 2014). Lecithins are purported to increase brain function, promote energy or prevent arteriosclerosis or cardiovascular disease (Radimer et al., 2000).

Pharmaceutical uses

Lecithins are used in pharmaceutical products as an active ingredient, as well as an excipient (Documentation provided to EFSA n.17).

The average single dosage of lecithins as an active ingredient for adolescents and adults in mono or combination products can be approximately up to 2,000 mg, whereas the average daily dosage might be up to 6,000 mg/day.[20] According to the draft monograph of the HMPC of the EMA, a traditional medicinal usage of soya bean lecithin can result in daily dosages in the range of 1,500–8,100 mg (divided into two or three intakes) (HMPC, 2016b; draft).

According to the EMA, lecithins are used as active ingredients which do not fulfil the criteria of traditional use in daily dosages up to 9,000 mg daily in several Member States of the EU (HMPC, 2016a; draft).

In many national and European authorised products, lecithins are used as an excipient in medicinal products for oral use for adolescents and adults starting from trace amounts up to approximately 30 mg as daily dosage/person.

3.5. Biological and toxicological data

Lecithins are natural constituents of all cells in the human body. Synthesis of phosphatides and the pathway of catabolism of lecithins in humans are well known. Hydrolysed lecithins are produced in the gut as a result of normal digestion of food.

The Panel noted that one of its metabolites, choline, is a precursor of the neurotransmitter acetylcholine. Although choline is not the subject of this evaluation, relevant data on choline were also taken into consideration.

Furthermore, for the toxicological evaluation, the Panel used available data on lecithins as a mixture of different phosphatides and, when available, purified phospholipids, such as phosphatidyl choline and phosphatidyl inositol.

3.5.1. Absorption, distribution, metabolism and excretion

3.5.1.1. Lecithins

In vivo studies

Several *in vivo* studies using radiolabelled lecithins were available in animals and humans.

Animal studies

Rats and monkeys were orally administered with radiolabelled soya phosphatidylcholine (1,2-diacylglycero-3-phosphorylcholine labelled with ^{3}H in the fatty acid moiety or with ^{14}C in the choline moiety) (Documents provided to EFSA n.4 and 5). Rats (four of each sex) and rhesus monkeys (three of each sex) received 250 mg ^{3}H- or ^{14}C-phosphatidylcholine/kg bw as a single dose or as a daily dose for five consecutive days. In these animals, tritium exchange with body water occurred extensively *in vivo* and a part of the ^{3}H radioactivity detected represented $^{3}H_2O$. The tissue distribution was investigated in rats; liver contained the higher amounts of radioactivity, although significant radioactivity was detectable after 6 h in striated muscle, depot fat and the kidneys. After repeated dosing over 5 days, there was a comparable organ distribution with additional small amounts of radioactivity in the lungs, testes, intestines, skin, thymus and thyroid gland. For both rats and monkeys receiving a single oral dose, the faecal excretion of ^{14}C radioactivity within 5 days corresponded to 3–7.4% of the dose, whereas, in rats, 30–47% of a single oral dose was exhaled as $^{14}CO_2$. The urinary excretion of ^{14}C radioactivity within 5 days amounted to 2.9–5.3% and 17–21% of the dose in rats and monkeys, respectively.

Le Kim and Betzing (1976) investigated the fate of polyunsaturated phosphatidylcholine in rats given 1,2-di-[9,10,12,13-$^{3}H_4$]linoleoyl-*sn*-glycero-3-phospho-[N-$^{14}CH_3$]-choline, 1-[1-^{14}C]linoleoyl-2-[9,10,12,13-$^{3}H_4$]-linoleoyl- or 1-[9,10,12,13-$^{3}H_4$]linoleoyl-2-[1-^{14}C]linoleoyl-*sn*-glycero-3-phosphocholine. Wistar rats (four males and four females) were given a single oral dose of 70 mg/kg bw of each radiolabelled substance and were kept in metabolic cages. The absorption rate of radioactivity from the gastrointestinal tract was rapid and 85% of the doses was absorbed within the first 8 h. One half of the orally administered polyunsaturated phosphatidylcholine was hydrolysed to 1-acyl-lysophosphatidylcholine and reacylated to phosphatidylcholine upon entering the mucosa cell. The other half was completely hydrolysed to free fatty acids and glycerophosphocholine. There was a relatively slow rate of degradation of the fatty acid in the 1-position, in contrast to the fatty acid esterified to the 2-position of phosphatidylcholine. In anaesthetised rats (six males), lymph samples

[20] Available online: http://www.kade.de/fileadmin/assets/beipackzettel/buer-lecithin-plus-vitamine-fluessigkeit-dr-kade.pdf

were collected every 1 h up to 24 h. Some 17–25% of the administered radioactivity appeared in the lymph chylomicrons within 6.5 h. This radioactivity was mainly located in phosphatidylcholine and neutral lipids fractions. From these data, it was considered that 'phosphatidylcholine is hydrolyzed to 1-acyl-lysophosphatidylcholine by pancreatic phospholipase A. This acyl-lyso compound is absorbed in the mucosal cells and is reacylated to form phosphatidylcholine by the lysolecithin acyltransferase. Part of the 1-acyl-lysophosphatidylcholine is further hydrolyzed in the intestinal tract by lysophospholipase to form glycerophosphocholine. The fatty acids are also absorbed and enter the Kennedy pathway to form triglycerides before appearing in the lymph chylomicrons'. Regarding tissue distribution, when ^{14}C radiolabelling was located on choline, the liver contained 30% of the applied ^{14}C-radioactivity and almost 10% of the applied ^{3}H-radioactivity. Minor amounts of radioactivity were distributed in all other organs analysed: lung, spleen, kidney, heart and brain. Blood contained 8% and 4% of ^{14}C-radioactivity and ^{3}H-radioactivity doses, respectively, and elimination half-lives for ^{14}C-radioactivity and ^{3}H-radioactivity were 20 and 30 h, respectively. Six hours after dosing, the respiratory excretions of $^{14}CO_2$ were 1.8%, 7.7% or 25% of the dose when ^{14}C-radioactivity was located in choline, in the 1- or 2-position of the fatty acid, respectively. The Panel noted that urinary and faecal excretions of radioactivity were not determined in this study.

Wistar rats (six males and six females) were given a single oral dose of 70 mg/kg bw radiolabelled phosphatidylcholine (Fox et al., 1979). Dilinoleoylphosphatidylcholine was labelled with ^{14}C in either the 1-position or the 2-position in the acyl moiety, or in the choline moiety. The same phosphatidylcholine was also labelled with ^{3}H in the acyl moiety and with ^{14}C in the choline moiety. Up to 84% of phosphatidylcholine was absorbed from the intestine within 19 h. The rates of absorption were equal for both the fatty acids and choline moieties. A considerable amount of radioactivity was found in the intestinal wall (40% of the dose after 3 h). The highest amounts of ^{3}H and ^{14}C radioactivities were found in the liver (38% of the dose after 6 h). Within 5 days after dosing, most of the radioactivity administered remained in the carcass (^{3}H: 58.8%; ^{14}C: 51.3%) or was expired (^{3}H: 6.6%; ^{14}C: 32%). Only minor amounts were excreted via faeces (^{3}H: 8.2%; ^{14}C: 3.2%) or urine (^{3}H: 15.6%; ^{14}C: 6.4%). In another experiment in dogs, using ^{3}H-^{14}C dilinoleoylphosphatidylcholine, it was shown that intestinal absorption of this compound was similar to that in rats and was not influenced by the vehicle in which phosphatidylcholine was administered (Fox et al., 1979).

Human studies

In humans (one female and four male fasted subjects), the metabolic fate of orally administered lecithins (1 g containing 150 μCi ^{3}H-polyenephosphatidylcholine and 50 μCi di[1′-^{14}C]linoleoyl-3-*sn*-glycerophosphocholine) was studied by Zierenberg and Grundy (1982). More than 90% of both isotopes were absorbed from the intestine. In blood, 70–85% of the ^{3}H-radioactivity was linked to phosphatidylcholine and 70% of the ^{14}C-radioactivity was in non-polar lipids (triglycerides and cholesteryl ester). According to the authors, it can be assumed that most of the phosphatidylcholine was hydrolysed to lysolecithin before absorption. After a lag time of about 2 h, radiolabelled lipids were measured in the blood. An examination of lipoproteins showed that the specific radioactivities of phosphatidylcholine in high-density lipoprotein (HDL) were 2–6 times higher than in apolipoproteina B-containing lipoproteins, and 2–20 times higher than that of red blood cells or total blood. This would indicate that absorbed phosphatidylcholine was incorporated preferentially into the HDL fraction of plasma. Within 7 days, only 2% and 4.5% of ^{3}H and ^{14}C, respectively, was excreted via faeces, whereas 6% and 1.2% of ^{3}H and ^{14}C, respectively, were excreted via urine. The Panel noted that, in this study, the radiolabelling of the only acyl moieties of lecithins did not permit an assessment of the fate of the free hydrolysed choline.

3.5.1.2. Metabolism of lecithins into choline

Among lecithins, phosphatidylcholine is hydrolysed to release choline in the cytidine-5-diphosphate-choline pathway in all cells of the body. Choline can also be synthesised *de novo* by the human body. It is a precursor of the neurotransmitter acetylcholine and it plays an important role in the metabolism and transport of lipids and cholesterol by lipoproteins, and is needed for the assembly and secretion of very low-density lipoproteins by the liver (EFSA NDA Panel, 2016).

The EFSA NDA Panel considered a total choline concentration of 145 mg/L for human milk (EFSA NDA Panel, 2016). According to older literature, human milk is reported to contain 160–210 mg (1.5–2 mmol)/L of total choline, delivered as choline, phosphocholine, glycerophosphocholine, phosphatidylcholine and sphingomyelin (Zeisel et al., 1986; Holmes-McNary et al., 1996).

In humans, dietary lecithins, namely phosphatidylcholines, are known to be hydrolysed by phospholipases to liberate choline. According to data from ELMA (Document provided to EFSA n.18), 1–3.38% of choline could theoretically be released from the food additive lecithins (E 322) (see Table 3). Following intestinal hydrolysis of phosphatidylcholine, choline is rapidly absorbed by a carrier-mediated saturable transport system and appears in plasma predominantly as free choline. Lecithins having escaped hydrolysis enter the lymph incorporated into chylomicrons. This metabolism was reviewed by Zeisel (1981) who reported the dietary sources of choline, as well as its biochemistry, physiology and pharmacology, and it was more recently described by EFSA in the scientific opinion on dietary reference values for choline (EFSA, 2016).

In humans, the relationship between dietary lecithin intake and plasma choline levels has been investigated in several studies.

For instance, Hirsch et al. (1978) determined choline serum levels in nine patients receiving either 3 g of choline chloride or a meal supplemented with an equivalent dose in the form of 100 g of lecithin granules, containing 10–20% lecithin and 80–90% mixed neutral lipids. After the consumption of a single meal containing 3 g of choline chloride, serum choline rose by 86%, attaining peak values after 30 min. When the same subjects ate the meal containing an equivalent amount of choline in the form of lecithin, serum choline levels rose by 33% after 30 min, and continued to rise for at least 12 h, to 265% over control values.

In six male subjects, Zeisel et al. (1980) examined plasma choline changes after ingestion of diets composed of common foodstuffs, with choline contents bracketing the average daily intake in the American diet, and the ingestion of diets supplemented with exogenous purified lecithin. A diet with low choline content did not increase plasma choline concentrations. A diet with high choline content doubled plasma choline levels. A lecithin supplemented (25 g of egg or soya lecithin; 80% phosphatidylcholine) low-choline diet increased plasma choline levels by four-fold at the peak value (6 h post-dosing).

Free choline is also found in maternal milk and its concentration changes during the progress of lactation and is influenced by maternal diet as reported in EFSA (2016).

Fischer et al. (2010) investigated, in pregnant women, the response of maternal plasma and breast milk choline concentrations to a phosphatidylcholine supplement (containing 750 mg choline/day per person, $n = 48$, from the 18 gestational weeks to 90 days post partum), compared to placebo ($n = 46$). The supplement was consumed in addition to a mean dietary choline intake of about 350 mg/day. Breast milk and maternal plasma concentrations were measured at 45 days post partum. There was a significant linear correlation between total choline intake (from foods and supplements; range about 150 to > 750 mg/day) and breast milk concentrations of phosphatidylcholine, phosphocholine, free choline and betaine when all subjects were taken into account. Mean breast milk concentrations of phosphocholine (722 vs 553 μmol/L) and free choline (106 vs 83 μmol/L) were significantly higher in the supplemented group than in the placebo group, whereas phosphatidylcholine was not significantly different. According to the authors, the study physician reported that unusual or unexpected events did not occur more frequently in women receiving the supplement compared to those receiving a placebo or to a normal obstetric population, and as well as in their nursed infants.

High doses of choline have been associated with a fishy body odour. This results from the excretion of excessive amounts of trimethylamine, a choline metabolite, as the result of bacterial action in the digestive system. Lecithin, as a group of choline-containing phospholipids, however, does not present a risk of fishy body odour. This is because the intestinal bacteria in general cannot cleave the esters, and hence do not form major amounts of trimethylamine from choline (Zeisel et al., 1983 cited in IOM 1998).

Conclusions

Overall, studies using radiolabelled phosphatidylcholine in animals and humans clearly indicated that, following oral administration, phosphatidylcholine is absorbed unchanged or as lysophosphatidylcholine or choline after intestinal hydrolysis. In intestinal mucosa cells, lysophosphatidylcholine would be reacylated into phosphatidylcholine or hydrolysed to glycerophosphocholine and free fatty acids. The fatty acids would be further utilised for the reassembly of triacylglycerides and phosphatidylcholine found in the chylomicrons. In humans, the absorbed phosphatidylcholine would be incorporated preferentially into the HDL fraction of plasma. Peak levels of phosphatidylcholine in blood are reached within 6 h. Besides the intestinal wall, the major target organ for distribution and metabolism of lecithins is the liver. Only minor amounts of radioactivity were excreted via urine and faeces demonstrating that the administered lecithins would undergo metabolism as for endogenous phospholipids. From the current database, the Panel noted that only minor levels of choline labelling radioactivity were detected in the brain.

In humans, dietary lecithins are known to be hydrolysed by phospholipases to liberate choline, which is rapidly absorbed by a carrier-mediated saturable transport system and appears in plasma predominantly as free choline. Consequently, an increased plasma-free choline concentration has been described as a consequence of increased dietary intake of lecithins. Moreover, a significant increase in breast milk concentrations of free choline was observed in lactating women receiving a phosphatidylcholine supplement in comparison with the placebo group.

3.5.2. Acute toxicity

Unpublished studies on acute oral toxicity of lecithins were presented by Cosmetic Ingredient Review (CIR) (2001), although the information on these data was limited.

In several studies, LD_{50} of more than 16,000 mg/kg bw in mice, more than 5,000 mg/kg bw in rats and 4,750 mg/kg bw in rabbits were reported (FDRL, 1973a,b; Leberco-Celsis Testing, 1997; FDRL, 1973c, as cited in CIR, 2001). The Panel noted that, in these studies, the test substance is not always characterised.

There were no deaths or clinical signs observed in male and female rats to which purified phosphatidylinositol from soya lecithin (Asahi Kasei PI) was orally administrated once in single doses up to 2,000 mg/kg bw (Honda et al., 2009).

3.5.3. Short-term and subchronic toxicity

3.5.3.1. Short-term studies

Rats

The SCF (1982) described a subacute toxicity study performed by Unilever (1978) as follows: 'a 3 week feeding study in rats comparing lecithin, hydrolysed lecithin and a control purified diet containing 10% ground nut oil showed no essential difference between lecithin and hydrolysed lecithin with respect to effects on body weight, food intake and growth. Level of 20% or more in the diet produced adverse effects on hematopoiesis and enlargement of the kidneys'.

Dogs

The effect of different batches of EPL (see Section 3.1.1) (without additional information on the composition) was tested by peroral administration to 18 pure-bred Beagle dogs (three animals per group) over a 6-week period (Document provided to EFSA n.11). Six more dogs received the solvent only and served as controls. The dosages used were 50, 250 and 2,500 mg EPL/kg bw per day in 5 mL of 1% aqueous carboxy ethyl cellulose gel by stomach tube. At all three dosages, the only effect observed was on lipid metabolism. After 6 weeks of treatment, the free cholesterol level was significantly lowered in animals receiving 2,500 mg EPL/kg bw per day. Total cholesterol and total lipid levels in serum were slightly lowered, although the values determined still lay within the normal range. Esterified and non-esterified fatty acids and neutral fats in serum were not affected. Behaviour, external appearances, feed and drinking water consumption, faeces, body weight development, haematological and electrocardiographic investigations, urine composition, examinations of the eyes, hearing and dentition, macroscopic inspection and visual comparison of the internal organs in section showed no evidence of adverse effects, even at the highest EPL dosage (2,500 mg/kg bw per day). Apart from the aforementioned influence on fat metabolism, no certain deviations could be seen in the clinical-biochemical parameters. The histopathological investigations also revealed no indication of injury. None of the animals died. According to the authors, the lowest toxic dose may be expected to be $>$ 2,500 mg EPL/kg bw per day. The alterations of lipid metabolism may be due to the pharmacodynamic properties of the preparation (Document provided to EFSA n.11).

3.5.3.2. Subchronic toxicity studies

Rats

A 90-day study has been performed in rats (Weanling SPF rats of the Carworth Farm E strain) with a mixture of ammonium compounds of phosphatidic acids derived from rapeseed oil and a proportion of triglycerides from the partially hardened oil (Gaunt et al., 1967). The soya bean lecithin (no additional information on the composition available) was used for comparison in this study.

Groups of 15 male and 15 female rats were fed diets containing 0.0% (control) or 6.0% soya bean lecithins, equivalent[21] to 4,860 mg/kg bw per day for males and 5,460 mg/kg bw per day for females, respectively. Body weight and food consumption were recorded weekly. Haematological investigations were made during week 6 with blood collected from the tail veins of 10 animals of each sex from the control, 6% test item and 6% lecithin groups, and terminally on all animals using blood collected from the dorsal aorta.

There was slight anaemia in females receiving 6% lecithin for 6 weeks but this effect was absent terminally. The osmotic fragility of the erythrocytes of rats on the 6% lecithin diet was comparable with that of the controls. There was no deviation from normality in respect of the terminal serum chemistry or renal function tests conducted at 6 or 13 weeks. No significant differences of relative organ weight were noted. At necroscopy, no gross changes were seen. The authors concluded that a minimum no-effect level was 6% of soya bean lecithins, equivalent to 4,860 mg/kg bw per day for male and 5,460 mg/kg bw per day for female rats, respectively.

The effect of EPL was tested in Wistar rats (male and female) over a period of 12 weeks using oral administration (Document provided to EFSA n.12). The test material was described as a product with active principle choline phosphoric acid diglyceride ester of natural origin with predominantly unsaturated fatty acids, particularly linolic acid (approximately 70%), linolenic and oleic acid. Four groups of 20 animals (10 males and 10 females) were administrated 0, 150, 750 and 3,750 mg EPL/kg bw per day. Distilled water was used as a solvent, and the solution was administered in a constant volume of 20.0 mL/kg bw per day by gavage. The control animals received the same volume of distilled water. No effect on behaviour, external appearance, body weight and intake of food and drinking water could be observed during the 12-week duration of the study. No changes were observed in the faeces. No modification of haematological and biochemical parameters, or urinanalysis, was noted. Histopathological examination did not detect changes induced by the test item. The authors concluded that the no-effect daily dose is $>$ 3,750 mg/kg bw per day. The Panel considered that, in this study, the no-observed-adverse effect (NOAEL) was 3,750 mg/kg bw per day, which is the highest dose tested.

In a 13-week study in male and female rats, purified phosphatidylinositol from soya lecithin (Asahi Kasei PI) was administered orally at daily doses of 0, 100, 300 and 1,000 mg/kg bw. Neither death nor any substance-related change with regard to body weight, food consumption, ophthalmoscopy, haematology, blood biochemistry, necropsy, organ weights or histopathology were observed in any of the treatment groups. Based on these results, the authors considered the NOAEL to be 1,000 mg phosphatidylinositol/kg bw per day for male and female rats, the highest dose tested (Honda et al., 2009).

Dogs

The effect of EPL by oral administration of 250, 500 and 1,000 mg/kg bw per day (three male and three female animals per group) in a capsule for 5 days/week for 1 year was investigated in beagle dogs (Document provided to EFSA n.15). A group of six dogs was taken as a control. During the whole treatment period, no visible signs of intolerance were detected. There was a slight but not dose-related increase in body weight in the treatment groups. Besides a slight increase (twice) in the amount of total lipids and a significant increase in triglyceride levels in females, no treatment-related differences in haematological, clinical-chemical, electrocardiographical and clinical data and urinanalysis could be detected. During sacrifice at the end of the study, no gross pathological changes were observed. The histopathological investigations of the tissues showed no significant substance-related differences. It was concluded that, under these experimental conditions, the no-effect dose was higher than 1,000 mg/kg bw per day.

3.5.4. Genotoxicity

No genotoxicity studies using lecithin preparations meeting the EU specifications for the food additive E 322 were available to the Panel. However, a number of *in vitro* and *in vivo* studies were available with a multivitamin preparation containing lecithins.

3.5.4.1. *In vitro*

Lecithin (no additional information on the composition available) was tested in an Ames test with *Salmonella* Typhimurium tester strains TA1535, TA1537 and TA1538 performed both in the absence

[21] EFSA guidance on selected default values. EFSA Journal 2012;10(3):2579, 32 pp.

and presence of S9 metabolic activation prepared from liver, lung and testis of rat, mouse and monkey (*Macaca mulatta*). A concentration of 0.02% was used in the plate test and concentrations of 0.01%, 0.02% and 0.04% were employed in the suspension test. The survival rate at the highest concentrations employed was 50% both in the plate and in suspension tests. No mutagenicity was observed. The Panel noted that the study is limited mainly for the incomplete set of the *S. typhimurium* tester strains employed (Litton Bionetics Inc., 1975).

In an unpublished report (Document provided to EFSA n.10), a multivitamin preparation (ESSENTIALE 303™) containing lecithin (50 mg/mL) was assessed. Lecithin was described as polyunsaturated phosphatidylcholine containing 60% unsaturated fatty acids (linoleic acid 80%, linolenic acid 5% and oleic acid 15%). This preparation was assessed for its mutagenicity in the reverse mutation assay using *S. typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 and in the forward mutation assay in *Schizosaccharomyces pombe* (strain P1), both in the absence and presence of rat liver S9 metabolism at concentrations of 200, 100, 50 and 25 μL/plate. No mutagenic activity was observed in any of the strains employed.

Another Ames test with *S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100 tester strains was performed both in the absence and presence of rat liver S9 metabolic activation. The test compound was added at 0.1, 1.0, 10.0 and 500.0 μg/plate as mixed micelles containing 169.3 mg/mL lecithins artificially decomposed by exposure to temperature of 80°C for 250 h (resulting in the decomposition of about 25% lecithins into fatty acids and lysolecithins). No indication of genotoxic activity was observed (Teelmann et al., 1984).

The preparation ESSENTIALE 303™ was also tested for induction of gene conversion in yeasts, both in the absence and presence of metabolic activation in two independent studies. In the first study, *Saccharomyces cerevisiae* (strain D4) was treated with lecithin at concentrations of 1.875%, 3.750% and 7.5% in dimethyl sulfoxide. The survival rate at the highest concentrations employed was 50% and no indication of genotoxic activity was observed (Litton Bionetics Inc., 1975). In the second study, the lecithin preparation (250 mg/5 mL polyunsaturated phosphatidylcholine containing 150 mg/5 mL unsaturated fatty acids) was employed for treatment at 200, 100, 50 and 25 μL for 2 h in *S. cerevisiae* (strain D4 and D7). The survival rate exceeded the value of 80% compared to the untreated control in both strains and at all concentrations assayed. No indication of genotoxicity was observed (Document provided to EFSA n.10).

In a study by Honda et al. (2009) purified phosphatidylinositol from soya lecithin (Asahi Kasei PI) was tested in an Ames test with *S. typhimurium* tester strains TA1535, TA1537, TA1538, TA100 and *Escherichia coli* WP2 uvrA, performed both in the absence and presence of S9 metabolic activation prepared from liver of rats pretreated with phenobarbital and 5,6-benzoflavone. A concentration in the range 315–5,000 μg/plate was employed in two experiments using the preincubation method and no increases in the number of revertant colonies were observed. The Panel noted that the study was performed according to the relevant OECD Guideline no. 471 adopted on 21 July 1997.

In an unscheduled DNA synthesis (UDS) assay in human embryonic epithelium (EUE) cells, the preparation ESSENTIALE 303™ was employed for treatment at 1×10^{-8}%, 1×10^{-6}%, 1×10^{-4}% and 1×10^{-2}%, for 1 h both in the absence and presence of S9 metabolic activation. At the end of the treatment, cultures were washed and ^{3}H-thymidine at 5 μCi/mL was added for 4 h to detect DNA repair events by the autoradiographic method. The results obtained did not indicate any induction of UDS (Document provided to EFSA n.10).

A purified phosphatidylinositol from soya lecithin (Asahi Kasei PI) was also tested for the induction of chromosomal aberration in a Chinese hamster lung fibroblast cell line, both in the absence and presence of S9 metabolic activation prepared from liver of rats pretreated with phenobarbital and 5,6-benzoflavone (Honda et al., 2009). The concentrations used, selected from preliminary dose-range finding experiments, were 1,250, 2,500 and 5,000 μg/mL. The highest dose-level selected, which is 2.5-fold higher than the recommended dose of 2,000 μg/mL in the current OECD Guideline no. 473, did not induce any cytotoxicity or reduction in cell growth. Cells were treated for 6 h both in the presence and absence of S9 metabolic activation with sampling at 24 h from the beginning of treatment in the short-term treatment time and for 24 and 48 h in the long-term treatment time. The results obtained indicated that the incidence of both structural and numerical (polyploidy) chromosomal aberration was similar to the untreated control. The Panel noted that the study was performed essentially in agreement with the current OECD Guideline no. 473.

3.5.4.2. *In vivo*

Groups of five male Swiss CD-1 mice were injected once, intraperitoneally, with 0.1, 1.0 and 2.0 mL/kg bw of the preparation ESSENTIALE 303™, and then kept in metabolic cages, and urine was collected for the following 24 h and filter sterilised. Volumes of 0.2 mL of urine, in the absence and presence of glucuronidase at 1,000 U/mL, were added to cultures of *S. cerevisiae* (strain D7) for induction of gene conversion. The survival rate exceeded the value of 80% compared to the untreated control at all concentrations assayed and no mutagenic activity was detected (Document provided to EFSA n.10).

In a host-mediated assay, groups of five male Swiss CD-1 mice were injected once, subcutaneously, with 0.1, 1.0 and 2.0 mL/kg bw of the preparation ESSENTIALE 303™ for 3 h. Immediately after treatment, 1 mL of a suspension containing about 2×10^9 cells of *S. cerevisiae* (strain D7) was injected into the peritoneum of each mouse. Three hours after the injection of the yeast, the mice were sacrificed and the yeast cells were aseptically washed out of the peritoneum of each animal and suspended in phosphate buffer at pH 7.1. Yeast cells were then plated under standard conditions to detect gene conversion. The survival rate exceeded the value of 85% compared to the untreated control at all concentrations assayed and no mutagenic activity was detected (Document provided to EFSA n.10).

In conclusion, no genotoxicity was observed in different *in vitro* assays with lecithins, which include the bacterial reverse mutation assay (Ames test), test for induction of gene conversion in *S. cerevisiae* (strains D4 and D7), an UDS assay in the human EUE cells *in vitro*, as well as in *in vivo* host-mediated and urinary assays. The Panel noted that investigations of structural and numerical aberrations that are two out of the three endpoints required for the assessment on the genotoxicity (EFSA Scientific Committee Guidance document, 2011) were only available for the purified phosphatidylinositol. However, the Panel considered that read-across from phosphatidylinositol to the other phospholipid components of lecithins was justified. Moreover, the substances known to induce structural chromosomal aberrations frequently also induce UDS and the Panel noted that the available UDS assay was negative. Overall, based on the data available, the Panel concluded that there is no concern with respect to the genotoxicity of lecithins.

3.5.5. Chronic toxicity and carcinogenicity

Mice

A study performed by Szepsenwol (1969) focussing on the development of brain nerve cell tumours in TM strain mice was regarded by the Panel as invalid due to several deficiencies (no complete histopathology performed, unknown mouse strain, no exact specification of the tumour type).

Rats

The effect of orally administered EPL (see Section 3.1.1) was tested in 25 female and male Wistar rats (25 of each sex per group) during 24 weeks (Document provided to EFSA n.13). The dosages were 0, 150, 750 and 3,750 mg EPL/kg bw per day. EPL was diluted in distilled water and the solution was administered in a constant volume of 20 mL/kg bw by gavage. The control animals received the same volume of the solvent. No influence on behaviour, external appearance, body weight, and food and water intake was observed during the test. Faeces did not show changes. There were no substance-related mortalities. The EPL administration did not affect the haematological, clinical-chemical and urinary parameters, nor the relative organ weights. Haemoglobin in the faeces was not detected during the 24-week test. No influence on hearing, growth of teeth and the visual system was observed. Macroscopic changes detected during necropsy were incidental findings and not substance-related. It was concluded that the NOAEL of this study is 3,750 mg EPL/kg bw per day.

The effect of EPL (see Section 3.1.1) was tested in Wistar rats (male and female) over a period of 48 weeks, using oral administration (Document provided to EFSA n.7). Four groups of 25 (male and female) were treated with 0, 150, 750 and 3,750 mg EPL/kg bw per day. Distilled water was used as a solvent, and the solution was administered in a constant volume of 20.0 mL/kg bw per day to the rats by gavage. The control animals received the same volume of distilled water. No influence on the behaviour, external appearance, body weight and the intake of food and drinking water could be observed during the 48-week duration of the test. No changes were observed in the faeces. In total, seven rats died during the study (three control animals, two animals from group I and one animal each from groups II and III), whereby the death of all animals is independent of the administration of the preparation. An influence resulting from the administration of the substance on hearing, the growth of teeth and the visual apparatus was not detectable. The haematological, clinical-chemical and urinary parameters, as well as the relative weight or the organs, were not influence by the administration of EPL over the 48-week period. Haemoglobin was not detectable in the faeces after the 48-week duration of the test. The macroscopically detected findings of necropsy of all animals at the end of the test can be considered to be chance findings and normal for rat populations, and thus independent of the test. For histological examination, paraffin sections of the following organs, stained with haemalum-eosin, were available: cerebrum, cerebellum, nervus ischiadicus, hypophysis, thyroid gland (2×), thymus gland, lung, heart, liver, oesophagus, stomach, duodenum, jejunum, pancreas, spleen, mesenteric lymph nodes, kidneys (2×), adrenal gland, skeletal muscle, testes, prostate gland, seminal vesicle and ovaries (2×), and uterus (2×). A Prussian-blue reaction of the lung and of the spleen was available for the detection of iron. Frozen sections stained with Sudan III were made for the detection of fat in the heart, liver and kidneys. Five male and female animals were then examined histopathologically in control and the lowest and middle doses, and 10 males and five females at the highest dose. With respect to the fatty changes, there was a tendency towards diffuse fatty changes in the heart in the case of the male higher dosage group (nine of 10 compared to three of five in controls), whereas there was no evidence of dosage-dependent fatty changes in the liver. The fatty changes in the liver were characterised by peripheral fatty deposits in the liver cells. According to the authors, this effect could be a chance finding, and they concluded that under the given circumstances of the test, the 'no-effect' dosage of EPL in Wistar rats may be expected, in the case of a 48-week per oral administration to be above 3,750 mg/kg bw per day.

The Panel noted that similar histopathological changes were observed in the heart in both control and treated animals. The Panel considered that these histopathological changes were likely to be a background finding in rats of this strain and age. Furthermore, the Panel noted that this study has some shortcomings.

In a 2-year study, groups of 48 male (100–130 g) and 48 female (90–120 g) weanling Wistar rats were fed diets containing either 0% (control), 2% or 6% a mixture of ammonium compounds of phosphatidic acids derived from rapeseed oil, and a proportion of triglycerides from the partially hardened oil or 4% soya lecithin (no additional information on the composition available), equal to 1,470 and 2,280 mg soya lecithin/kg bw per day in male and female rats, respectively, for 2 years (Brantom et al., 1973). Body weights and food consumption were recorded at intervals up to week 95. Necropsies were carried out on all rats. The animals were examined for macroscopic abnormalities and the brain, pituitary, thyroid, heart, liver, spleen, stomach, small intestine, caecum, kidneys, adrenal glands and gonads were weighed. Samples of these organs and samples of salivary gland, trachea, lung, aortic arch, skeletal muscle, lymph nodes, colon, rectum, pancreas, spinal cord, bone and uterus and any other tissue that appeared abnormal were preserved in 10% buffered formalin. All tissues from control animals and those fed 4% soya lecithin were prepared for microscopic examination. No abnormalities were seen in the behaviour of the rats. The body weights of females fed 4% soya lecithin were significantly higher than those of controls from week 62 onwards. The food intakes of all treated male groups were slightly higher than those of controls, whereas females from treated and control groups consumed similar amounts of food daily. There were no statistically significant differences between treated and control animals with respect to the results of serum analyses or the tests of renal concentrating ability, and haematological investigations did not reveal any significant differences between treated and control animals. At necropsy, it was noted, mainly in males, that small nodules were present on the surface of the thyroids of four controls and seven or eight animals in each treated group. Histopathological examination of these tissues revealed enlarged hyperplastic parathyroids. This lesion was also found in rats in which no nodules were seen at necropsy. Regarding the incidence of tumours, the commonest was chromophobe adenoma of the pituitary and fibroadenoma of the mammary tissue. Benign tumours affecting the liver, pancreas, pituitary, thyroid, adrenals, testes, skin, brain salivary gland, ovary, uterus, prostate and connective tissue were also found. Malignant tumours were found in all groups affecting the pancreas, thymus, salivary gland, mammary tissue, uterus, skin and connective tissue. However, the incidence of tumours was not influenced by feeding with soya lecithin.

The authors concluded that, although tumours were observed in this study, in no case could these be taken as an indication of a carcinogenic effect of the test item. On the basis of the present study, soya lecithin can be considered as not carcinogenic when fed to rats for 2 years at dietary levels of up to 4%. Similarly, no toxic effects that could be attributed to the ingestion of the soya lecithin were found in this study and a no-untoward effect level of 4% in the diet, equal to 1,470 and 2,280 mg soya lecithin/kg bw per day in males and females, respectively, was identified by the authors. The Panel agreed with this conclusion.

3.5.6. Reproductive and developmental toxicity

3.5.6.1. Reproductive toxicity studies

No reproductive toxicity studies with lecithins were available.

3.5.6.2. Developmental studies

Several prenatal developmental toxicity studies with lecithins were conducted in CD1 mice, Wistar rats and Dutch belted rabbits (FDA, 1974). Animals were administered different doses of lecithin suspended in anhydrous corn oil by gavage; the control groups were vehicle treated.[22] Body weights were recorded at regular intervals during gestation and all animals were observed daily for appearance and behaviour. All dams were subjected to caesarean section, and the numbers of implantation sites, resorption sites, live and dead fetuses, and body weight of live fetuses were recorded. All fetuses were examined grossly for external abnormalities, one-third underwent detailed visceral examinations and two-thirds were stained and examined for skeletal defects.

Mice

In a mice study, groups of 21–23 pregnant albino CD-1 mice were dosed via gavage with 0, 16, 74.3, 345 or 1,600 mg/kg bw per day lecithin in corn oil (dose volume 10 mL/kg bw) from gestational day (GD) 6 to 15 (FDA, 1974). Body weights were recorded on GD 0, 6, 11 and 15, and at necropsy on GD 17. For both dams and fetuses, no adverse effects were noted at doses of up to 1,600 mg/kg bw per day.

Rats

In a rat study (FDA, 1974), groups of 22–24 pregnant albino Wistar rats were dosed via gavage with 0, 16, 74.3, 345 or 1,600 mg/kg bw per day lecithin in corn oil from GD 6 to 15. The dose volume of the vehicle was 1, 1, 1, 2 or 6.4 mL/kg bw, respectively). Body weights were recorded on days 0, 6, 11 and 15, and at necropsy on day 20. Dams and fetuses were examined as described in the above study with mice. No adverse effects for both dams and fetuses were noted at doses of up to 1,600 mg/kg bw per day.

The effect of a preparation containing choline phosphoric acid diglyceride ester of natural origin with mainly unsaturated fatty acids, particularly linolic acid (approximately 70%), linolenic and oleic acid, was tested on rats. Groups of 25 pregnant rats received, throughout pregnancy and lactation, oral doses of 0, 150, 750 and 3,750 mg/kg bw per day, from GD 16 to the third week of lactation (Document provided to EFSA n.9). Distilled water was used as a solvent, and the solution was administered in a constant volume of 20 mL/kg bw per day to the rats by gavage. No influence of the preparation on behaviour, appearance, body weight, food and water intake or the faeces of the dams was recorded. There were no mortalities. No abnormalities were seen regarding the duration of gestation. The number of dead pups was somewhat higher in the 750 mg/kg bw per day group compared to the control. However, the effect was not dose-dependent and the changes in the 750 mg/kg bw per day group were within the historical background range expected for this strain. No morphological abnormalities could be detected in the offspring. Regarding lactation and viability index, as well as rearing rate, no substance-specific influences were seen. It was stated that this preparation in oral doses up to 3,750 mg/kg bw per day exerts no influence on peri- and postnatal development of rats.

EPL (see Section 3.1.1) was administered to pregnant Wistar rats (n = 24 per group) at doses of 0, 100, 500 and 1,000 mg/kg bw by gavage (dosing volume 10 mL/kg bw) from GD 6 to 15 (Document provided to EFSA n.14). The substance was stirred with distilled water and allowed to swell. Administration of the substance had no effect on behaviour, external appearance, weight development, water consumption and faeces of the dams. A reduction on food intake after the treatment phase in the animals of the mid- and high dose group was considered by the authors of little or no significance because no effect on weight development could be found. There were no deaths. Macroscopic examination at necropsy showed no pathological findings in the dams. Corpora lutea, implantations,

[22] Taking into account the statement from the teratology study in rats (FDRL, 1973a,b,c) that 'the controls were sham treated with the vehicle at a level equivalent to the group receiving the highest test dose', the Panel assumed that control group was treated with the vehicle, corn oil.

resorptions, litter size, fetal and placental weights, and pre- and post-implantation losses showed no marked differences between treated animals and controls. No treatment-related effects were observed on external, visceral or skeletal examination of the fetuses. The Panel agreed with the authors and considered the NOAEL for maternal and developmental effects to be 1,000 mg/kg bw per day (the highest dose tested).

EPL (see Section 3.1.1) US 10% was given intravenously to pregnant Wistar rats ($n = 24$ per group) in doses of 0, 1.0, 3.16 and 10 mL/kg bw per day (dosing volume 10 mL/kg bw in 0.9% NaCl solution) from GD 6 to 15 (Document provided to EFSA n.8). After the treatment phase (GD 15), an increase in food intake in the animals of the mid- and high dose group was observed. There were no deaths. Macroscopic examination at necropsy showed no pathological findings in the dams. Corpora lutea, implantations, resorptions, litter size, fetal and placental weights, pre- and post-implantation losses showed no marked differences between treated animals and controls. No treatment-related effects were observed on external, visceral or skeletal examination of the fetuses. The Panel agreed with the authors and considered the NOAEL for maternal and developmental effects to be 10 mL/kg bw per day approx. 1,000 mg/kg bw per day (the highest dose tested).

Rabbits

In a rabbit study (FDA, 1974), groups of 10–14 pregnant Dutch-belted rabbits were dosed via gavage with 0, 4.75, 22.1, 100.3 or 475 mg/kg bw per day lecithin in corn oil on GD 6–18. The dose volume of the vehicle was 1, 1, 1, 1 or 2 mL/kg bw. Body weights were determined on days 0, 6, 12 and 18, and at necropsy on GD 29. In addition, live fetuses of each litter were placed in an incubator for 24 h for evaluation of neonatal survival. For both dams and fetuses, no adverse effects were noted at doses of up to 475 mg/kg bw per day.

The effect of PPC-R (containing 95.2% of phosphatidylcholine, 1.3% lysolecithins and 0.13% kephalin) was tested after administration by gavage from GD 1 to 6 in 12 pregnant rabbits per group (Document provided to EFSA n.6). PPC-R was taken up in 0.8% aqueous hydroxypropyl-methylcellulose gel and administered at doses of 0, 250, 500 or 1,000 mg PPC-R/kg bw per day by gavage (volume: 5 mL/kg bw per day). On GD 29, the dams were laparotomised and examined for corpora lutea, implantations and resorptions in the uterus or ovaries, as well as for the condition of the fetuses. The pre-implantation loss was not increased and the development of embryos and fetuses showed no substance-related influence after administration of PPC-R compared to the control group. The authors concluded that PPC-R administration by gavage up to 1,000 mg PPC-R/kg bw per day (treatment from GD 1 to 6) did not influence the implantation in rabbits and the further development of the fetuses. The Panel agreed with this conclusion.

Overall, with respect to reproductive toxicity, no reproductive studies with lecithins are known. In the prenatal developmental studies in mice, rat and rabbits with lecithins, no developmental effects were induced up to the highest dose tested (1,600 mg/kg bw per day, mice and rat and 475 mg/kg bw per day in rabbits). The Panel noted the lack of details in the report of these studies and a lack of description of the statistical methods. In a peri- and post-natal study in rats with a preparation containing choline phosphoric acid diglyceride ester of natural origin with mainly unsaturated fatty acids, particularly linolic acid (approximately 70%), linolenic and oleic acid, no treatment-related effects were observed up to the highest dose tested, 3,750 mg/kg bw per day. PPC-R (containing 95.2% of phosphatidylcholine, 1.3% lysolecithins and 0.13% kephalin) as administered by gavage up to 1,000 mg PPC-R/kg bw per day (treatment from GD 1 to 6) did not influence the implantation in rabbits and the of the fetuses.

3.5.6.3. Neurodevelopmental toxicity studies

Mice

Effects of phospholipids on behavioural maturation were studied in mice by Gozzo et al. (1982). The pregnant females (10 per group) were fed the test diet from GD 14 and continued throughout lactation. At weaning, the pups were fed the control diet until they were sacrificed on post-natal day (PND 60). The control diet contained 10% of lipids (9% made up from margarine and 1% corn oil). The 10% of lipids in the control diet were replaced by commercial soya lecithin in the test diet. Pups were subjected to a series of test of reflex responses, locomotor activity and avoidance leaning between PND 1 and 21. On PND 60, an avoidance learning session of five consecutive days was performed. Body weights of the lactating dams and the pups were not affected (data not shown only for day birth). Fore limb grasping and vibrissae placing were achieved earlier in the pups of the soya bean lecithin group compared to the control group. On PND 2, 4 and 8, locomotor activity was decreased. The number of avoidances in the learning sessions (from PND 60 onwards) of the soya lecithin group was increased. The number of mice, litters and pups used for each measurement was not clear to the Panel, nor was the selection of these animals for the measurements.

Several studies on the effects of soya lecithin on neurochemical and behavioural effects were reported by the same group (Bell and Lundberg, 1985; Bell and Slotkin, 1985; Bell et al., 1986).

Rats

Against the background that choline availability as a precursor of acetylcholine may possibly influence neurotransmitter systems, Bell and Lundberg (1985) studied the effects of 2% and 5% soya lecithin in the diet of pregnant rats (equivalent to 1,250 or 2,500 mg soya lecithin/kg bw per day). The diets were fed from 2 weeks before mating until weaning of their litters. The control animals were fed AIN 76 diet. After weaning, half of the litters were placed on control litters, whereas the others remained on their respective diets. The authors stated that based on an average consumption of 10 g, the control animals received 8.9 mg and the soya lecithin groups received 14.0 or 22 mg choline/day. Neurobehavioural toxicity in rats was assessed using a developmental test battery from PND 3 to 20. Furthermore, a number of post-weaning tests were performed. Choline acetyltransferase was measured in whole brain of PND 1 pups and in the forebrain on PND 21, 42 and 67. In the 5% group, reflex righting and swimming development were delayed. In this group, the brain to bodyweight and acetylcholine levels were increased. Animals exposed also after weaning to 2% and 5% soya lecithin were shown to be hypoactive and to have neurochemical abnormalities. For several tests, there was no clear dose relationship detected between the 2% and the 5% concentration groups. The results for the measurement of choline acetyltransferase of F1 pups/animals were presented for dams fed lecithin pre- and/or post-natally. From these results, no clear indication can be given which period the F1 pups/animals were more sensitive to changes in this parameter.

Bell and Slotkin (1985) fed control (AIN) or diets containing 5% soya lecithin to pregnant rats (equivalent to 2,500 mg soya lecithin/kg bw per day). The diet was fed from GD 7 until termination of the study. The control diet contained 0.2% choline bitartrate. The authors stated that, based on an average consumption of 10 g, the control received 9 mg choline/day and the soya lecithin group 22 mg choline/day. Latencies for righting responses (measured on PND 1–4) and negative geotaxis (measured on PND 5–8) were shorter in the soya lecithin group. Behavioural differences were still present in adulthood as response to analgesia was reduced in the soya lecithin group at that time. Biochemical markers in the cerebellum and the cerebral cortex were different in the soya lecithin treated groups compared to the control. However, the Panel noted that the number of pregnant animals and the number of litters and the sex of the pups in the control and treated groups used in the assessment for neurotoxicity were not described in sufficient detail. In addition, the length of gestation and the pup weight at birth and during the tests were not presented.

Bell et al. (1986) studied the effects of replacing 5% corn oil with 5% commercial lecithin in the diet of pregnant Sprague–Dawley rats (equivalent to 2,500 mg soya lecithin/kg bw per day). The diet was fed from GD 7 until the end of lactation and pups were also fed the same diet until adulthood. The authors stated that, based on an average consumption of 10 g, the control received 9 mg choline/day and the soya lecithin group 22 mg choline/day. The description and selection of animals, pups/litter and pups for each measurement is not clear to the Panel. Catecholamine, noradrenaline and dopamine levels were measured in several brain regions. The authors concluded that transmitter uptake capabilities in the brain were affected by developmental exposure to soya bean lecithin.

Overall, the Panel noted the following flaws for the study by Gozzo et al. (1982) in mice and the studies of Bell and co-workers in rats (Bell and Lundberg, 1985; Bell and Slotkin, 1985; Bell et al., 1986) with soya lecithin. The number of pregnant animals, the number of litters and the sex of the pups in the control and treated groups as used in the assessment for neurotoxicity was not described in sufficient detail. In addition, the length of gestation and the pup weight at birth and during the tests was not presented in all publications. In neurodevelopmental toxicity studies, the selection of pups, the sex used in the tests, the pup weight and the corresponding developmental windows of the animals are very important. Therefore, the Panel concluded that the relevance of the studies is limited, although, at concentrations of 5% soya lecithin and higher in the diet during the gestation, lactation and post-weaning period, there were indications for alterations in the development of the brain.

The report by the Ministry of Agriculture and Fisheries and Food of the UK (1992) reported the following on these studies rats (Bell and Lundberg, 1985; Bell and Slotkin, 1985; Bell et al., 1986): 'These studies are of limited quality and the results were not considered relevant to the general use of lecithins as additives in food'. In 1996, the SCF (1997) also addressed the possible behavioural effects described in the studies of Bell and co-workers (Bell and Lundberg, 1985; Bell and Slotkin, 1985; Bell et al., 1986) and proposed that the maximum level of lecithins in infant formulae should be restricted to that of human milk (1 g/L). The Panel agreed with this conclusion.

3.5.7. Hypersensitivity, allergenicity and food intolerance

3.5.7.1. Humans

Adults

There are several case reports and studies available that describe a possible allergenic potential of lecithins (E 322).

In an occupational study, inhaled soya bean lecithin was reported to cause immunological (20 males) and respiratory changes (19 males) (Zuskin et al., 1990, 1991). All workers reacted to intradermal skin tests with soya bean dust and almost all reacted to soya bean antigen prepared after separation of oil (94.7%). Increased levels of soya-specific immunoglobulin (Ig) E were noted in only three of 19 individuals. There was a higher incidence of chronic respiratory symptoms compared to controls not exposed to soya bean dust (significantly different for dyspnoea: 47.4% vs 9.7% in controls).

Lavaud et al. (1994) reported two cases of soya bean-lecithin-induced asthma in bakers. Both individuals tested positive in skin tests and also the radioallergosorbent test gave a positive result for soya bean.

Awazuhara et al. (1998) investigated the antigenicity of soya lecithin and soya oil proteins with regard to soya bean allergy. The proteins present in soya lecithin and soya oil were determined according to an established method and analysed by SDS-PAGE. The IgE- and IgG4-binding abilities of the soya lecithin proteins were investigated by immunoblotting with sera from 30 soya bean-sensitive patients, including seven with a positive challenge test. The results of SDS-PAGE demonstrated the presence of only three proteins, with molecular weights of about 58–67 kDa in soya oil, and suggested that soya lecithin also contains these proteins. The soya lecithin also contained many proteins besides these. The proteins with molecular weights of 58–67 kDa rarely bound to serum IgE. Only one of the patients who presented a positive challenge test had IgE antibodies bound to soya lecithin proteins. Neither the IgE, nor the IgG4 present in the patients' sera reacted to any soya oil protein. The authors concluded that the proteins present in soya lecithin and soya oil have little antigenicity with regard to soya bean allergy.

Gu et al. (2001) isolated soya lecithin proteins following solvent extraction of lipid components and then separated them by SDS-PAGE. The level of protein in six lecithin samples obtained from commercial suppliers ranged from 100 to 1,400 ppm. Immunoblotting with sera from soya-sensitive individuals showed IgE binding to bands corresponding to 7, 12, 20, 39 and 57 kDa. The authors concluded that soya lecithin contains a number of IgE-binding proteins and therefore might represent a source of hidden allergens. According to the authors, these allergens may be a more significant concern for soya-allergic individuals consuming lecithin products as a health supplement.

Müller et al. (1998) investigated six commercial soya lecithins for residual allergenicity and compared with extracts from raw and heat-treated soya bean. The protein content was determined by enzyme-linked immunosorbent assay and allergens were analysed with specific IgE from patients' sera using the enzyme allergosorbent test (EAST). The EAST studies revealed that three of six sera from patients with allergy to soya beans contained IgE to four soya lecithins with the content of residual proteins higher than 20 mg/kg. EAST inhibition showed that the allergens from soya lecithin were immunologically more closely related to allergens from heat-treated soya beans than to those from raw soya beans.

Martin-Hernandez et al. (2005) performed quantification and characterisation of residual proteins in lecithins. The SDS-PAGE protein pattern of the standard soya lecithin was very similar to that of soya flour. The seed maturation protein P34 from the 7S globulin fraction of soya proteins, reported as the most allergenic protein in soya bean, has also been identified in soya lecithins.

According to the EFSA NDA Panel (2014), the prevalence of clinically confirmed soya allergy in unselected populations in Europe appears to be low, although available studies are scarce. Higher rates of anaphylactic reactions to soya protein have been reported among peanut-allergic patients. Serological and clinical cross-reactions have been described between soya and other legumes, with the pollen allergen Bet 1 v, and with bovine casein. Thermal processing, high hydrostatic pressure treatments and fermentation have been shown to reduce the IgE-binding capacity of soya proteins, depending on the conditions and duration of the processes. The lowest MED reported in soya-allergic patients undergoing DBPCFC was 0.2 mg of soya protein, although the majority of patients only reacted to higher doses.

The possibility of residual allergenicity in food products manufactured using egg lecithin has been reported in a DBPCFC. Both egg white- and egg yolk-derived proteins have been described to trigger clinical allergic reactions. Heat denaturation and other food-processing treatments do not reliably reduce the allergenicity of eggs. The MEDs of ingested egg proteins reported to trigger objective reactions in clinical studies range from few micrograms to milligrams (EFSA NDA Panel, 2014).

Infants and children

According to the Annex II of the Regulation (EU) No 1169/2011[23], soya beans and products thereof and eggs and products thereof are listed as substances or products causing allergies or intolerances, and information on their presence in food should be given to the consumers.

Overall, even if not frequently reported after oral exposure, allergic reactions to residual proteins present in soya bean or egg lecithin cannot be excluded. Therefore, it should be specified that the amount of these residual proteins in the food additive lecithins (E 322) must be kept as low as possible.

The Panel considered it advisable to reduce as much as possible the presence of proteinaceous compounds by introducing appropriate purification steps in the manufacturing process.

3.5.8. Other studies

3.5.8.1. Animal studies

The effect of supplementing the diet with natural/dietary emulsifiers was examined by Lecomte et al. (2016). Four groups of C57BL6 mice (21–23 g and 6 weeks old) received either a low-fat diet (n = 10), a high-fat diet (n = 12), a high-fat diet containing soya bean lecithin (n = 12) or a high-fat diet containing a polar lipid emulsifier from milk (n = 12) for 8 weeks. The three high-fat diet formulations contained the same amount of lipids, proteins and carbohydrates, differing only by the lack or the presence of 1.2% by weight of polar lipids (equivalent to 600 mg/kg bw per day) from soya bean or milk. Compared with the high-fat diet group, the group maintained on a high-fat diet containing soya bean lecithin diet had increased white adipose tissue mass ($p < 0.05$), with larger adipocytes ($p < 0.05$) and increased epidydimal adipose expression of tumour necrosis factor α, monochemoattractant protein-1, lipopolysaccharide-binding protein and leptin ($p < 0.05$). These changes were not observed in the group treated with a high-fat diet containing a polar lipid emulsifier from milk. Liver weight did not differ among groups. However, the group fed a high-fat diet containing soybean lecithin had a higher hepatic lipid content compared to the groups fed either a high-fat diet or a high-fat diet containing a polar lipid emulsifier from milk ($p < 0.01$ and $p < 0.05$, respectively). The group fed a high-fat diet containing soya bean lecithin also had a greater proportion of hepatic triglycerides compared to the groups fed either a high-fat diet or a high-fat diet containing a polar lipid emulsifier from milk ($p < 0.001$ and $p < 0.01$, respectively) and a lower proportion of hepatic phospholipids compared to the high-fat group ($p < 0.05$). No differences were observed among groups regarding plasma lipid concentrations. The Panel noted that, when feeding a high-fat diet to mice, addition of soya bean lecithin compared to addition of polar lipid emulsifier lead to an increase in white adipose tissue mass and greater portion of hepatic triglycerides.

3.5.8.2. Human data: information from pharmaceutical uses

Contraindications, warnings and undesirable effects for lecithin as an excipient are not known in dosages used. In the literature, it is always emphasised that the sensitisation of atopic patients is possible due to residual proteins in lecithin, resulting in hypersensitivity (Palm et al., 1999; HMPC, 2006). At higher amounts, such as a daily dosage of 1.5–2.7 g of lecithin (containing 73–79% phosphatidyl-choline), occasional gastrointestinal effects (such as stomach pain, loose stool and diarrhoea) were described (Blumenthal et al., 1998).

[23] Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004.

From the European Economic Area, there are only few cases of a wide range of adverse effects reported without proven cause–effect relationship.[24]

According to the recently published draft monograph of the HMPC of EMA, the traditional medicinal usage of soya bean lecithin (deoiled, enriched phospholipids from soya bean) by oral administration at the dosage of 750–2,700 mg (two or three times daily) corresponding to 1,500–8,100 mg/day could be verified for 'the relief of temporary fatigue and sensation of weakness' in adolescents, adults and elderly. The undesirable effects reported were: 'Allergic reactions including severe anaphylaxis and angioedema have been reported. The frequency is not known. Skin reactions like pruritus, dermatitis, exanthema and urticaria have been reported. The frequency is not known. Gastrointestinal disorders like stomach discomfort and diarrhoea have been reported' (HMPC, 2016b; draft).

Adults

Dechent et al. (1999) studied the effects of oral administration of choline (short-term study) or lecithin (long-term study) on the metabolite concentrations in the human brain. In the short-term study, three women and three men (age 28.0 ± 3.5 years, mean weight 71 ± 10 kg) ingested a single dose of 50 mg/kg bw of free choline as choline bitartrate. These dose levels were chosen because Stoll et al. (1995) and Cohen et al. (1995) observed a doubling of the plasma choline levels at this dose. In the long-term study, three women and three men (aged 27.7 ± 3.8 years; weighing 72.7 ± 10 kg) received 2 × 16 g of lecithin (containing 95% phosphatidylcholine) per day. The choline levels in the brain in both studies were not increased.

Infants

A 3-year-old boy with retarded bodyweight growth due to chronic diarrhoea showed abdominal pain and post-prandial emesis (Renaud et al., 1996). Testing with native soya lecithin caused a diarrhoeal bout, whereas placebo had no effect. During provocation, there was a sharp rise in the urinary lactulose/mannitol ratio compared to a fasting test (4.25% vs 1.34%), which is indicative for an alteration of intestinal permeability. In a test with placebo, there was no significant change in urinary lactulose/mannitol ratio (1.82% vs 1.59%).

Healthy full-term infants were fed from birth exclusively human milk (n = 16), standard term formula (n = 15) or the same formula supplemented with egg yolk lecithin providing docosahexaenoic a(DHA) 0.15% and arachidonic acids (AA) 0.30% (n = 18) (Bondía-Martínez et al., 1998). Fatty acid composition of plasma and erythrocytes were determined at birth, as well as at day 7, 1 month and 3 months. At 1 and 3 months, the infants of the non-supplemented formula group showed a decreased in DHA and AA in the serum. No differences were observed between the group fed breast milk and the group fed supplemented formula during the study period.

4 Discussion

Lecithins are mixtures or fractions of phosphatides obtained by physical procedures from animal or vegetable foodstuffs. They also include the corresponding hydrolysed products obtained through the use of harmless and appropriate enzymes, although the final product must not show any signs of residual enzyme activity. The lecithins may be slightly bleached in aqueous medium by means of hydrogen peroxide, although the oxidation must not chemically modify the lecithin phosphatides (Commission Regulation (EU) No 231/2012).

Lecithins (E 322) are authorised as food additives in the EU and have been previously evaluated by JECFA in 1973 (JECFA, 1974a,b) and by the SCF in 1982 (SCF, 1982). The Panel noted that, although Commission Regulation (EU) No 231/2012 includes both types of lecithins (non-hydrolysed and hydrolysed) under the same food additive (E 322), JECFA differentiated between them and treated them as different food additives (INS 322i and INS 322ii) with separate specifications.

The Panel noted that the protein content in crude, fluid and deoiled soya lecithins are in the range of 115–27,000 mg/kg, 232–1,338 mg/kg and 65–480 mg/kg, respectively, and in egg lecithins 49 mg/kg ((Document provided to EFSA n.18); Porras et al., 1985; Müller et al., 1998; Gu et al., 2001; Paschke et al., 2001; Martin-Hernandez et al., 2005). According to EFSA NDA Panel (2014), the lowest MED reported in soya-allergic patients undergoing DBPCFC was 0.2 mg of soya protein, and from a few micrograms to a few milligrams of egg proteins. The Panel agreed with the opinion from NDA Panel (2014) that the hypersensitivity to soya and egg lecithins is due to the residual proteins in

[24] From the table provided from EMA (Eudravigilance).

lecithins (E 322) and therefore considered it necessary to develop the limit for the presence of residual protein in the EU specifications.

The Panel noted that, based on the data provided by the industry, it is feasible to lower the specification limits for toxic elements: lead, mercury and arsenic. The Panel also noted that the limit for cadmium should be included in the EU specifications.

The Panel noted that the composition of the preparations used in the various studies was different. However, because all of the constituents were qualitatively similar, the Panel considered the studies relevant for the risk assessment of lecithins.

Lecithins are natural constituents of all cells in the human body and also are natural components of the diet. Hydrolysed lecithins are produced in the gut as a result of normal digestion (SCF, 1982). Among lecithins, phosphatidylcholine is hydrolysed in choline in the cytidine-5-diphosphate-choline pathway in all cells of the body. The content of choline that can theoretically be released from phosphatidylcholine containing two linoleate groups is 13.2%. Choline is a precursor of the neurotransmitter acetylcholine and plays an important role in the metabolism and transport of lipids (EFSA NDA Panel, 2016).

For choline, the EFSA NDA Panel (2016) prepared a scientific opinion on DRVs in 2016. In this opinion, the NDA Panel considered dietary choline including choline compounds (e.g. glycerophosphocholine, phosphocholine, phosphatidylcholine, sphingomyelin). The NDA Panel concluded that ARs and PRIs for choline could not be derived for adults, infants (aged 7–11 months) and children, and therefore defined AIs for total choline (free and bound). For infants during the first 6 months of life, the amount of total choline provided in human milk was considered adequate. With regard to an excessive intake of choline, the NDA Panel referenced on the setting of ULs for choline by the US IOM (1998) and noted that no UL was established by IOM for infants. According to IOM, the only source of intake of choline for infants should be from food or formula to prevent high levels of intake.

Studies using radiolabelled phosphatidylcholine in animals and humans clearly indicated that, following oral administration, phosphatidylcholine is absorbed intact or as lysophosphatidylcholine or choline after intestinal hydrolysis. In intestinal mucosa cells, lysophosphatidylcholine would be reacylated into phosphatidylcholine or hydrolysed to glycerophosphocholine and free fatty acids. The fatty acids would be further utilised for the reassembly of triacylglycerides and phosphatidylcholine found in the chylomicrons. In humans, the absorbed phosphatidylcholine would be incorporated preferentially into the HDL fraction of plasma. In humans, dietary lecithins are known to be hydrolysed by phospholipases to liberate choline which is rapidly absorbed by a carrier-mediated saturable transport system and appears in plasma predominantly as free choline. Consequently, an increased plasma-free choline concentration has been described as a consequence of increased dietary intake of lecithins. Moreover, a significant increase in breast milk concentrations of free choline was observed in pregnant women receiving a phosphatidylcholine supplementation compared to the placebo group.

The acute toxicity of lecithins (E 322) in mice, rats and rabbits is low. The Panel noted that in these studies the test substance is not always characterised.

Subchronic toxicity studies in rats and dogs did not report any adverse effect, even at the highest doses tested (3,750 mg EPL (see Section 3.1.1)/kg bw per day, 1,000 mg soya phosphatidylinositol or EPL/kg bw per day in rats and dogs, respectively, and 5,460 mg lecithins/kg bw per day in rats).

The Panel considered the available genotoxicity data on lecithins (E 322) to be sufficient to conclude that there is no concern with respect to genotoxicity.

Chronic toxicity studies in rats did not report any adverse effects, even at the highest dose tested (3,750 mg EPL/kg bw per day). No carcinogenic effects were reported in rats, even at the highest dose tested (1,470 and 2,280 mg soya lecithin/kg bw per day in males and females, respectively) for 2 years.

The Panel considered that no adverse effects were observed in the developmental toxicity studies performed in mice, rat and rabbits up to the highest dose tested. However, the Panel noted that no reproductive toxicity studies were available.

Against the background that choline availability as a precursor of acetylcholine may possibly influence neurotransmitter systems, several neurodevelopmental toxicity studies were conducted with lecithin. The Panel noted that the neurodevelopmental toxicity studies of Gozzo et al. (1982) in mice and the studies of Bell and co-workers in rats (Bell and Lundberg, 1985; Bell and Slotkin, 1985; Bell et al., 1986) had several limitations, such as the number of pregnant animals, the number of litters, and the sex of the pups in the control and treated groups not being described in sufficient detail. In addition, the length of gestation and pup weight at birth, as well as during the tests, were not presented in all publications. Therefore, the Panel concluded that the relevance of the studies is limited but, at concentrations of 5% soya lecithin and higher in the diet during the gestation, lactation and the post-weaning period, there were indications for alterations in the development of the brain.

The UK Ministry of Agriculture Fisheries and Food (1992) reported the following on these rat studies (Bell and Lundberg, 1985; Bell and Slotkin, 1985; Bell et al., 1986): 'These studies are of limited quality and the results were not considered relevant to the general use of lecithins as additives in food'. In 1996, the SCF (SCF, 1997), also addressed the possible behavioural effects described in the studies of Bell and co-workers (Bell and Lundberg, 1985; Bell and Slotkin, 1985; Bell et al., 1986) and proposed that the maximum level of lecithins in infant formulae should be restricted to that of human milk (1 g/L). The Panel agreed with this conclusion. Furthermore, the Panel considered it prudent that lecithins (E 322) use in infant formulae should not lead to choline intakes higher than the amount of total choline provided in human milk considered adequate by the NDA Panel (EFSA 2016).

The Panel noted that, in Annex II of Regulation (EC) No 1333/2008, the use levels of lecithins (E 322) in food for infants under the age of 12 weeks are included in categories 13.1.1, 13.1.5.1 and 13.1.5.2. The Panel considered that these uses would require a specific risk assessment in line with the recommendations given by JECFA (1978) and the SCF (1998) and endorsed by the Panel (EFSA ANS Panel, 2012). Therefore, the current re-evaluation of lecithins (E 322) as a food additive is not considered to be applicable for infants under the age of 12 weeks.

The present re-evaluation includes the use of lecithins (E 322) in foods for infants from 12 weeks of age and for young children.

Concerning uses of lecithins in food for infants and young children the Panel concurs with the SCF (SCF, 1998, 2003) '... the SCF considered it prudent that the number and amounts of additives used in foods for infants and young children should be kept at the minimum necessary. The SCF confirmed its long standing view that additives should not be permitted in foods specially prepared for infants. Rarely, exceptional technological circumstances may justify the use of an additive.'

The Panel acknowledged that consumption with respect to the concerned food categories would be short and also noted that it is prudent to keep the number of additives used in foods for infants and young children to the minimum necessary and that there should be strong evidence of need, as well as safety, before additives can be regarded as acceptable for use in infant formulae and foods for infants and young children.

The Panel noted that, if lecithins are added in combination with mono- and diglycerides of fatty acids (E 471), citric acid esters of mono- and diglycerides of fatty acids (E 472c) and sucrose esters of fatty acids (E 473) to food of the categories 13.1.1, 13.1.2, 13.1.4 or 13.1.5, the maximum level established for lecithins should not be exceeded by the total concentration of these substances.

To assess the dietary exposure to lecithins (E 322) from its use as a food additive, the exposure was calculated based on (1) maximum levels of data provided to EFSA (defined as *the maximum level exposure assessment scenario*) and (2) the reported use levels (defined as the *refined exposure assessment scenario*). Dietary exposure through this latter scenario was assessed using reported use levels data considering levels not exceeding the MPLs for food categories for which direct addition of lecithins is authorised (Annex II to Regulation No 1333/2008).

Based on the available data set, the Panel calculated two refined exposure estimates based on different assumptions: a *brand-loyal consumer scenario* and a *non-brand-loyal scenario* (see Section 3.4.1).

The main contributing food category to the total mean exposure estimates in the maximum scenario was bread and rolls for all age groups. The Panel noted that the estimated long-term exposures based on this scenario are very likely conservative because this scenario assumes that all foods and beverages listed under the Annex II to Regulation No 1333/2008 contain lecithins (E 322) as a food additive at the maximum reported use levels.

From the *refined estimated exposure scenario* considering only food categories for which direct addition of lecithins (E 322) to food is authorised, in the *brand-loyal scenario*, mean exposure to lecithins (E 322) ranged from 7 mg/kg bw per day in adolescents to 82 mg/kg bw per day in children. The 95th percentile exposure to lecithins (E 322) ranged from 15 mg/kg bw per day in adolescents to 187 mg/kg bw per day in children. In the *non-brand-loyal scenario*, mean exposure to lecithins (E 322) ranged from 3 mg/kg bw per day in adults/elderly to 22 mg/kg bw per day in toddlers. The 95th percentile exposure to lecithins (E 322) ranged from 6 mg/kg bw per day in adults/elderly to 62 mg/kg bw per day in infants. The main contributing food categories in the non-*brand-loyal scenario* were foods for infants and young children for infants and toddlers, fine bakery wares, bread and rolls for children, adolescents, adults and the elderly. The main contributing food categories in the *brand-loyal* *scenario* were foods for infants and young children for infants, fine bakery wares, and bread and rolls for the other age groups.

The Panel considered that the refined exposure assessment approach resulted in more realistic long-term exposure estimates compared to the *maximum level exposure assessment scenario*. This approach is based on the extensive range of analytical data available and assumes that people, in the long term, are exposed to foods and beverages that contain the food additive at a mean concentration level for all products (*non-brand-loyal scenario*) or that one product contains the food additive at the maximum concentration level (*brand-loyal scenario*) and the remaining products contain the additive at a mean concentration level. For lecithins (E 322), reported use levels were available. However, not all available data could be included in the assessment as a result of specific restrictions/exceptions regarding products not referenced in the FoodEx classification. This may have resulted in an underestimation of exposure to lecithins (E 322).

The Panel considered that dietary intakes of lecithins from the regular diet could be estimated in average ranging from 4 to 71 mg/kg bw per day across all population age groups.

Moreover, the Panel noted that mean dietary intakes to lecithins from the regular diet are in the range of the mean estimated exposure from the use of the food additive itself for the non-brand loyal consumer scenario.

Lecithins (E 322) is used as emulsifying and stabilising agents of water-oil/fat mixtures in a wide range of foods and it is therefore not expected that brand-loyalty will result in higher exposure in general population, except in specific populations consuming foods for special medical purposes and in infants and young children consuming infant formulae and/or follow-on formulae. The Panel therefore selected the brand-loyal refined scenario as the most relevant exposure scenario for this additive in these specific situations when justified.

Overall, the Panel considered, that in view of the limited information on health effects of excessive intake of lecithins or choline, respectively, especially by infants, children, pregnant and lactating women, estimated total choline intake including the use of lecithins (E 322) as a food additive should not lead to a significant exceedance of AIs for choline for infants or ULs defined by IOM (1998). Maximum levels of lecithins (E 322) in all types of infant formulae should be restricted to that of human milk (1 g/L).

The Panel considered that lecithins added during food processing may increase the average daily per capita consumption of phosphatidylcholine by 1.5 mg/kg of body weight for adults (this corresponds to 0.225 mg/kg of body weight of choline moiety).

5. Conclusions

I. General population

a) Above 1 year of age

Following the conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010 (EFSA, 2014), and given that:

- adequate exposure data were available and the highest relevant exposure estimate calculated in the refined exposure assessment scenario based on the reported data from food industry was for toddlers (12–35 months) up to 175 mg lecithins/kg bw per day at the 95th percentile (brand-loyal scenario),
- exposure via natural occurrence as reported by JECFA provided a daily mean intake of several grams of lecithin (approximately 1–5 g corresponding to 14–71 mg/kg bw for a 70-kg adult population),
- lecithins are natural constituents of all cells in the human body and also are natural components of the diet,
- toxicity database for lecithins was overall sufficient but not adequate regarding the endpoint of neurobehavioural developmental effects,
- there was no concern with respect to genotoxicity,
- no adverse effects were reported in chronic and carcinogenicity study in rats at the highest dose tested of 3,750 mg lecithins/kg bw per day,

the Panel concluded that there was no need for a numerical ADI for lecithins (E 322) and that there was no safety concern for the general population from more than 1 year of age at the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive.

Moreover, taking into consideration that:

- hydrolysed lecithins and choline are produced in the gut as a result of normal digestion of lecithins. Choline is rapidly absorbed and appears in plasma predominantly as free choline,
- choline is a precursor of the neurotransmitter acetylcholine,
- the content of choline, that can theoretically be released from phosphatidylcholine containing two linoleate groups, is up to 13.2%, and the measured content of choline from commercial lecithins (E 322) up to 3.4%,
- 13.2% release would result in exposure up to 23 mg choline/kg bw per day at the 95th percentile intake of lecithins in toddlers (brand loyal scenario),
- total choline intake considering regular diet (estimated in average ranging from 4 to 18 mg/kg bw per day) across all population age groups and choline intake resulting from lecithins (E 322) used as a food additive are below the UL for choline defined by the IOM (1998),

the Panel concluded that there is no safety concern for the exposure to the choline from lecithins (E 322) as a food additive at use and use levels reported by industry.

b) Infants (from 12 weeks up to 11 months of age)

Taking further into consideration that:

- adequate exposure estimates calculated in the refined exposure assessment scenario based on the reported data from food industry for infants (12 weeks to 11 months) was up to 163 mg/kg bw per day at the 95th percentile (brand-loyal scenario),
- 13.2% release would result in exposure up to 22 mg choline/kg bw per day at the 95th percentile dietary exposure of lecithins (E 322) in infants (brand loyal scenario),
- total choline intake considering regular diet in the same population group (estimated in average ranging from 9 to 16 mg/kg bw per day), and choline intake resulting from lecithins used as a food additive were in the same order as the adequate intake levels (AI) (EFSA NDA, 2016),

the Panel concluded that there was no safety concern at the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive and for the choline from lecithins (E 322) as a food additive at use and use levels reported by industry.

II. Infants and young children consuming foods for special medical purposes

Taking further into consideration that:

- with respect to the exposure estimates calculated based on the reported data from food industry for infants (12 weeks to 11 months) and young children, the highest exposure was 232 mg lecithins/kg bw per day for toddlers (12–35 months) at the 95th percentile (brand-loyal scenario),
- 13.2% release would result in exposure up to 31 mg choline/kg bw per day at the 95th percentile dietary exposure of lecithins (E 322) in toddlers (brand loyal scenario),
- total choline intake considering regular diet in the same population group (estimated on average as ranging from 13–18 mg/kg bw per day), and choline intake resulting from lecithins used as a food additive, are in the same order as the AI (EFSA NDA, 2016),

the Panel concluded that there was no safety concern with respect to the refined exposure assessment for the reported uses of lecithins (E 322) as a food additive and for exposure to choline resulting from these uses of lecithins (E 322).

6. Recommendations

The Panel recommended that the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EU specification for lecithins (E 322) should be revised in order to ensure that lecithins (E 322) as a food additive will not be a significant source of exposure to those toxic elements in food. The Panel recommended that the limit for cadmium should be included in the specifications.

The Panel noted some case reports of hypersensitivity reactions associated with soya and egg lecithins (see Section 3.5.7). The Panel agree with the opinion from EFSA NDA Panel (2014) that this hypersensitivity is due to the residual proteins in lecithins (E 322) and therefore their content should be reduced as much as possible.

Regarding the results of the inadequate neurobehavioural studies, to clarify the relevance of the data, a study with lecithins (E 322) in compliance with the current OECD TG 426 would be warranted.

In case the food additive lecithins (E 322) is used in infant formulae and follow-on formulae supplemented with choline or choline salts (see Section 1.2), the Panel recommended that the intake of choline from all sources including the use of the food additive lecithins (E 322) via infant formulae (category 13.1.1), follow-on formulae (category 13.1.2) or other food should be in the order of the AIs defined by the EFSA NDA Panel (2016).

The Panel noted discrepancies between the data reported from industry and the Mintel database, where lecithins (E 322) is labelled in more products than in food categories for which data were reported from industry. Therefore, the Panel recommended collection of data of usage and use levels of lecithins (E 322) in order to perform a more realistic exposure assessment. Moreover, there are several authorised uses that are not supported by data submitted by industry nor by the Mintel database.

Documentation provided to EFSA

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Glossary [and/or] Abbreviations

AA	arachidonic acid
ADI	acceptable daily intake
AESGP	Association of the European Self-Medication Industry
AI	adequate intake
AMFEP	Association of Manufacurers and Formulators of Enzyme Products
ANS	Panel on Food Additives and Nutrient Sources added to Food
AOAC	Association of Analytical Communities
AR	average requirement
CAS	Chemical Abstracts Service
cfu	colony-forming unit
CIR	Cosmetic Ingredient Review
DBPCFC	double-blind placebo-controlled food challenge
DHA	docosahexaenoic acid
DRV	dietary reference value
EAST	enzyme allergosorbent test
EFEMA	European Food Emulsifiers Manufacturers Association
EFSA FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
EFSA NDA	EFSA Panel on Dietetic Products, Nutrition and Allergies
EINECS	European Inventory of Existing Commercial Chemical Substances
ELMA	European Lecithin Manufacturers Association
EMA	European Medicines Agency
EPL	essential phospholipid
EUE	human embryonic epithelium cells
FAO/WHO	Food and Agriculture Organization/World Health Organisation
FCS	Food Classification System
FDA	Food and Drug Administration
FDE	Food Drink Europe
FDRL	Food and Drug Research Laboratories
FSMP	foods for special medical purposes
GD	gestational day
GNPD	Global New Products Database
GRAS	'Generally Recognised As Safe'
HDL	high-density lipoprotein
HMPC	Committee on Herbal Medicinal Products
HPLC	high-performance liquid chromatography
ICGA	International Chewing Gum Association

Ig	immunoglobulin
INS	International Numbering System for Food Additives
IOM	Institute of Medicine
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD_{50}	lethal dose, 50%, i.e. dose that causes death among 50% of treated animals
LOD	limit of detection
MED	minimum eliciting dose
MPL	maximum permitted level
NMR	nuclear magnetic resonance (spectroscopy)
NOAEL	no-observed-adverse effect
PND	post-natal day
PRI	population reference intake
QS	*quantum satis*
SCF	Scientific Committee on Food
SDS-PAGE	sodium dodecyl sulfate-polyacrylamide gel electrophoresis
SNE	Specialised Nutrition Europe
TLC	thin-layer chromatography
UDS	unscheduled DNA synthesis
UL	upper intake level

Appendix A – Summary of reported use levels of lecithins (E 322) (mg/kg or mg/L as appropriate) provided by industry

Food category number[(a)]	Food category name	MPL	Restrictions/exceptions	Information provided by	N	Typical mean	Maximum
01.5	Dehydrated milk as defined by Directive 2001/114/EC	QS		European Lecithin Manufacturers Association	3	1,000	12,000
01.6.3	Cream and cream powder	QS		European Lecithin Manufacturers Association	1	1,000	12,000
01.7.1	Unripened cheese excluding products falling in category 16	QS	Except mozzarella	European Lecithin Manufacturers Association	1	1,000	12,000
01.8	Dairy analogues, including beverage whiteners	QS		FDE Food and Drink Europe	10	1,222	2,750
01.8	Dairy analogues, including beverage whiteners	QS		European Lecithin Manufacturers Association	2	2,000	10,000
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	QS		FDE Food and Drink Europe	6	2,296	7,500
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	QS		European Lecithin Manufacturers Association	4	2,450	15,000
03	Edible ices	QS		BABBI Confectionary Industry	1	3,000	3,000
03	Edible ices	QS		FDE Food and Drink Europe	26	902	6,497
03	Edible ices	QS		European Lecithin Manufacturers Association	1	1,000	5,000
04.2.5.4	Nut butters and nut spreads	QS		European Lecithin Manufacturers Association	1	5,000	5,000
04.2.5.4	Nut butters and nut spreads	QS		FDE Food and Drink Europe	1	1,000	10,000
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	QS		Rudolf Wild GmbH & Co. KG	1	600	600
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	QS		Stollwerck	1	6,000	6,500
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC	QS		FDE Food and Drink Europe	146	6,978	12,283
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC	QS		European Lecithin Manufacturers Association	11	2,486	30,000

Food category number[(a)]	Food category name	MPL	Restrictions/exceptions	Information provided by	N	Typical mean	Maximum
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC	QS		BABBI Confectionary Industry	1	2,000	2,000
05.2	Other confectionery including breath freshening microsweets	QS		FDE Food and Drink Europe	3	862	7,000
05.2	Other confectionery including breath freshening microsweets	QS		European Lecithin Manufacturers Association	3	2,250	8,000
05.3	Chewing gum	QS		European Lecithin Manufacturers Association	2	13,000	50,000
05.3	Chewing gum	QS		INTERNATIONAL CHEWING GUM ASSOCIATION	1	13,600	50,000
05.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4	QS		FDE Food and Drink Europe	62	3,811	25,943
05.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4	QS		European Lecithin Manufacturers Association	2	1,000	12,000
06.3	Breakfast cereals	QS		European Lecithin Manufacturers Association	1	3,000	3,000
07.1	Bread and rolls	QS	Except products in 7.1.1 and 7.1.2	FDE Food and Drink Europe	3	887	5,000
07.1	Bread and rolls	QS	Except products in 7.1.1 and 7.1.2	European Lecithin Manufacturers Association	3	3,000	30,000
07.2	Fine bakery wares	QS		Rudolf Wild GmbH & Co. KG	1	10	10
07.2	Fine bakery wares	QS		FDE Food and Drink Europe	37	3,342	20,000
07.2	Fine bakery wares	QS		BABBI Confectionary Industry	1	3,000	3,000
07.2	Fine bakery wares	QS		European Lecithin Manufacturers Association	13	2,000	25,000
08.3.2	Heat-treated meat products	QS	Except foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben	FDE Food and Drink Europe	1	165	318

Food category number[(a)]	Food category name	MPL	Restrictions/exceptions	Information provided by	N	Typical mean	Maximum
08.3.2	Heat-treated meat products	QS	Except foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben	European Lecithin Manufacturers Association	3	1,000	10,000
12.2.2	Seasonings and condiments	QS		European Lecithin Manufacturers Association	3	1,000	12,000
12.5	Soups and broths	QS		FDE Food and Drink Europe	5	336	2,839
12.5	Soups and broths	QS		European Lecithin Manufacturers Association	1	2,000	10,000
12.6	Sauces	QS		FDE Food and Drink Europe	13	1,459	10,688
12.6	Sauces	QS		European Lecithin Manufacturers Association	1	2,000	10,000
13.1.1	Infant formulae as defined by Commission Directive 2006/141/EC	1,000	(b)	FDE Food and Drink Europe	3	383	600
13.1.1	Infant formulae as defined by Commission Directive 2006/141/EC	1,000	(b)	SNE Specialised Nutrition Europe	7	455	1,000
13.1.1	Infant formulae as defined by Commission Directive 2006/141/EC	1,000	(b)	European Lecithin Manufacturers Association	1	1,000	1,000
13.1.2	Follow-on formulae as defined by Directive 2006/141/EC	1,000	(b)	FDE Food and Drink Europe	1	550	600
13.1.2	Follow-on formulae as defined by Directive 2006/141/EC	1,000	(b)	SNE Specialised Nutrition Europe	5	399	950
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Commission Directive 2006/125/EC	1,0000	Only biscuits and rusks, cereal-based foods, baby foods	SNE Specialised Nutrition Europe	3	1,412	2,600
13.1.4	Other foods for young children	1,0000	(b)	European Lecithin Manufacturers Association	2	1,000	10,000
13.1.4	Other foods for young children	1,0000	(b)	SNE Specialised Nutrition Europe	2	285	500
13.1.5.1	Dietary foods for infants for special medical purposes and special formulae for infants	1,000	(b)	SNE Specialised Nutrition Europe	9	513	1,000

Food category number[(a)]	Food category name	MPL	Restrictions/exceptions	Information provided by	N	Typical mean	Maximum
13.1.5.2	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC	1,000	[(b)]	SNE Specialised Nutrition Europe	6	572	930
13.1.5.2	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC	1,0000	Only biscuits and rusks, cereal-based foods, baby foods[(b)]	SNE Specialised Nutrition Europe	40	2,057	8,000
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	QS		European Lecithin Manufacturers Association	1	1,000	30,000
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	QS		FDE Food and Drink Europe	1	25	484
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	QS		SNE Specialised Nutrition Europe	74	1,753	4,215
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	QS		SNE Specialised Nutrition Europe	5	34,173	100,000
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	QS		FDE Food and Drink Europe	2	5,619	10,397
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	QS		European Lecithin Manufacturers Association	1	1,000	30,000
14.1.4	Flavoured drinks	QS		FDE Food and Drink Europe	4	25	25
14.1.5.2	Other	QS	Excluding unflavoured leaf tea; including flavoured instant coffee	FDE Food and Drink Europe	1	369	437
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15% of alcohol	QS		FDE Food and Drink Europe	1	20	20

Food category number[(a)]	Food category name	MPL	Restrictions/exceptions	Information provided by	N	Typical mean	Maximum
15.2	Processed nuts	QS		FDE Food and Drink Europe	1	62	62
16	Desserts excluding products covered in categories 1, 3 and 4	QS		FDE Food and Drink Europe	7	536	8,280
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	QS		CHEPLAPHARM Arzneimittel GmbH	1	0.02	0.02
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	QS		Nathura	4	715	1,350
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	QS		FDE Food and Drink Europe	2	5,226	15,000
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	QS		European Lecithin Manufacturers Association	2	12,750	20,000
17.3	Food supplements supplied in a syrup-type or chewable form	QS		AESGP – Association of the European Self-Medication Industry	1	14,706	18,387

MPL: maximum permitted levels; QS: *quantum satis*.

(a): FCS, Food Categorisation System (food nomenclature) presented in the Annex II to Regulation (EC) No 1333/2008.

(b): If more than one of the substances E 322, E 471, E 472c and E 473 is added to a foodstuff, the maximum level established for that foodstuff for each of those substances is lowered with that relative part as is present of the other substances together in that foodstuff.

Appendix B – Number and percentage of food products labelled with lecithins (E 322) out of the total number of food products present in Mintel GNPD per food subcategory between 2011 and 2016

Mintel sub-category[(a)]	Total number of products	Products labelled with lecithins (E 322)	
		Number	%
Individually wrapped chocolate pieces	2,380	2,044	85.9
Chocolate countlines	2,112	1,804	85.4
Seasonal chocolate	5,171	4,359	84.3
Non-individually wrapped chocolate pieces	4,798	3,832	79.9
Chocolate spreads	991	791	79.8
Other chocolate confectionery	266	212	79.7
Baby formula (6–12 months)	251	181	72.1
Gum	1,332	949	71.2
Growing up milk (1–4 years)	227	159	70
Baby formula (0–6 months)	235	162	68.9
Chocolate tablets	7,566	5,184	68.5
Growing up milk (4+ years)	3	2	66.7
Sweet biscuits/cookies	15,850	8,848	55.8
Snack/cereal/energy bars	4,345	2,205	50.7
Other frozen desserts	1,471	716	48.7
Margarine & other blends	903	429	47.5
Caramel & cream spreads	245	105	42.9
Cakes, pastries & sweet goods	11,977	5,047	42.1
Toffees, caramels & nougat	1,757	740	42.1
Dairy-based frozen products	7,236	2,991	41.3
Malt & other hot beverages	930	331	35.6
Meal replacements & other drinks	1,010	303	30
Soy-based frozen products	73	21	28.8
Mixed assortments	276	78	28.3
Beverage mixes	798	219	27.4
Cold cereals	5,621	1,539	27.4
Popcorn	991	223	22.5
Baby biscuits & rusks	274	55	20.1
Chilled desserts	5,726	1,152	20.1
Nut spreads	651	130	20
Other sugar confectionery	963	183	19
Baking ingredients & mixes	8,180	1,409	17.2
Rice snacks	363	52	14.3
Baby cereals	629	89	14.1
Dessert toppings	575	81	14.1
Wheat & other grain-based snacks	1,748	237	13.6
Rice/nut/grain & seed based drinks	963	130	13.5
Other snacks	118	15	12.7
Soy yogurt	364	44	12.1
Savoury biscuits/crackers	4,298	515	12
Snack mixes	1308	142	10.9
Lollipops	342	37	10.8
Hot cereals	1,022	96	9.4
Standard & power mints	808	67	8.3

Mintel sub-category[(a)]	Total number of products	Products labelled with lecithins (E 322)	
		Number	%
Boiled sweets	870	71	8.2
Shelf-stable desserts	2,972	241	8.1
Cream	1,471	116	7.9
Soft cheese desserts	1,397	103	7.4
Spoonable yogurt	9,079	590	6.5
Bread & bread products	9,063	555	6.1
Water-based frozen desserts	1,097	66	6
Pizzas	3,995	227	5.7
Sandwiches/wraps	2,457	136	5.5
Flavoured milk	1,316	70	5.3
Pastry dishes	1,755	91	5.2
Pastilles, gums, jellies & chews	3,411	174	5.1
Hors d'oeuvres/canapes	3,704	183	4.9
Liquorice	690	34	4.9
Stocks	1,276	60	4.7
Potato snacks	4,500	201	4.5
Marshmallows	436	18	4.1
Instant noodles	1,014	40	3.9
Medicated confectionery	931	29	3.1
Corn-based snacks	1,981	57	2.9
Meal kits	1,851	49	2.6
Baby fruit products, desserts & yogurts	1,423	35	2.5
Baby juices & drinks	339	8	2.4
Oils	3,880	87	2.2
Baby snacks	262	5	1.9
Cassava & other root-based snacks	269	5	1.9
Dry soup	1,516	29	1.9
Processed cheese	1,913	37	1.9
Fresh cheese & cream cheese	2,519	45	1.8
Other sauces & seasonings	862	15	1.7
Prepared meals	10,058	172	1.7
RTD (iced) coffee	810	11	1.4
Shortening & lard	72	1	1.4
Coffee	6,932	88	1.3
Butter	1,294	15	1.2
Liqueur	1,476	18	1.2
Sports drinks	728	9	1.2
Bean-based snacks	183	2	1.1
Instant pasta	567	6	1.1
Fish products	11,023	111	1
Meat substitutes	1,949	20	1
Tea	8,103	79	1
Rice	2,986	26	0.9
Wet soup	3,817	33	0.9
Cooking sauces	4,528	34	0.8
Fruit snacks	2,912	24	0.8
Instant rice	124	1	0.8
Liquid dairy other	119	1	0.8

Mintel sub-category[a]	Total number of products	Products labelled with lecithins (E 322)	
		Number	%
Meat pastes & pates	2,785	23	0.8
Poultry products	5,535	44	0.8
Soy based drinks	619	5	0.8
Stuffing, polenta & other side dishes	2,024	17	0.8
Pasta	9,091	63	0.7
Potato products	2,943	22	0.7
Sandwich fillers/spreads	910	6	0.7
Sweetened condensed milk	134	1	0.7
White milk	2,004	12	0.6
Creamers	189	1	0.5
Dark rum	219	1	0.5
Dips	1,306	7	0.5
Nuts	4,091	19	0.5
Pasta sauces	3,483	16	0.5
Savoury vegetable pastes/spreads	1,469	7	0.5
Seasonings	8,604	44	0.5
Artificial sweeteners	273	1	0.4
Eggs & egg products	1,303	5	0.4
Noodles	492	2	0.4
Fortified & other wines	386	1	0.3
Meat products	14,094	36	0.3
Table sauces	5,470	18	0.3
Whisky	688	2	0.3
Baby savoury meals & dishes	1,546	3	0.2
Confiture & fruit spreads	4,375	9	0.2
Dressings & vinegar	3,125	6	0.2
Drinking yogurt & liquid cultured milk	2,967	7	0.2
Mayonnaise	816	2	0.2
Soft cheese & semi-soft cheese	5,070	9	0.2
Vegetable snacks	517	1	0.2
Vegetables	9,418	20	0.2
Vodka	496	1	0.2
Energy drinks	1,539	2	0.1
Flavoured alcoholic beverages	1,816	1	0.1
Fruit	2,488	3	0.1
Fruit/flavoured still drinks	2,637	2	0.1
Hard cheese & semi-hard cheese	5,973	5	0.1
Honey	1,541	1	0.1
Nectars	3,633	5	0.1
Salads	2,378	2	0.1
Sucrose	983	1	0.1
Carbonated soft drinks	5,024	1	0
Juice	7,067	1	0
Pickled condiments	5,050	1	0
Wine	3,589	1	0
Total sample	**373,237**	**52,373**	**14.0**[b]

(a): According to the Mintel food categorisation.
(b): In total, around 14% of the foods available on the Mintel GNPD are labelled with lecithins (E 322) between 2011 and 2016.

Appendix C – Concentration levels of food additive lecithins (E 322) used in the refined exposure scenarios (mg/kg or mL/kg as appropriate)

FCS category number	FCS food category	Restrictions/exception	MPL	Concentration levels used in the refined exposure assessment scenario (only reported use levels)		Comments
				Mean	Maximum	
01.3	Unflavoured fermented milk products, heat-treated after fermentation		QS	–	–	Not taken into account (no concentration data)
01.4	Flavoured fermented milk products including heat treated products		QS	–	–	Not taken into account (no concentration data)
01.5	Dehydrated milk as defined by Directive 2001/114/EC		QS[(a)]	–	–	Not taken into account in the refined scenarios (no concentration data)
01.6.3	Cream and cream powder		QS[(a)]	–	–	Not taken into account in the refined scenarios (no concentration data)
01.7.1	Unripened cheese excluding products falling in category 16	Except mozzarella	QS[(a)]	–	–	Not taken into account in the refined scenarios (no concentration data)
01.7.5	Processed cheese		QS	–	–	Not taken into account (no concentration data)
01.7.6	Cheese products (excluding products falling in category 16)		QS	–	–	Not taken into account (no concentration data)
01.8	Dairy analogues, including beverage whiteners		QS	1,222	2,750	
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	Except virgin oils and olive oils	30,000	–	–	Not taken into account in the refined scenarios (no concentration data)
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions		QS	2,296	7,500	

FCS category number	FCS food category	Restrictions/exception	MPL	Concentration levels used in the refined exposure assessment scenario (only reported use levels)		Comments
				Mean	Maximum	
02.3	Vegetable oil pan spray		QS	–	–	Not taken into account (no consumption and no concentration data)
03	Edible ices		QS	981	6,497	
04.2.1	Dried fruit and vegetables		QS	–	–	Not taken into account (no concentration data)
04.2.2	Fruit and vegetables in vinegar, oil, or brine		QS	–	–	Not taken into account (no concentration data)
04.2.4.1	Fruit and vegetable preparations excluding compote		QS	–	–	Not taken into account (no concentration data)
04.2.5.4	Nut butters and nut spreads		QS	1,000	10,000	
04.2.6	Processed potato products		QS	–	–	Not taken into account (no concentration data)
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC		QS	6,894	12,283	
05.2	Other confectionery including breath freshening microsweets		QS	862	7,000	
05.3	Chewing gum		QS	13,600	50,000	
05.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4		QS	3,811	25,943	
06.2.2	Starches		QS	–	–	Not taken into account (no concentration data)
06.3	Breakfast cereals		QS[(b)]	–	–	Not taken into account in the refined scenarios (no concentration data)
06.4.1	Fresh pasta		QS	–	–	Not taken into account (no concentration data)

FCS category number	FCS food category	Restrictions/exception	MPL	Concentration levels used in the refined exposure assessment scenario (only reported use levels)		Comments
				Mean	Maximum	
06.4.2	Dry pasta	Only gluten-free and/or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC	QS	–	–	Not taken into account (no concentration data)
06.4.3	Fresh pre-cooked pasta		QS	–	–	Not taken into account (no concentration data)
06.4.4	Potato Gnocchi	Except fresh refrigerated potato gnocchi	QS	–	–	Not taken into account (no concentration data)
06.4.5	Fillings of stuffed pasta (ravioli and similar)		QS	–	–	Not taken into account (no concentration data)
06.5	Noodles		QS	–	–	Not taken into account (no concentration data)
06.6	Batters		QS	–	–	Not taken into account (no consumption and no concentration data)
06.7	Precooked or processed cereals		QS	–	–	Not taken into account (no consumption and no concentration data)
07.1	Bread and rolls	Except products in 7.1.1 and 7.1.2	QS	887	5,000	
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt		QS	–	–	Not taken into account (no concentration data)
07.1.2	Pain courant francais; Friss búzakenyér, fehér és félbarna kenyerek		QS	–	–	Not taken into account (no concentration data)
07.2	Fine bakery wares		QS	3,247	20,000	
08.3	Processed meat	Except foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben	QS	165	318	

FCS category number	FCS food category	Restrictions/exception	MPL	Concentration levels used in the refined exposure assessment scenario (only reported use levels)		Comments
				Mean	Maximum	
09.2	Processed fish and fishery products including molluscs and crustaceans		QS	–	–	Not taken into account (no concentration data)
09.3	Fish roe	Only processed fish roe	QS	–	–	Not taken into account (no concentration data)
10.2	Processed eggs and egg products		QS	–	–	Not taken into account (no concentration data)
11.2	Other sugars and syrups		QS	–	–	Not taken into account (no concentration data)
12.1.2	Salt substitutes		QS	–	–	Not taken into account (no consumption and no concentration data)
12.2.2	Seasonings and condiments		QS[(a)]	–	–	Not taken into account in the refined scenarios (no concentration data)
12.3	Vinegars		QS	–	–	Not taken into account (no concentration data)
12.4	Mustard		QS	–	–	Not taken into account (no concentration data)
12.5	Soups and broths		QS	336	2,839	
12.6	Sauces		QS	1,459	10,688	
12.7	Salads and savoury based sandwich spreads		QS	–	–	Not taken into account (no concentration data)
12.8	Yeast and yeast products		QS	–	–	Not taken into account (no concentration data)
12.9	Protein products, excluding products covered in category 1.8		QS	–	–	Not taken into account (no concentration data)
13.1.1	Infant formulae as defined by Commission Directive 2006/141/EC		1,000	433	1,000	

FCS category number	FCS food category	Restrictions/exception	MPL	Concentration levels used in the refined exposure assessment scenario (only reported use levels)		Comments
				Mean	Maximum	
13.1.2	Follow-on formulae as defined by Directive 2006/141/EC		1,000	424	950	
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Commission Directive 2006/125/EC	Only biscuits and rusks, cereal-based foods, baby foods	10,000	1,412	2,600	
13.1.4	Other foods for young children		10,000	285	500	
13.1.5.1	Dietary foods for infants for special medical purposes and special formulae for infants		1,000	513	1,000	
13.1.5.2	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC		1,000	572	930	
13.1.5.2	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC	Only biscuits and rusks, cereal-based foods, baby foods	10,000	2,057	8,000	
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)		QS	1,730	4,215	
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)		QS	26,014	100,000	
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) No 41/2009	Including dry pasta	QS	–	–	Not taken into account (no concentration data)

FCS category number	FCS food category	Restrictions/exception	MPL	Concentration levels used in the refined exposure assessment scenario (only reported use levels)		Comments
				Mean	Maximum	
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	Only vegetable juices	QS	–	–	Not taken into account (no concentration data)
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	Only vegetable nectars	QS	–	–	Not taken into account (no consumption and no concentration data)
14.1.4	Flavoured drinks		QS	25	25	
14.1.5.2	Other non-alcoholic beverages	Excluding unflavoured leaf tea; including flavoured instant coffee	QS	369	437	
14.2.3	Cider and perry		QS	–	–	Not taken into account (no concentration data)
14.2.4	Fruit wine and made wine		QS	–	–	Not taken into account (no concentration data)
14.2.5	Mead		QS	–	–	Not taken into account (no concentration data)
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Except whisky or whiskey	QS	–	–	Not taken into account (no concentration data)
14.2.7.1	Aromatised wines		QS	–	–	Not taken into account (no concentration data)
14.2.7.2	Aromatised wine-based drinks		QS	–	–	Not taken into account (no concentration data)
14.2.7.3	Aromatised wine-product cocktails		QS	–	–	Not taken into account (no concentration data)
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15% of alcohol		QS	20	20	
15.1	Potato-, cereal-, flour- or starch-based snacks		QS	–	–	Not taken into account (no concentration data)

FCS category number	FCS food category	Restrictions/exception	MPL	Concentration levels used in the refined exposure assessment scenario (only reported use levels)		Comments
				Mean	Maximum	
15.2	Processed nuts		QS	62	62	
16	Desserts excluding products covered in categories 1, 3 and 4		QS	536	8,280	
17.1/17.2/17.3	Food supplements		QS	4,002	18,387	
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children		QS	–	–	Not taken into account (no concentration data)

FCS: Food Classification System; MPL: maximum permitted level; QS: *quantum satis*.
(a): A level of 12,000 mg/kg was used in the maximum scenario.
(b): A level of 3,000 mg/kg was used in the maximum scenario.

Appendix D – Summary of total estimated exposure of lecithins (E 322) from their use as a food additives for the maximum level exposure scenario and the refined exposure assessment scenarios per population group and survey: mean and 95th percentile (mg/kg bw per day)

Population group	Number of subjects	MPL scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	P95	Mean	P95	Mean	P95
Infants							
Bulgaria (NUTRICHILD)	659	140	337	56	163	19	62
Germany (VELS)	159	178	368	44	108	21	49
Denmark (IAT 2006_07)	826	140	306	32	67	17	39
Finland (DIPP_2001_2009)	500	50	109	18	49	15	42
United Kingdom (DNSIYC_2011)	1,369	124	273	36	88	20	48
Italy (INRAN_SCAI_2005_06)	12	67	–	36	–	16	–
Toddlers							
Belgium (Regional_Flanders)	36	365	–	78	–	22	–
Bulgaria (NUTRICHILD)	428	295	520	76	175	18	36
Germany (VELS)	348	257	422	63	136	21	41
Denmark (IAT 2006_07)	917	253	392	39	65	13	23
Spain (enKid)	17	187	–	45	–	17	–
Finland (DIPP_2001_2009)	500	69	130	16	39	11	29
United Kingdom (NDNS-RollingProgrammeYears1-3)	185	228	401	60	137	16	32
United Kingdom (DNSIYC_2011)	1,314	208	395	50	122	15	35
Italy (INRAN_SCAI_2005_06)	36	158	–	51	–	12	–
Netherlands (VCP_kids)	322	320	517	73	162	21	38
Children							
Austria (ASNS_Children)	128	257	442	64	151	17	38
Belgium (Regional_Flanders)	625	291	482	71	141	20	34
Bulgaria (NUTRICHILD)	433	314	576	82	187	19	39
Czech Republic (SISP04)	389	231	396	60	135	17	34
Germany (EsKiMo)	835	186	317	37	80	13	27
Germany (VELS)	293	250	379	64	135	21	38
Denmark (DANSDA 2005-08)	298	215	338	34	55	12	23
Spain (enKid)	156	203	353	53	131	15	32
Spain (NUT_INK05)	399	211	331	46	99	14	25
Finland (DIPP_2001_2009)	750	71	119	16	31	7	14
France (INCA2)	482	213	362	73	145	19	35
United Kingdom (NDNS-RollingProgrammeYears1-3)	651	206	350	58	130	15	29
Greece (Regional_Crete)	838	261	476	69	165	14	31
Italy (INRAN_SCAI_2005_06)	193	182	373	54	117	13	27
Latvia (EFSA_TEST)	187	216	475	56	124	15	33
Netherlands (VCP_kids)	957	283	453	66	148	19	35
Netherlands (VCPBasis_AVL2007_2010)	447	250	408	61	140	18	33
Sweden (NFA)	1,473	205	346	59	133	16	32
Adolescents							
Austria (ASNS_Children)	237	147	276	35	86	9	19
Belgium (Diet_National_2004)	576	124	234	31	70	9	18
Cyprus (Childhealth)	303	88	165	24	57	6	14

Population group	Number of subjects	MPL scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	P95	Mean	P95	Mean	P95
Czech Republic (SISP04)	298	177	324	45	108	11	27
Germany (National_Nutrition_Survey_II)	1,011	118	235	29	77	8	20
Germany (EsKiMo)	393	145	256	28	62	10	20
Denmark (DANSDA 2005-08)	377	113	212	18	35	7	15
Spain (AESAN_FIAB)	86	94	189	25	57	6	14
Spain (enKid)	209	148	300	35	85	10	22
Spain (NUT_INK05)	651	138	248	31	67	9	17
Finland (NWSSP07_08)	306	32	59	7	15	4	8
France (INCA2)	973	122	234	39	90	10	21
United Kingdom (NDNS-RollingProgrammeYears1-3)	666	115	215	37	86	9	18
Italy (INRAN_SCAI_2005_06)	247	115	234	32	80	8	18
Latvia (EFSA_TEST)	453	169	316	41	96	11	25
Netherlands (VCPBasis_AVL2007_2010)	1,142	163	290	40	87	12	23
Sweden (NFA)	1,018	137	239	40	93	11	21
Adults							
Austria (ASNS_Adults)	308	118	237	34	84	9	19
Belgium (Diet_National_2004)	1,292	107	204	25	59	7	14
Czech Republic (SISP04)	1,666	111	211	25	66	6	14
Germany (National_Nutrition_Survey_II)	10,419	106	202	26	65	8	17
Denmark (DANSDA 2005-08)	1,739	81	139	13	23	4	9
Spain (AESAN)	410	72	143	18	52	5	11
Spain (AESAN_FIAB)	981	70	142	18	47	4	11
Finland (FINDIET2012)	1,295	87	164	21	50	6	13
France (INCA2)	2,276	92	169	24	55	6	13
United Kingdom (NDNS-RollingProgrammeYears1-3)	1,266	75	136	22	53	6	12
Hungary (National_Repr_Surv)	1,074	101	179	14	28	4	8
Ireland (NANS_2012)	1,274	88	156	19	42	5	11
Italy (INRAN_SCAI_2005_06)	2,313	73	145	17	43	4	9
Latvia (EFSA_TEST)	1,271	117	235	25	65	7	15
Netherlands (VCPBasis_AVL2007_2010)	2,057	112	199	26	56	8	16
Romania (Dieta_Pilot_Adults)	1,254	71	134	9	20	3	6
Sweden (Riksmaten 2010)	1,430	87	172	29	78	8	17
The elderly							
Austria (ASNS_Adults)	92	116	198	30	74	8	16
Belgium (Diet_National_2004)	1,215	110	199	22	48	7	14
Germany (National_Nutrition_Survey_II)	2,496	108	197	26	64	7	16
Denmark (DANSDA 2005-08)	286	77	132	12	21	4	7
Finland (FINDIET2012)	413	81	160	19	48	5	11
France (INCA2)	348	93	174	22	43	6	10
United Kingdom (NDNS-RollingProgrammeYears1-3)	305	73	133	20	50	5	10
Hungary (National_Repr_Surv)	286	95	163	14	29	3	8
Ireland (NANS_2012)	226	86	160	21	45	5	11
Italy (INRAN_SCAI_2005_06)	518	72	143	15	32	3	8
Netherlands (VCPBasis_AVL2007_2010)	173	106	182	23	45	7	16
Netherlands (VCP-Elderly)	739	103	169	21	39	7	12

Population group	Number of subjects	MPL scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	P95	Mean	P95	Mean	P95
Romania (Dieta_Pilot_Adults)	128	81	170	11	25	3	6
Sweden (Riksmaten 2010)	367	81	152	24	54	6	13

MPL: maximum permitted level; P95: 95th percentile.
–: P95 of exposure was only calculated for those population groups where the sample size was sufficiently large to allow this calculation (EFSA, 2011a).