# EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies) , 2013. Scientific Opinion on the safety of " coriander seed oil " as a Novel Food ingredient .

**EFSA Publication; Tetens, Inge; Poulsen, Morten**

*Link to article, DOI:*
10.2903/j.efsa.2013.3422

*Publication date:*
2013

*Document Version*
Publisher's PDF, also known as Version of record

## SCIENTIFIC OPINION

# Scientific Opinion on the safety of "coriander seed oil" as a Novel Food ingredient[1]

**EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)**[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

## ABSTRACT

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a scientific opinion on "coriander seed oil (CSO)" as a novel food ingredient (NFI) in the context of Regulation (EC) No 258/97. Petroselinic acid (PA) is the major fatty acid in CSO. Conventional edible oil technologies are used to manufacture the NFI. The NFI is intended to be marketed as a food supplement for healthy adults, at a maximum level of 600 mg per day (i.e. 8.6 mg/kg bw per day for a 70 kg person), which would lead to significantly higher intakes of CSO and PA than current background intakes. There are no safety concerns regarding genotoxicity. In rats fed high amounts of CSO, increased liver weight, marked to severe fat infiltration in the liver, and lower tissue arachidonic acid concentrations were observed. In the same study, similar affects were observed when feeding other vegetable oils, although not as severe as that seen for CSO. The dose level of CSO was more than a thousand fold higher than the proposed use level. In a subchronic study using 150, 450 or 1 000 mg/kg bw per day of CSO, a treatment-related effect was observed on blood glucose concentrations of male rats. Although this effect was not accompanied by any toxicological findings, its biological relevance is unclear and therefore the Panel considers the dose level of 450 mg/kg bw per day to be the NOAEL in rats. This is more than 50 fold higher than the proposed use level. No treatment-related adverse effect was observed in one human study using the NFI at the proposed use level for six months. The Panel concludes that the novel food ingredient, CSO, is safe under the proposed uses and use levels.



**KEY WORDS**

coriander seed oil, petroselenic acid, novel food, ingredient

[1] On request from the European Commission, Question No EFSA-Q-2013-00232, adopted on 10 October 2013.

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Suggested citation: EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2013. Scientific Opinion on the safety of "coriander seed oil" as a Novel Food ingredient. EFSA Journal 2013;11(10):3422, 20 pp. doi:10.2903/j.efsa.2013.3422

Available online: www.efsa.europa.eu/efsajournal

## SUMMARY

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a scientific opinion on "coriander seed oil" as a novel food ingredient in the context of Regulation (EC) No 258/97, taking into account the comments and objections of a scientific nature raised by Member States.

Coriander seed oil is a triglyceride oil, in which the monounsaturated fatty acid petroselinic acid is the main fatty acid (60-75 % of coriander seed oil). The novel food ingredient (NFI) also contains small quantities of other fatty acids such as linoleic acid, oleic acid, palmitic acid and stearic acid. The NFI is manufactured from seeds of *Coriandrum sativum* L. using conventional edible oil technologies. The applicant provided sufficient information regarding the composition, specification, manufacture and stability of the NFI.

Coriander seed oil is intended to be marketed as a food supplement for healthy adults, at a maximum level of 600 mg per day. At this use level, the intake of coriander seed oil from the NFI is estimated to be about 30-40 times higher than estimated current mean background intake of coriander seed oil, while the intake of petroselinic acid is estimated to be about 15 times higher than the intake coming from estimated current background intake of this fatty acid.

The applicant has provided *in vitro* genotoxicity studies on coriander seed oil. Based on the results of these studies, the Panel concludes that it has no safety concerns regarding genotoxicity.

Data from rats receiving a diet containing 12 % coriander seed oil (approximately 12 g/kg bw per day) or other vegetable oils for 10 weeks indicate that triacylglycerols containing petroselinic acid are hydrolysed and absorbed from the small intestine, and that petroselinic acid is metabolised to the fatty acid cis-4-hexadecenoic acid. Incorporation of petroselinic acid into the adipose triacylglycerols of the rats receiving the coriander seed oil was observed. Increased liver weight, marked to severe fat infiltration in the liver, and lower tissue arachidonic acid concentrations were seen in a 10-week rat study using 12 % coriander seed oil in the diet. These effects are not unexpected when feeding animals with high levels of an oil that has a specific fatty acid profile. In the same study, feeding of olive oil, rapeseed oil, and sunflower oil at the same level also led to marked fat infiltration in the liver, although not as severe as that seen for coriander seed oil. The dose level of coriander seed oil was more than a thousand fold higher than the proposed use level of the NFI (i.e. 8.6 mg/kg bw per day for a 70 kg person).

In a 13-week subchronic oral toxicity study in rats, 150, 450 or 1 000 mg/kg bw per day of coriander seed oil was given to three groups of 10 male and 10 female rats. A dose-dependent increase in serum glucose levels in males was observed, which reached statistical significance and was reported to be beyond background values at the high-dose level. No effect on serum glucose levels was seen in females. No other treatment-related effects were observed. Although the effect on glucose concentrations observed in male rats was not accompanied by any toxicologically relevant findings, the biological relevance of this effect is unclear and therefore the Panel considers that the dose level of 450 mg/kg bw per day is the NOAEL in this study.

Data from a controlled randomised double-blind study in healthy women, where participants received coriander seed oil at the intended use level for six months, showed no effect of coriander seed oil consumption on haematological parameters, nor on blood glucose and fatty acids concentrations, including arachidonic acid. No treatment-related adverse effect was observed.

The risk of allergic reactions to the NFI is considered not to be higher than that of other products containing coriander seeds.

There is a margin of more than 50 between the intended intake level of the NFI and the NOAEL of 450 mg/kg bw per day determined in rats, and no treatment-related adverse effect was observed in one human study at the intended dose level.

The Panel concludes that the novel food ingredient, coriander seed oil, is safe under the proposed uses and use levels.

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## BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

On 21 July 2011, the company Nestec Ltd. submitted a request under Article 4 of the Novel Food Regulation (EC) N° 258/97 to place on the market "Coriander seed oil" as a novel food ingredient (NFI).

On 19 October 2011, the competent authorities of Ireland forwarded to the Commission their initial assessment report, which came to the conclusion that coriander seed oil may be placed on the market.

On 8 November 2011, the Commission forwarded the initial assessment report to the other Member States. Several of the Member States submitted comments or raised objections.

The concerns of a scientific nature raised by the Member States can be summarised as follows:

- No data were provided on the level of tocopherols and other phenols.
- No data were provided on the NFI content of volatile compounds, which are typically contained in coriander essential oil.
- The bioavailability of petroselinic acid in the NFI vs. background diet should be considered in estimating the exposure.
- Insufficient data was provided on the metabolism of petroselinic acid and its impact on other fatty acid bioavailability and metabolism (in particular, in view of its probable action on desaturases), at doses relevant to intended exposure.
- Medium and long-term consequences have not been sufficiently evaluated, in particular with respect to potential accumulation of lipids in the liver (petroselinic acid appears to be a poor substrate for beta-oxidation and for hepatic lipase or hormone-sensitive lipase).
- The results of a study in rats has shown both a reduction of arachidonic acid in several tissues and adverse effects on the liver (Weber et al., 1995; Richter et al., 1996). The relevance of these findings to human health has to be addressed.
- The allergic potential of residual proteins or their degradation products contained in the NFI has to be further addressed.

## TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002, the European Food Safety Authority is asked to carry out the additional assessment for "Coriander seed oil" as a novel food ingredient in the context of Regulation (EC) No 258/97.

EFSA is asked to carry out the additional assessment and to consider the elements of a scientific nature in the comments raised by the other Member States.

## ASSESSMENT

In accordance with Commission Recommendation 97/618/EC[4], coriander seed oil is allocated to Class 2.1, i.e. "complex NF from non-GM source. The source of the NF has a history of food use in the Community". The assessment of the safety of this novel food ingredient (NFI) is based on data supplied in the original application, the initial assessment by the competent authority of Ireland, the concerns and objections of the other Member States and the responses of the applicant. The data are required to comply with the information required for novel foods of Class 2.1, i.e. structured schemes I, II, III, IX, X, XI, XII and XIII of Commission Recommendation 97/618/EC. In the text these structured schemes are listed 1 to 8. The intention is to market coriander seed oil for use in food supplements for skin and hair benefits. This assessment only concerns risk that might be associated with consumption, and is not an assessment of the efficacy of coriander seed oil with regard to any claimed benefit.

### 1. Specification of the Novel Food Ingredient (NFI)

Coriander seed oil (CAS No. 8008-52-4) is a triglyceride oil that is produced from the seeds of the coriander plant *Coriandrum sativum* L.[5]. The product specifications are presented in Table 1.

Petroselinic acid, a monounsaturated fatty acid, is the major fatty acid in coriander seed oil (60-75 % of the oil). Petroselinic acid (cis-6-octadecenoic acid, cis-C18:1(n-12)), is a regioisomer of oleic acid (cis-9-octadecenoic acid, cis-C18:1(n-9)).

The NFI also contains small quantities of other fatty acids, such as linoleic acid (12-19 %), oleic acid (8-15 %), palmitic acid (2-5 %) and stearic acid (< 1.5 %). The applicant provided analyses (by accredited laboratories) of the fatty acid contents of 3 non-consecutive batches of the NFI, which complied with the specifications (Table 2). The applicant provided separated analyses of the *trans* fatty acid content of the three batches (0.26 %, 0.04 % and 0.27 %, respectively), which complied with the specification.

**Table 1:** Specifications for coriander seed oil, as proposed by the applicant

| | **Specification** | **Method** |
|---|---|---|
| **Characteristics** | | |
| Colour | Slight yellow | NGD C20-1976 |
| Odour and taste | Bland | GI-31.107-1 |
| Refractive index (at 20°C) | 1.466 to 1.474 | IUPAC 2.102 |
| Acid value | Max. 0.6 mg KOH/g | Nestec LI-00.516 |
| Peroxide value | Max. 5 meq/kg | Nestec LI-03.512 |
| Iodine Value | 88 to 102 units | Nestec LI-03.507 |
| Saponification value | 186 to 198 mg KOH/g | NGD C8-1976 |
| Unsaponifiable matter | Max. 15 g/kg | IUPAC 2.401 |
| **Composition of Fatty Acids** | | |
| Palmitic acid (C16:0) | 2 to 5 % | IUPAC 1.122 |
| Stearic acid (C18:0) | < 1.5 % | IUPAC 1.122 |
| Petroselinic acid (cis-C18:1(n-12)) | 60 to 75 % | IUPAC 1.122 |
| Oleic acid (cis-C18:1(n-9)) | 8 to 15 % | IUPAC 1.122 |

[4] Commission Recommendation 97/618/EC: Commission Recommendation of 29 July 1997 concerning the scientific aspects and the presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients and the preparation of initial assessment reports under Regulation (EC) No 258/97 of the European Parliament and of the Council. OJ L 253, 16.9.1997, p. 1-36

[5] Taxonomic classification: Kingdom: *Plantae*; Phylum: *Magnoliophyta*; Class: *Magnoliopsida*; Order: *Apiales*; Family: *Apiaceae* (*Umbelliferae*); Genus: *Coriandrum* L.; Species: *Coriandrum sativum* L.

| | Specification | Method |
|---|---|---|
| Linoleic acid (C18:2) | 12 to 19 % | IUPAC 1.122 |
| α-Linolenic acid (C18:3) | < 1.0 % | IUPAC 1.122 |
| Trans Fatty Acids | Max. 1% | IUPAC 1.122 |

IUPAC: International Union of Pure and Applied Chemistry; KOH: potassium hydroxide;

**Table 2:** Batch Analysis of fatty acid content of coriander seed oil

| | Specification | Batch IZXFK | Batch IBRDF | Batch JCAKG |
|---|---|---|---|---|
| Petroselinic acid (cis-C18:1(n-12)) | 60 to 75 % | 71.41 | 67.5 | 62.08 |
| Linoleic acid (C18:2) | 12 to 19 % | 13.82 | 15.66 | 17.3 |
| Oleic acid (cis-C18:1(n-9)) | 8 to 15 % | 9.01 | 10.45 | 13.29 |
| Palmitic acid (C16:0) | 2 to 5 % | 3.19 | 3.68 | 4.02 |
| Stearic acid (C18:0) | < 1.5 % | 0.68 | 0.89 | 1.02 |
| α-Linolenic acid (C18:3) | < 1.0 % | 0.32 | 0.20 | 0.70 |
| Vaccenic acid (trans-C18:1(n-7)) | n.a. | 0.79 | 0.81 | 0.82 |
| Palmitoleic acid (C16:1) | n.a. | 0.33 | 0.33 | 0.28 |
| Arachidic acid (C20:0) | n.a. | 0.09 | 0.13 | 0.18 |
| Margaric acid (C17:0) | n.a. | 0.06 | 0.07 | 0.07 |
| Myristic acid (C14:0) | n.a. | 0.06 | 0.06 | 0.05 |
| Behenic acid (C22:0) | n.a. | 0.04 | 0.04 | 0.07 |
| Not identified | n.a. | 0.20 | 0.18 | 0.12 |
| Total fatty acids (%) | | 100 | 100 | 100 |

The applicant also provided analyses of the characteristics of four non-consecutive batches of the NFI, which complied with the specifications (Table 3).

**Table 3:** Batch analysis of the characteristics of coriander seed oil

| | Specification | Batch IBRDF | Batch JCAKH | Batch JCDTH | Batch JCDTI |
|---|---|---|---|---|---|
| Refractive index (at 20°C) | 1.466 to 1.474 | 1.471 | 1.472 | 1.472 | 1.472 |
| Acid value | Max. 0.6 mg KOH/g | 0.12 | 0.10 | 0.14 | 0.14 |
| Peroxide value | Max. 5 meq/kg | < 0.20 | 0.20 | 0.20 | 0.20 |
| Iodine value | 88 to 102 units | 99.0 | 99.5 | 98.8 | 98.8 |
| Saponification value | 186 to 198 mg KOH/g | 190 | 188 | 191 | 191 |
| Unsaponifiable matter | Max. 15g/kg | 11.60 | 13.88 | 9.42 | 9.42 |

The NFI exhibits a content of total sterols ranging from 2.4 to 3.7 g/kg. The predominant phytosterols are ß-sitosterol, stigmasterol, campesterol and δ-7-stigmastenol.

In three batches of the NFI, the protein content was lower than the limit of quantification (0.1 g/100 g) for the analytical method applied (Kjeldahl method). Following a request from a Member State (MS), an additional analysis was performed. The coriander seed oil was extracted with acetone-hexane followed by centrifugation and colorimetric quantification of the protein content. The level of protein in the five batches tested was below the detection limit of 1.5 mg/kg.

In response to a MS's request with respect to the tocopherol content of the NFI, the applicant provided the analytical results of 3 batches of the NFI, where tocopherols were below the limit of quantification (LOQ = 2 mg/100 g; analysed by HPLC).

The NFI is obtained by hexane extraction (Section 2). Results of the analysis of potential residual levels of hexane have been provided for three batches of the NFI, and were all below the limit of quantification of 0.5 mg/kg. This is in accordance with the maximum residue limit of 1 mg hexane/kg set for fats, oils and cocoa butter in Directive 2009/32/EC[6].

Regarding heavy metals, dioxins/PCBs, polycyclic aromatic hydrocarbons (specifically benzo[a]pyrene) and pesticides residues, the applicant provided test results for three batches of the NFI, which were lower than the maximum levels set in Commission Regulation (EC) No 1881/2006[7], or than the quantification limits for the analytical methods applied.

In response to an MS's request concerning the presence of volatile compounds in the NFI, the applicant indicated that the oil undergoes vacuum deodorisation for 3.5 hours at 200 °C, and is therefore unlikely to contain any significant levels of such compounds.

The Panel considers that the information provided on the composition, specification and data from batch testing do not raise safety concerns.

*Stability*

The NFI has to be stored in light protected and airtight conditions, under cool and dry conditions with temperature not exceeding 20 °C. Under these storage conditions, data provided by the applicant confirms that the NFI is stable for at least 12 months.

The analyses of the acid value and the peroxide value of the NFI indicate that when stored under appropriate conditions, the coriander seed oil would not be significantly oxidised or hydrolysed.

The Panel considers that the data provided sufficient information with respect to the stability of the NFI.

## 2. Effect of the production process applied to the NFI

Coriander seed oil is manufactured from seeds of the coriander plant *Coriandrum sativum* L.. Seeds are mechanically pressed, then processed on a rolling mill to obtain a flaked cake. The crude oil is extracted using hexane and neutralised with a sodium hydroxide solution. The oil is then washed with water and subsequently bleached with 1.5 % bleaching earth, 1.0 % activated carbon, and 0.5 % amorphous silica gel. The bleached oil is winterised with perlite 1200S to absorb impurities from the oil, and is deodorised with steam to obtain the fully refined coriander seed oil.

The applicant provided the specifications for the coriander seeds used for the manufacturing process with respect to their oil content (> 20 %), water content (< 9 %), level of impurity (< 2 %) and broken seeds (< 5 %). The applicant indicates that the other materials are typically used in the oil refining industry. Activated carbon (Carbopal®) is used to remove dissolved organic compounds such as polycyclic aromatic hydrocarbons in oils, and for controlling odour and taste. Bleaching earth (Tonsil® Supreme 110 FF) is acidified, and is used to remove polar compounds via adsorption. Amorphous silica gel (TriSyl®) is also used in the refining of the oil.

[6] Directive 2009/32/EC of the European Parliament and of the Council of 23 April 2009 on the approximation of the laws of the Member States on extraction solvents used in the production of foodstuffs and food ingredients (Recast) (Text with EEA relevance), OJ L 141, 6.6.2009, p. 3-11

[7] Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs, OJ L 364, 20.12.2006, p. 5-24.

The applicant's manufacturing subsidiary for speciality oils is independently certified to have a valid HACCP system in place in accordance with Regulation (EC) N. 852/2004[8]. The applicant also applies ISO 22000:2005[9].

The manufacturer uses conventional edible oil manufacturing procedures. The Panel concludes that the production process is sufficiently described and does not raise safety concerns.

## 3. History of the organism used as a source

The applicant indicates that the seeds used come from *Coriandrum sativum* L.. Ground or whole coriander seeds are commonly used as food seasonings (Kiralan et al., 2009). The ground seeds are one of the major constituents of curry powder.

## 4. Anticipated intake/extent of the use of the NFI

Coriander seed oil is proposed to be supplied as a food supplement at a maximum level of 600 mg per day (three 200 mg tablets per day; equivalent to 8.6 mg/kg bw/day for a 70 kg person).

The applicant indicates that these supplements are intended for healthy adults. It is not aimed at children and pregnant and lactating women.

## 5. Information from previous exposure to the NFI or its source

Coriander-distilled essential oil has been in use as a food flavouring and fragrance ingredient since the 1900s (Opdyke, 1973). Coriander essential oil also has a long history of use as a traditional medicine (Burdock and Carabin, 2009). Coriander essential oil has been approved for use in medicines (as active ingredient or excipient) and flavourings in Canada (Health Canada, 2007, 2009), Australia (Therapeutic Goods Administration, 2007) and the United States (U.S. FDA, 2011).

Use of coriander seeds as a source of flavouring materials was considered by the Council of Europe, and was concluded to be acceptable for addition to foodstuffs as a herb, spice or seasoning with possible limitation of the active principle in the final product (Council of Europe, 1981).

### 5.1. Background consumption of coriander seeds

The applicant provided estimates of the background intakes of coriander seed in the UK population using consumption data from the UK National Diet and Nutrition Survey (NDNS). Alcoholic beverages (e.g. coriander-flavoured spirits) and curry powder were considered as the main sources of exposure. Calculations were based on the assumption that all curries consumed by individuals in the UK NDNS were made with curry powder containing 23 % coriander seed.

Estimates of the daily intake of coriander seed were calculated at individual level, and represent projected 7-day averages. The distribution from which mean and high percentile intake estimates were produced was comprised of these average amounts. Results are provided in Table 4.

[8] Regulation (EC) No 852/2004 of the European Parliament and of the Council of 29 April 2004 on the hygiene of foodstuffs, OJ L 139, 30.4.2004, P. 1-54

[9] ISO 22000:2005 specifies requirements for a food safety management system, for any organisation in the food chain.

**Table 4:** Summary of the estimated daily intake of coriander seed from all background food categories in the UK by population group (UK NDNS data)

| Population Group | Age Group (Years) | % User | Actual Number of Total Users | All-Person Consumption | | | | All-Users Consumption | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Mean (mg) | Percentile (mg) | | | Mean (mg) | Percentile (mg) | | |
| | | | | | 90 | 95 | 97.5 | | 90 | 95 | 97.5 |
| Children | 1½ -4½ | 43.0 | 709 | 13 | 34 | 47 | 63 | 31 | 51 | 69 | 101 |
| Young People | 4-10 | 62.2 | 521 | 36 | 61 | 118 | 249 | 58 | 95 | 206 | 323 |
| Female Teenager | 11-18 | 64.1 | 286 | 95 | 115 | 519 | 998 | 127 | 149 | 697 | 1 051 |
| Male Teenager | 11-18 | 69.5 | 289 | 100 | 147 | 605 | 1 117 | 139 | 286 | 933 | 1 128 |
| Female Adult | 16-64 | 61.1 | 585 | 61 | 99 | 217 | 630 | 95 | 145 | 520 | 986 |
| Male Adult | 16-64 | 67.6 | 518 | 76 | 128 | 254 | 810 | 104 | 172 | 486 | 991 |

According to the applicant, coriander seeds contain up to 20 % oil. The estimated mean daily intake of coriander seed oil from intake of coriander seeds is thus around 15 and 20 mg for adult all-persons (i.e. total population) and adult all-users (i.e. consumers of coriander seeds containing products only), respectively. The intake coming from the proposed 600 mg coriander seed oil from supplements is about 30-40 times higher than the estimated mean background intake of coriander seed oil. For adult all-users in the 95$^{th}$ percentile, the estimated daily intake of coriander seed oil from the intake of coriander seed is about 100 mg.

### 5.2. Background consumption of petroselinic acid

The applicant indicates that petroselinic acid is also present in other seeds for human consumption, including seeds from anise, dill, parsley, fennel and celery. Estimates of the background intakes of petroselinic acid were calculated using consumption data from the UK NDNS and ingredient lists of food product containing these seeds, such as alcoholic beverages, curry powders, industry-prepared curry sauces, pickles, seasonings and spice mixes and soup powders. The petroselinic acid content in seeds was derived from published literature sources, and based on the amount of fatty acids in the seed oil per seed type. The maximum percentage content of petroselinic acid from all seed types (18.1 %) was used in the calculation. The resulting estimated daily intake of petroselinic acid from all background food categories are shown in Table 5.

**Table 5:** Summary of the estimated daily intake of petroselinic acid from all background food categories in the UK by population group (UK NDNS Data)

| Population Group | Age Group (Years) | % User | Actual Number of Total Users | All-Person Consumption | | | | All-Users Consumption | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Mean (mg) | Percentile (mg) | | | Mean (mg) | Percentile (mg) | | |
| | | | | | 90 | 95 | 97.5 | | 90 | 95 | 97.5 |
| Children | 1½ -4½ | 77.2 | 1,273 | 10 | 21 | 28 | 36 | 12 | 24 | 30 | 43 |
| Young People | 4-10 | 91.5 | 766 | 19 | 29 | 43 | 72 | 20 | 31 | 44 | 77 |
| Female Teenager | 11-18 | 87.4 | 390 | 39 | 43 | 213 | 394 | 39 | 43 | 159 | 394 |
| Male Teenager | 11-18 | 92.1 | 383 | 41 | 55 | 240 | 393 | 44 | 56 | 297 | 420 |
| Female Adult | 19-64 | 80.4 | 770 | 25 | 32 | 57 | 234 | 29 | 35 | 110 | 271 |
| Male Adult | 19-64 | 86.9 | 666 | 30 | 43 | 69 | 325 | 32 | 45 | 71 | 337 |

According to the intake data provided by the applicant, the estimated mean daily intake of petroselinic acid from all background sources would be around 30 mg for adults. The amount of petroselinic acid (ca. 450 mg) coming from the proposed 600 mg coriander seed oil from supplements is about 15 times higher than the intake coming from estimated mean background intake of petroselinic acid. For adult all-users in the 95$^{th}$ percentile, the daily intake of petroselinic acid is about 100 mg.

The Panel notes that these estimates are based on a number of assumptions which overestimate actual background intakes of coriander seed oil and petroselinic acid by the population.

## 6. Nutritional information on the NFI

The main constituent of the NFI is petroselinic acid, which is a monounsaturated fatty acid (60-75 % of coriander seed oil). Lower proportions of other fatty acids such as linoleic, oleic, palmitic and stearic acid are also present (Section 1).

The applicant indicates that coriander seed oil is intended to be marketed as a food supplement and is not anticipated to replace other foods in the diet.

The Panel considers that consumption of the NFI is not nutritionally disadvantageous.

## 7. Microbiological information on the NFI

The applicant provided results for three batches of the NFI. Total aerobic count and *Enterobacteria* were lower than the quantification limit (10 UFC/mL) and *Salmonella spp.* were absent in 25 g.

The Panel considers that the microbiological information provided does not raise safety concern.

## 8. Toxicological information on the NFI

### 8.1. Absorption, Distribution, Metabolism and Excretion

In a study by Heimermann et al. (1973), fifteen triacylglycerols, containing C12:0, C14:0, C16:0, C18:2 and positional isomers of cis-C18:1 fatty acids, were hydrolysed by pancreatic lipase and the resulting free fatty acids were analysed by gas liquid chromatography. The study indicated that the presence of a double-bond near the carboxyl group of an acid, like in petroselinic acid, slows its hydrolysis from a triacylglycerol. Another study by Seher and Fiebig (1983) also describes that the incubation (5 min) of model mixtures of petroselenic-containing triglycerols with pancreatic lipase and fungal lipases, respectively, resulted in maximum hydrolysis rates of 20 %. Thus, both of the two *in vitro* studies indicate that triacylglycerols containing petroselinoyl moieties are hydrolysed at slower rates than other triacylglycerols.

A number of publications addressed the effects of a diet containing 12 % coriander oil (72 % petroselinic acid) given to rats for 10 weeks on hepatic lipid profile (Weber et al., 1997), the concentrations of arachidonic acid in body tissues (blood, liver, and heart) (Weber et al., 1995), and the distributions of fatty acid moieties contained within triacylglycerols of adipose tissue (Weber et al., 1999; Weber et al., 2003). Considering the composition of the oil used, the Panel assumes that it was derived from coriander seeds.

Groups of 10 male Wistar rats were administered coriander seed oil, olive oil, high-oleic sunflower oil (HOS), rapeseed oil, or conventional sunflower oil in the diet, at concentrations of 12 % for a period of 10 weeks (Weber et al., 1995). The Panel notes that this is equivalent to approximately 12 g/kg bw (EFSA SC, 2012).

No early deaths were recorded, and body weights, food intake and efficiency were comparable among the groups. Liver weights of rats in the coriander seed oil-treated group were significantly higher than in the four other groups. Liver lipid levels were significantly higher in the coriander and olive oil groups compared to the HOS group. Heart, spleen, kidney, and testes weights were comparable among all groups, as were levels of plasma total cholesterol, high-density lipid (HDL) cholesterol, and triacylglycerols. Rats in the coriander seed oil group had significantly lower levels of faecal triacylglycerols compared to the HOS and olive oil groups. No significant differences in fat absorption were seen between the groups. Rats fed coriander seed oil had petroselinic acid incorporated in their heart, liver and blood lipids, whereas arachidonic acid levels were significantly lower (up to 50 %) compared to the HOS group. Additionally, significantly higher levels of linoleic acid were observed in

tissue and blood lipids from the coriander seed oil group compared to the HOS group. Thus, the data indicate that *in vivo* the triglycerides in coriander seed oil are hydrolysed by lipases and petroselinic acid is absorbed. According to the authors, petroselinic acid at this high dose level partially inhibits the processes that lead to the formation of arachidonic acid (i.e. desaturation and chain elongation) in rats.

In order to determine the metabolic fate of petroselinic acid in the liver, and its effect on hepatic lipid profile, groups of male Wistar rats (10 per group) were provided coriander or high-oleic sunflower oil in the diet at concentrations of 12 % for a period of 10 weeks (Weber et al., 1997). The coriander seed oil comprised petroselinic acid (72.4 %), linoleic acid (18.6 %), palmitic acid (5.4 %), oleic acid (2.5 %), stearic acid (0.4 %), and other fatty acids (0.7 %). In comparison, the high-oleic sunflower oil contained oleic acid (75.0 %), linoleic acid (14.7 %), palmitic acid (5.9 %), stearic acid (2.8 %), and other fatty acids (1.6 %). Following the 10-week test feeding period, rats were necropsied and the livers were removed and analysed for fatty acid composition of the lipid fraction.

Petroselinic acid was only observed in the liver lipids from rats provided coriander seed oil. Likewise, only coriander seed oil-treated rats were observed to accumulate cis-8-eicosenoic acid (C20:1(n-12)) and cis-4-hexadecenoic acid (C16:1(n-12)) in their livers. Based on the absence of these two fatty acids in the high-oleic sunflower oil group, the authors suggested that petroselinic acid is subject to elongation, resulting in cis-8-eicosenoic acid, and β-oxidation, forming cis-4-hexadecenoic acid. No metabolites resulting from desaturation-elongation reactions were observed in the coriander seed oil-fed group. In comparison to the high-oleic sunflower oil group, higher levels of linoleic acid were observed in the coriander seed oil group (16.1 % vs. 9.0 %), accompanied by lower levels of arachidonic acid (10.0 % vs. 16.7 %), suggesting that petroselinic acid interfers with synthesis of arachidonic acid from linoleic acid. According to the authors, inhibition may be the result of petroselinic acid inhibiting Δ-desaturase which converts linoleic acid to γ-linolenic acid by mimicking a product of Δ-desaturase. Overall, petroselinic acid was shown to be absorbed and primarily metabolised to cis-8-eicosenoic acid and cis-4-hexadecenoic acid.

In two other papers by the same group (Weber et al., 1999; Weber et al., 2003), the fatty acid composition of adipose tissue (epididymal, subcutaneous and perirenal) of the rats was found to broadly reflect the fatty acid composition of the oils administered. It was shown that petroselinic acid from the coriander seed oil was extensively incorporated into adipose triacylglycerols. It was further demonstrated that also the regiospecific distribution of the major acyl moieties of the subcutaneous adipose tissue broadly reflected the distribution of the acyl moieties in the oils given to the rats.

In another experiment, petroselinic acid, oleic acid and cis-C18:1(n-10) were given in concentrations up to 5 % of the diet to groups of six rats for three weeks, through a combination of parsley seed oil, sunflower seed oil, olive oil and ethyl-cis-8-octadecenoate (Hoy and Holmer, 1981). Diets differed in their content in octadecenoic acids but had similar contents of saturated, mono-unsaturated and poly-unsaturated fatty acids. Petroselinic acid was shown to be incorporated into lipids in the liver and into adipose tissue, but at a slower rate than cis-C18:1(n-10). The fatty acids in the total lipids of adipose tissue were mirroring the dietary intake of fatty acids; no difference between groups was observed in the adipose tissue profile for the other major fatty acids analysed (C14:0, C16:0, C16:1, C18:0, C18:2). The fatty acids in the diet did not affect the amount of polyunsaturated fatty acids in the phospholipids of the liver mitochondrial membrane.

The Panel concludes that triacylglycerols containing petroselinic acid appear to be hydrolysed *in vivo* and absorbed from the small intestine. Some data indicate that petroselinic acid is metabolised to the fatty acid cis-4-hexadecenoic acid (Weber et al., 1997). Coriander seed oil, at high concentrations (12 % in the diet) and as the primary lipid source, appears to interfere with the formation of arachidonic acid from linoleic acid, probably through an effect on desaturation and elongation pathways (Weber et al., 1995; Weber et al., 1997). At high doses, lipid profiles of liver and other tissues have been observed to be altered (Weber et al., 1995; Weber et al., 1997; Weber et al., 1999; Weber et al., 2003).

Changes in liver tissue arachidonic acid concentrations or hepatic lipid profiles have also been observed with high doses of other fats and oils. In a study by Caster et al. (1966), rats were given diets with 10 % common natural fats or oils, and mixtures hereof for 66 days. The diets with the different fats and oils resulted in significant changes in the liver lipid profile. Feeding rats with up to 21 % of isomeric cis- and trans- octadecenoic acid in the diet lowered the level of arachidonic acid in the liver lipids by 35 % compared with control animals given an isocaloric diet with primarily beef tallow (Lawson et al., 1983).

The Panel notes that it is generally recognised that the rat is not a good model for studying fatty acid metabolism in humans.

The applicant provided preliminary results from a 4-week randomised controlled human trial in 72 healthy women, measuring plasma concentrations of petroselinic acid after daily consumption of 600 mg of coriander seed oil (3 x 200 mg/day, n = 24 or 600 mg/day, n = 24) or a placebo (paraffin oil, n = 24) (unpublished study report by Lissy et al. (2012)), which indicate that petroselinic acid is absorbed. The Panel notes that the information available from the graphs provided on the level of absorption of petroselenic acid were scarce, and that limited conclusions can be drawn from these data.

### 8.2. Genotoxicity

The coriander seed oil was tested using the *in vitro* bacterial reverse mutation assay (plate incorporation and pre-incubation methods) with *Salmonella typhimurium* strains (TA98, TA100, TA1535, TA1537, and TA102) with and without metabolic activation (compliant with OECD test guideline No 471 and GLP (Good Laboratory Practice)) (unpublished study report by Chalendard and Liang (2009a)). The coriander seed oil was tested as an emulsion, dispersed in ethanol. To account for the state of the test substance (i.e. emulsion), bacteria were exposed to concentrations of up to 16 000 µg/plate of coriander seed oil. Coriander seed oil was tested negative for mutagenicity in the absence and presence of metabolic activation in the five *S. typhimurium* strains tested.

The coriander seed oil was tested using an *in vitro* mouse lymphoma TK+/- assay (L5178Y mouse lymphoma cells), following a long exposure period (24 hours) without metabolic activation and with a short exposure period (four hours), with or without metabolic activation (compliant with OECD test guideline No 476 and GLP) (unpublished study report by Chalendard and Liang (2009b)). The coriander seed oil was in the form of an emulsion (in ethanol) and concentrations of up to 8 000 µg/mL were tested. Coriander seed oil tested negative for genotoxicity in the absence and presence of metabolic activation.

The Panel concludes that the NFI is not genotoxic under the conditions of these assays.

### 8.3. Acute Toxicity Studies

The applicant did not provide data on the acute toxicity of coriander seed oil.

### 8.4. Subchronic/Chronic Toxicity Studies

One study conducted with a coriander oil includes a number of parameters that can be used in a safety assessment, although it is not a conventional safety study (Richter et al., 1996). In this study, male Wistar rats (85-90 g) were divided into groups of 10 and fed a diet containing 12 % coriander oil (approximately 12 g/kg bw, see Section 8.1) and 2 % corn oil, for a period of 10 weeks. The coriander oil contained 72 % petroselinic acid. Considering the composition of the oil, the Panel assumes that it was derived from coriander seeds. Additional groups of rats were given 12 % high-oleic sunflower oil, sunflower oil, olive oil, or rapeseed oil. A control group (n = 5) was administered a standard diet with 4 % fat. At termination, anatomical and histological examinations of the liver, heart, aorta, stomach and spleen were performed.

All high-fat diets induced fatty livers with total lipid contents of 7.1-9.7 %. At the histological examination of the livers, hepatocytes with mixed-size lipid vesicles, mainly periportal, were seen in all groups given high-fat diets. In the group given coriander seed oil, the fat infiltration was more pronounced (average degree: 2.3 vs. 1.6-1.9), and large macrovesicular lipid droplets (fatty cysts) were seen as well. Only a very low degree of these effects was seen in the control group. In various animals fed coriander seed oil, enlarged nuclei were observed in liver cells without fat infiltration when compared to animals fed standard diet. No such effect was observed in the other groups. No indications of inflammatory reactions were observed in these animals. Histological examination of the heart, aorta, stomach and spleen revealed no histopathological lesions in these organs. The authors suggest that the observed severe fat infiltration in the liver of coriander seed oil-fed rats could be due to the low activity of the liver lipase to hydrolyse triacylglycerols containing petroselinic acid, and the limited metabolism of petroselinic acid. In addition, it is suggested that the enlarged nuclei of some of the liver cells could have been caused by a stimulation in response to cell degeneration or cell death (e.g. as a result of fatty cyst formation).

The Panel considers that the significant fat infiltrations observed in all groups except the control group is most likely a result of the high fat level in the diet. However, the Panel notes that the fat infiltration and histopathological alterations observed in the coriander seed oil group appeared to be more pronounced.

The applicant commissioned a 13-week subchronic oral toxicity study in rats (unpublished study report by Giorgi et al. (2010)), which followed the OECD test guideline No 408 and the principles of GLP. The study was carried out by giving (oral gavage) 150, 450 or 1 000 mg/kg body weight per day of coriander seed oil to three groups of 10 male and 10 female Wistar Crl:WI (Han) rats for 13 weeks. A group of 10 rats per sex received the vehicle (1 % carboxymethylcellulose in water with 5 % Tween 80) and served as the negative control. Two additional groups of five male and five female animals were administered the high dose or vehicle for 13 weeks, and received a standard rodent diet for four weeks thereafter (recovery group). Rats were housed in groups of five of the same sex. During the study, the following parameters were monitored: clinical condition, functional observation, body weight, food consumption, ophthalmic examination, haematology, blood chemistry, urinalysis, organ weight, macropathology and histopathological investigations.

Mean body weight and body weight gains over the 13-week period were noted to be slightly lower (less than 10 %) in treated males, particularly at the low- and mid-dose levels compared to controls (not statistically significant). During the four week post-treatment period, significantly lower body weight gains were observed in some weeks in the high-dose males of the recovery group. The body weights of female rats were not affected. Food consumption was slightly lower (up to 10 %), but not statistically significant, in male and female rats given the coriander seed oil. The effect was more pronounced in the medium and high dose groups. The same tendency was seen for males but not females in the post-treatment period. The reduced food consumption of the dosed animals is most likely due to the daily intake of coriander seed oil through gavage. The decreased body weight gain of males is probably a consequence of the reduced feed intake, and is not considered to be adverse.

In haematology, a statistically significant increased count of large unstained cells was seen for the medium and high dose group in males compared to the control group. No difference for this parameter was seen for the recovery group and females. A significantly higher activated partial thromboplastine time was seen in high dose males, but in the recovery group only. These are regarded as incidental findings.

For the clinical chemistry parameters, a dose-dependent increase in serum glucose levels in males was observed, which reached statistical significance at the high-dose level (mean ± SD, control group: 7.53 ± 1.24 mmol/L; low dose group: 7.59 ± 0.64 mmol/L; intermediate dose group: 8.01 ± 0.05 mmol/L; high dose group: 10.00 ± 1.51 mmol/L). The glucose concentration in the male high dose group was reported to be beyond background values in male rats (6.25 ± 0.91 mmol/L), and

is probably a treatment-related effect. No effect on serum glucose levels was seen in the male recovery group and in females.

A significant reduced sodium and increased creatinine level were seen for the high dose male group. For the medium and high dosed males a reduced total bilirubin level was observed. None of the above-mentioned effects in relation to clinical chemistry was apparent in the recovery and female groups. All female dose groups had increased calcium levels, which showed no dose-response. Activity of aspartate aminotransferase was significantly reduced in the female high dose group. A significantly higher protein concentration was seen in the male recovery group compared to the control group. The observed differences in relation toclinical chemistry parameters were either seen in only one sex, were not dose-related, did not appear in the recovery group, or appeared only in the recovery group.

For the urinalysis, a significant reduction in urine volume in all male test groups compared to controls was seen at the end of the treatment period. The decreased urine volume could be a physiological response, but no measurements of water intake were performed during the study that could clarify this.

The relative mean thymus weights were significantly greater in mid-dose males compared to controls. Given the absence of a dose-dependent response, this was not considered to be biologically significant. In females, absolute brain and heart weights were significantly lower compared to controls, but only in the recovery group. No significant differences were seen for any organ, including the liver, at the macro- and microscopic examinations.

Although the effect on glucose concentrations observed in male rats was not accompanied by any toxicologically relevant findings, the biological relevance of this effect is unclear, and therefore the Panel considers that the dose level of 450 mg/kg bw per day is the NOAEL in this study.

### 8.5. Developmental and Reproductive Toxicity Studies

The applicant did not provide data on the reproductive and developmental toxicity of coriander seed oil.

### 8.6. Human Studies

The applicant provided results from a human clinical study conducted to investigate potential beneficial effects of the NFI (unpublished study report by Hoffmann (2013)). In this controlled randomised double-blind study in healthy Caucasian women aged between 18 and 50 years, one group received the test product coriander seed oil (600 mg/day, n = 72) and the other group received the placebo, paraffin oil (n = 71), for six months. Blood samples were collected at baseline (day 1), day 20-28, day 76-84 and day 160-168 (termination of study) and analysed for haematological parameters, triglycerides, cholesterol, urea, creatinine and glucose concentrations. No significant difference between the placebo group and the coriander seed oil group was observed for any of the blood parameters. The coriander seed oil was well tolerated and no adverse effects related to treatment with coriander seed oil were observed.

In response to an MS comment, the applicant performed analyses of serum fatty acid content in a sub-group of 16 subjects of the placebo group and 20 subjects of the treatment group (unpublished study results). Concentrations of arachidonic acid, docosahexaenoic acid (DHA), oleic acid and cis isomers, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids 18:2 and 18:3, long-chain polyunsaturated fatty acids and total fatty acids were measured. In both sub-groups, no significant change from baseline was observed for any parameter. No between-group comparisons were performed. The applicant also provided raw data of serum content of C18:1 fatty acid isomers in both sub-groups (unpublished study results).

The Panel considers that no treatment-related adverse effects were observed in healthy women consuming the NFI at a dose of 600 mg/day for six months.

## 9. Allergenicity

Allergenicity (including dermatitis) to coriander has been previously described in case reports (Suhonen et al., 1979; Kanerva and Soini, 2001; Ebo et al., 2006). Sensitisation to the Apiaceae family of spices was reported to be high following skin prick tests in children (< 15 years old) and adults (Moneret-Vautrin et al., 2002). A case report of a 26 year-old woman who presented with multiple systemic reactions including urticaria and laryngeal angioedema following ingestion of carrots cooked in sunflower oil and margarine was identified (Moneret-Vautrin et al., 2002). Subsequent food allergen tests revealed highly positive results to Apiaceae and Compositae. A double-blind, placebo-controlled food challenge (DBPCFC) to 265 mg coriander resulted in sneezing and rhinorrhea. Nasal dysfunction increased 1 hour 30 minutes after ingestion. Conjunctivitis occurred an hour later.

The applicant indicates that no reports of allergenicity to coriander seed oil have been reported in the literature to date.

The applicant notes that the ingredient intended for use as a food supplement is the seed oil, rather than any protein containing fraction. Based on UK NDNS survey data, the applicant estimated a daily mean background exposure to coriander seed proteins from the diet of around 10-15 mg. Assuming the sensitivity of the Kjeldahl test method, the applicant calculated that, assuming an intake of 600 mg coriander seed oil, an exposure of 0.6 mg per person per day (or 0.2 mg per serving) of coriander seed protein would result from consumption of the NFI, which is much lower than the amount of protein inducing allergic reactions in the DBPCFC study by Moneret-Vautrin et al. (2002). It would therefore constitute no additional risk of allergenicity to the general population.

The Panel considers that the risk of allergic reactions to the NFI is not higher than that of other products containing coriander seeds.

## DISCUSSION

Coriander seed oil is a triglyceride oil which is produced from the seeds of the coriander plant *Coriandrum sativum* L.. Petroselinic acid, a monounsaturated fatty acid, is the major fatty acid of coriander seed oil (60-75 %). The NFI also contains small quantities of other fatty acids such as linoleic acid, oleic acid, palmitic acid and stearic acid.

The Panel notes that the information provided on the manufacturing process, as well as on the composition, specification and nutritional value of the NFI, is sufficient, and does not raise safety concerns.

Coriander seed oil is proposed for use as a food supplement for healthy adults at a maximum level of 600 mg per day. The estimated mean and 95$^{th}$ percentile daily adult intake of coriander seed oil from intake of coriander seed is around 20 mg and 100 mg for all-users, respectively. The anticipated intake of the NFI is about 30 and 6 times higher than estimated background intake, respectively. The estimated mean and 95$^{th}$ percentile daily adult intake of petroselinic acid from all background sources is around 30 mg and 100 mg, respectively. The anticipated intake of petroselinic acid through the NFI is about 15 and 5 times higher than the estimated background intake of this fatty acid, respectively. The anticipated intake of the NFI will therefore be significantly higher than current background consumption of coriander seed oil and petroselinic acid.

Triacylglycerols containing petroselinic acid appear to be hydrolysed *in vivo* and absorbed from the small intestine, although at a slower rate than other fatty acids of similar chain length.

The Panel notes that significantly increased liver weight and marked-to-severe fat infiltration in the liver were seen in a 10-week rat study using a high dose level of coriander seed oil (12 % in the diet). In addition, changes in the fatty acid composition of hepatic and adipose tissues were observed, including lower concentrations of arachidonic acid. These effects were to some extent to be expected when feeding animals with high levels of an oil that has a specific fatty acid profile. In the same studies, feeding of olive oil, rapeseed oil, and sunflower oil at the same level also led to marked fat

infiltration in the liver, although not as severe as that seen for coriander seed oil. The dose level of coriander seed oil in these studies was approximately 12 g/kg bw per day, which is more than a thousand fold higher than the exposure to the NFI estimated under the proposed conditions of use as a food supplement (i.e. 600 mg/day or 8.6 mg/kg bw/day for a 70 kg person).

Although the effect on glucose concentrations observed in male rats in the subchronic 13-week toxicity study was not accompanied by any toxicological relevant findings, the biological relevance of this effect is unclear, and therefore the Panel considers that the dose level of 450 mg/kg bw per day is the NOAEL in this study. This dose is about 50 fold higher than the anticipated exposure under the proposed conditions of use.

Data from the controlled randomised double-blind study in healthy women where participants received coriander seed oil (600 mg/day) for six months showed no effect on haematological parameters, nor on blood glucose and fatty acid concentrations, including arachidonic acid.

The Panel considers the nature of the NFI, the fact that the margin between the intended intake and the NOAEL of 450 mg/kg bw per day in the subchronic 13-week rat toxicity study is sufficient, and the fact that no adverse effect was observed in one human study at the intended dose level.

## CONCLUSIONS

The Panel concludes that the novel food ingredient, coriander seed oil, is safe under the proposed uses and use levels.

## DOCUMENTATION PROVIDED TO EFSA

1. Dossier "Application for the Approval of Coriander Seed Oil for Use in Foods for the General Population and Food Supplements Under Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 Concerning Novel Foods and Novel Food Ingredients" received on 19 February 2013. Submitted by Nestec Ltd. on 21 July 2011. Additional data were provided on 02 July 2013.
2. Letter from the European Commission to the European Food Safety Authority with the request for an opinion on the safety of 'Coriander Seed Oil'. SANCO/E6/Ak/ks D (2013) 196714, dated 14 February 2013.
3. Initial assessment report carried out by the Food Safety Authority of Ireland: 'Safety Assessment of Coriander Seed Oil'.
4. Member States' comments and objections.
5. Response by the applicant to the initial assessment report and the Member States' comments and objections.

## REFERENCES

Burdock GA and Carabin IG, 2009. Safety assessment of coriander (Coriandrum sativum L.) essential oil as a food ingredient. Food and Chemical Toxicology, 47, 22-34.

Caster WO, Mohrhauer H and Holman RT, 1966. Effects of twelve common fatty acids in the diet upon the composition of liver lipid in the rat. Journal of Nutrition, 89, 217-225.

Chalendard M and Liang C, 2009a. Coriander Seed Oil, Type C – Bacterial Reverse Mutation Test (Plate Incorporation and Pre-incubation Methods). (Study number: AA78240). Unpublished proprietary study report. Prepared by MDS Pharma Services, Lyon, France for Nestlé Research Center, Chemical Food Safety, Quality & Safety Department, Lausanne, Switzerland. 49 pp.

Chalendard M and Liang C, 2009b. Coriander Seed Oil, Type C – In Vitro Mammalian Cell Gene Mutation Test on L5178Y Mouse Lymphoma Cells TK+/- (Microwell Method). (Study number: AA78241). Unpublished proprietary study report. Prepared by MDS Pharma Services, Lyon,

France for Nestlé Research Center, Chemical Food Safety, Quality & Safety Department, Lausanne, Switzerland. 70 pp.

Council of Europe, 1981. Coriander. In: Flavouring Substances and Natural Sources of Flavourings, 3rd ed. Strasbourg, France, p. 76.

Ebo DG, Bridts CH, Mertens MH and Stevens WJ, 2006. Coriander anaphylaxis in a spice grinder with undetected occupational allergy. Acta Clinica Belgica, 61, 152-156.

EFSA SC (EFSA Scientific Committee), 2012. Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. EFSA Journal 2012;10(3):2579, 32 pp. doi:10.2903/j.efsa.2012.2579.

Giorgi H, Drevon-Gaillot E, Howroyd P and Liang C, 2010. Coriander Seed Oil, Type C-13-week Oral (Gavage) Toxicity Study in Rat Followed by a 4-week Treatment-Free Period. (Study number: AA78242). Unpublished proprietary study report. Prepared by MSDS Pharma Services for Nestlé Research Center, Chemical Food Safety, Quality & Safety Department, Lausanne, Switzerland. 540 pp.

Health Canada, 2007. Search results for 'Coriander oil'. In: Natural Health Products Ingredients Database. Health Canada, Natural Health Products Directorate (NHPD), Ottawa, Ontario; 2007. Available online: http://webprod.hc-sc.gc.ca/nhpidbdipsn/ingredReq.do?id=3855&lang=eng

Health Canada, 2009. Search results for product name 'Coriander' (Natural Product number: 80015479). In: Licensed Natural Health Products Database. Health Canada, Natural Health Products Directorate (NHPD), Ottawa, Ontario. Available online: http://webprod.hc-sc.gc.ca/lnhpd-bdpsnh/start-debuter.do?lang=eng

Heimermann WH, Holman RT, Gordon DT, Kowalyshyn DE and Jensen RG, 1973. Effect of double bond position in octadecenoates upon hydrolysis by pancreatic lipase. Lipids, 8, 45-47.

Hoffmann R, 2013. Evaluation of the effect of a nutritional supplement versus placebo on hair loss. Study N. BTS520/10//10E Coriander 2. Proprietary unpublished study report., 178 pp.

Hoy CE and Holmer G, 1981. Incorporation of cis-octadecenoic acids into the rat liver mitochondrial membrane phospholipids and adipose tissue triglycerides. Lipids, 16, 102-108.

Kanerva L and Soini M, 2001. Occupational protein contact dermatitis from coriander. Contact Dermatitis, 45, 354-355.

Kiralan M, Calikoglu E, Ipek A, Bayrak A and Gurbuz B, 2009. Fatty acid and volatile oil composition of different coriander (Coriandrum sativum) registered varieties cultivated in Turkey. Chemistry of Natural compounds, 45, 100-102.

Lawson LD, Hill EG and Holman RT, 1983. Suppression of arachidonic acid in lipids of rat tissues by dietary mixed isomeric cis and trans octadecenoates. Journal of Nutrition, 113, 1827-1835.

Lissy M, Koch M, Lehnick D, Gonzalo F and Piskol G, 2012. Study Protocol. Comparative bioavailability study of petroselinic acid after coriander seed oil consumption. Study No 11.15.NRC., 47 pp.

Moneret-Vautrin DA, Morisset M, Lemerdy P, Croizier A and Kanny G, 2002. Food allergy and IgE sensitization caused by spices: CICBAA data (based on 589 cases of food allergy). Allergie et Immunologie, 34, 135-140.

Opdyke DLJ, 1973. Monographs on fragrance raw materials: coriander oil. Food and Cosmetics Toxicology, 11, 1077.

Richter KD, Mukherjee KD and Weber N, 1996. Fat infiltration in liver of rats induced by different dietary plant oils: high oleic-, medium oleic- and high petroselinic acid-oils. Zeitschrift fur Ernahrungswissenschaft, 35, 241-248.

Seher A and Fiebig H-J, 1983. Stereospezifische Analyse von Triacylglycerinen mit selten vorkommenden Fettsäuren. [Stereospecific analysis of triacylglycerides with rarely occurring fatty acids]. Fette, Seifen, Anstrichmittel 85, 333-338.

Suhonen R, Keskinen H, Bjorksten F, Vaheri E and Zitting A, 1979. Allergy to coriander. A case report. Allergy, 34, 327-330.

Therapeutic Goods Administration, 2007. Substances That May Be Used in Listed Medicines in Australia. Therapeutic Goods Administration (TGA), Australian Government Department of Health and Aging. Available online: http://www.tga.gov.au/cm/listsubs.pdf

U.S. FDA, 2011. Search results for 'coriander oil '. In: Inactive Ingredient Search for Approved Drug Products. U.S. Food and Drug Administration (U.S. FDA), Center for Drug Evaluation and Research (CDER), Office of Generic Drugs, Rockville. Available online: http://www.accessdata.fda.gov/scripts/cder/iig/index.cfm

Weber N, Richter KD, Schulte E and Mukherjee KD, 1995. Petroselinic acid from dietary triacylglycerols reduces the concentration of arachidonic acid in tissue lipids of rats. Journal of Nutrition, 125, 1563-1568.

Weber N, Vosmann K, Brühl L and Mukherjee KD, 1997. Metabolism of dietary petroselinic acid: a dead-end metabolite of desaturation/chain elongation reactions. Nutrition Research, 17, 89-97.

Weber N, Schonwiese S, Klein E and Mukherjee KD, 1999. Adipose tissue triacylglycerols of rats are modulated differently by dietary isomeric octadecenoic acids from coriander oil and high oleic sunflower oil. Journal of Nutrition, 129, 2206-2211.

Weber N, Klein E and Mukherjee KD, 2003. Stereospecific incorporation of palmitoyl, oleoyl and linoleoyl moieties into adipose tissue triacylglycerols of rats results in constant sn-1:sn-2:sn-3 in rats fed rapeseed, olive, conventional or high oleic sunflower oils, but not in those fed coriander oil. Journal of Nutrition, 133, 435-441.

## ABBREVIATIONS

| | |
|---|---|
| CSO | corander seed oil |
| DBPCFC | double-blind, placebo-controlled, food challenge |
| DHA | docosahexaenoic acid |
| GLP | good laboratory practice |
| HACCP | hazard analysis and critical control points |
| HDL | high density lipid |
| HOS | high-oleic sunflower oil |
| HPLC | high performance liquid chromatography |
| IUPAC | International Union of Pure and Applied Chemistry |
| LOQ | limit of quantification |
| MS | Member State |
| NDNS | National Diet and Nutrition Survey |
| NF(I) | Novel Food (Ingredient) |
| NOAEL | no observed adverse effect level |
| OECD | Organisation for Economic Co-operation and Development |
| PA | petroselinic acid |
| PCBs | polychlorinated biphenyls |
| SD | standard deviation |
| UFC | colony forming unit |