Potential Dietary Intakes of Calcium Lignosulfonate

Report for consideration by the
European Food Safety Authority

Prepared for

DSM Nutritional Products Europe Ltd

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1. Introduction

Lignosulfonates have a long history of use as binders and dispersants in a wide variety of applications including animal feed additives (E565; binders, anti-caking agents and coagulants)[1]. DSM now wishes to extend their use as carriers for vitamins and nutrients in food and is seeking an opinion on their safety for food uses from the Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) of the European Food Safety Authority (EFSA).

The EFSA Scientific Committee has expressed an Opinion on exposure assessments used to support its work and that of the Panels responsible for different types of food hazards[2]. They noted that internationally accepted guidance exists, at least for initial assessments, in most areas of EFSA's work where exposure assessment is required and recommended that EFSA Panels use guidance that is established in their own area, which has the advantage of increasing acceptance and comparison of the EFSA assessments internationally.

The Joint FAO/WHO Secretariat of the JECFA has laid down Guidelines for intake estimation (FAO/WHO Joint Secretariat, 2001)[3]. This follows a tiered approach in which simple, conservative screening methods are used to provide initial intake estimates, which are gradually refined using national production figures and finally food consumption data. These methods rely on information about the usage of a food additive, such as annual production figures and levels in food. Since lignosulfonates are presently not authorised for use in foods it is not possible to follow this approach. However, many regulatory authorities have approved the vitamins and nutrients that the company would like to use lignosulfonates as carriers for. The ratio of active principle (vitamin or nutrient) to lignosulfonate as a carrier is fixed for technological reasons. Therefore, estimates of high-level intakes of the respective vitamins and nutrients can be used to predict potential high-level intakes of lignosulfonates. These estimates will represent a potential worst case because lignosulfonate will not be used in all vitamin and nutrient applications because it is applicable mainly to water dispersible (i.e. not oil-based) formulations.

Lignin is a natural constituent of many plants and is a component of dietary fibre. It is estimated that western diets provide 1 to 1.7 g per day[4 5].

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[1] List of the authorised additives in feedingstuffs published in application of Article 9t (b) of Council Directive 70/524/EEC concerning additives in feedingstuffs. (2004/C 50/01). 25.2.2004 EN Official Journal of the European Union C 50. 0001 – 0144.

[2] European Food Safety Authority (2005). Opinion of the Scientific Committee on a request from EFSA related to Exposure Assessments. (Request No EFSA-Q-2003-107), adopted on 22 June 2005. The EFSA Journal (2005) 249, 1-26.

[3] FAO/WHO Joint Secretariat (2001). Guidelines for the preparation of working papers on intake of food additives for the Joint FAO/WHO Expert Committee on Food Additives. Geneva.

[4] Tungland B C and Meyer D (2002). Nondigestible Oligo- and Polysaccharides (Dietary Fiber): Their Physiology and Role in Human Health and Food. Comprehensive reviews in Food Science and Food Safety, Vol. 1, 73 –77.

[5] Wenlock, R W, Buss, D H and Agatter, I B (1984). New estimates of fibre in the diet in Britain. British Medical Journal 288, 1873.

2. Proposed food applications for lignosulfonate.

Lignosulfonates are proposed as carriers for various carotenoids and nutrients, such as beta-carotene, zeaxanthin, lutein, lycopene, canthaxanthin, beta-apo-8'-carotenal and fat soluble vitamins A, E, D and K.

Lignosulfonate will be used as a carrier in formulations of oil-soluble vitamins and carotenoids only where these are presented in water dispersible forms (i.e. not in oily suspensions). The carrier would typically provide about 50% of the mass of vitamin or nutrient products with the active ingredient ranging from 0.5% to 10%, the rest being made up of starch, sugar and other ingredients. However, for technological reasons the actual ratio of active principle to lignosulfonate in water dispersible products will vary between products (Table 1).

Table 1. Ratios of active principal to lignosulfonate (confidential)

	Active principle : Lignosulfonate
Carotenoids	1 : 5
Vitamin E	1 : 1
Vitamin A	1 : 4
Vitamin D	1 : 200
Vitamin K	1 : 18

Since lignosulfonate will be used mainly in the water dispersible (powdered) product forms this affects intakes, especially for the vitamin products, because only a sub-set of available products will contain lignosulfonate. About 50% of sales of carotenoid products are in water dispersible forms. The ratio of water dispersible formulation sales to oily forms for vitamin products is provided in Table 2. Care should be taken when applying market share data to intake estimates. If product use is widespread and an individual consumer could derive intakes from a wide range of products, then it is reasonable to apply this factor. If, however, the main source of intake is from one product, then an individual consumer may always choose that product and so the market share factor should not be applied. In this report, intake estimates will be provided with and without application of this market share factor.

Table 2. Proportion of vitamins sold in water dispersible form

	Water dispersible forms	**Oily/fluid forms**
Vitamin A	45%	55%
Vitamin D	35%	65%
Vitamin E	50%	50%

DSM has provided previous submissions on zeaxanthin, lutein and lycopene to the JECFA. These data can be used as the basis for lignosulfonate intake estimates from its use in carotenoid products.

3. Methods for estimating intakes.

The JECFA guidelines suggest several methods for estimating intakes of additives. 'Poundage' or 'disappearance' data rely on information about sales volumes – which are

not available for food uses of lignosulfonates since they are not presently approved. Similarly food consumption data, whether from household budget surveys of from individual food consumption surveys cannot be used because it would be necessary to know the level of lignosulfonate use associated with each food. Since lignosulfonate has no nutrient role in the food because it is there only as a carrier for the nutrient or vitamin, the levels of use would be difficult to predict. Estimates of poundage or disappearance might be based on production figures for the carotenoids and nutrients that lignosulfonate is intended to support. However, since these substances may be used in other applications not associated with lignosulfonate, this estimate would be unreliable.

A more direct method of estimating lignosulfonate intakes would be to base them on information already available about intakes of the nutrients and vitamins they are intended to provide a carrier for. Since the ratio of the active principle to the carrier is fixed, the maximum intake of the nutrient or vitamin can be used to predict the maximum intake of lignosulfonate.

4. Lignosulfonate intakes based on carotenoid intakes.

For the lignosulfonate use linked to carotenoids, intake estimates will be based around estimated intakes of carotenoids previously prepared for EFSA, JECFA or other safety assessment authorities. Such intake assessments usually take account of exposure to nutrients from various sources, including natural sources. However, for the purpose of assessing the risks associated with lignosulfonate intake only exposures from added sources such as fortification, supplementation or food additive applications should be taken into account. Estimates of lignosulfonate intake based on such intake estimates will tend to be conservative because they assume that all of the carotenoid presented as a nutrient, supplement or food additive is dispersed in lignosulfonates. In practice, lignosulfonate can be used only in water dispersible formulations, which account for approximately 50% of all uses.

4.1 Beta Carotene

In 2000 the EU Scientific Committee on Food was unable to determine a tolerable upper intake level for beta-carotene[6]. However, they identified three general ß-carotene sources associated with ranges of intake:

a) natural food sources that may contribute around 2-5 mg/European person/day,
b) food additives (1-2 mg/person/day), and
c) supplements.

The UK expert group on vitamins and minerals[7] identified the use of beta-carotene in vitamin and mineral supplements at levels ranging from 0.4 mg to 20 mg per day.

The report on intakes of beta-carotene from its use as a food additive, fortificant and dietary supplement in France, Germany and the UK by Tennant *et al*[8] reported intake

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[6] Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Beta Carotene (expressed on 19 October 2000). SCF/CS/NUT/UPPLEV/37 Final. 28 November 2000.

[7] Expert Group on Vitamins and Minerals (2003). Safe Upper Levels for Vitamins and Minerals. Food Standards Agency, UK. ISBN 1-904026-11-7

[8] Tennant, D.R., Gedrich, K, Godfrey, D, and Davidson, J (2004). Intakes of beta-carotene from its use as a food additive, fortificant and dietary supplement in France, Germany and the UK. British Food Journal 106/6, 436 – 456.

estimates of beta-carotene from food colour uses ranging from 0.4 to 1.9 mg/day. Although intakes from nutritional supplements could range from less than 1 mg/day to 100 mg/day, for the majority of products recommended daily doses were less than 10 mg/day. These figures were based on a study conducted in 2001 and very high dosage supplements are no longer marketed. The upper limit is presently nearer to 20 mg/day. The report estimated theoretical intakes from fortified drinks above 5 mg/day but this level of intake would be unlikely to be maintained in the longer term.

When used as a carrier for beta-carotenes in a ratio of one unit of beta-carotene to five units of lignosulfonate, intakes of lignosulfonate would be in the following ranges (Table 3):

Table 3. Potential intakes of lignosulfonate resulting from use as a carrier for beta-carotene.

		Beta carotene				API:LS = 1 : 5			
Source		**Intake range**				**LS Intakes**			
SCF	Food additive	1	to	2	mg/day	**5**		**10**	
	Supplements			> 20	mg/day			**> 100**	
UK EGVM	Supplements	0.4		20	mg/day	**2**	**to**	**100**	mg/day
				0.11	mg/kg bw/day			**0.55**	mg/kg bw/day
Tennant *et al*	Food colour	0.4	to	2	mg/day	**2**	**to**	**10**	mg/day
	Nutritional supplement	< 1	to	20*	mg/day	**< 5**	**to**	**100**	mg/day
	Fortifying agent	2	to	5	mg/day	**10**	**to**	**25**	mg/day

* modified from original source

Intakes of lignosulfonate from use as a carrier for beta-carotene could result in intakes ranging from less than 10 to over 100 mg/day, depending on the application and dose. Lignosulfonate will be used only in water dispersible forms, which means that fewer applications are possible. For example, margarine would not be enriched with a water dispersible form. If the proportion of product supplied in the water dispersible form (approximately 50%) is taken into account in the intake estimates, then high level lignosulfonate intakes would range up to about 50 mg/day. Also, a significant share of food supplements use oil suspensions of beta-carotene, for which lignosulfonate-based formulations would not be suitable.

4.2 Zeaxanthin

In 2004 DSM Nutritional Products submitted a dossier[9] to the JECFA that contained information about potential intakes of zeaxanthin from its use as a food ingredient in the USA and in Europe (based on UK data). Data were provided for average consumers and for 90th percentiles (US) and 97.5th percentiles (UK) to represent high-level consumers.

Although zeaxanthin is not presently authorised in the EU, the ingredient can provide a useful illustration of potential intakes of lignosulfonate, if used as a carrier. The use of

[9] Estimated Dietary Intakes for Zeaxanthin from Use as a Food Ingredient (2004). For consideration by the Joint FAO/WHO Expert Committee on Food Additives 63rd Meeting, Geneva, 8-17 June 2004. DSM Nutritional Products, Basel, Switzerland.

lignosulfonate as a carrier for zeaxanthin in a ratio of one unit of zeaxanthin to five units of lignosulfonate would give rise to intakes of lignosulfonate in the following ranges (Table 4):

Table 4. Potential intakes of lignosulfonate resulting from use as a carrier for zeaxanthin in food

	Zeaxanthin Intake range			API:LS = 1 : 5 **LS Intakes**		
Population group	**Mean**	**90th**		**Mean**	**90th**	
US Infants	0.84	1.68	mg/day	**4.2**	**8.4**	mg/day
US Children	1.32	2.22	mg/day	**6.6**	**11.1**	mg/day
US Female teenagers	1.58	2.66	mg/day	**7.9**	**13.3**	mg/day
US Male teenagers	2.14	3.72	mg/day	**10.7**	**18.6**	mg/day
US Female adults	1.24	2.3	mg/day	**6.2**	**11.5**	mg/day
US Male adults	1.6	3.04	mg/day	**8**	**15.2**	mg/day
US Total population	1.42	2.68	mg/day	**7.1**	**13.4**	mg/day
US Infants	0.07	0.15	mg/kg bw/day	**0.35**	**0.75**	mg/kg bw/day
US Children	0.05	0.09	mg/kg bw/day	**0.25**	**0.45**	mg/kg bw/day
US Female teenagers	0.03	0.05	mg/kg bw/day	**0.15**	**0.25**	mg/kg bw/day
US Male teenagers	0.03	0.06	mg/kg bw/day	**0.15**	**0.3**	mg/kg bw/day
US Female adults	0.02	0.04	mg/kg bw/day	**0.1**	**0.2**	mg/kg bw/day
US Male adults	0.02	0.04	mg/kg bw/day	**0.1**	**0.2**	mg/kg bw/day
US Total population	0.03	0.06	mg/kg bw/day	**0.15**	**0.3**	mg/kg bw/day
	Mean	97.5th		**Mean**	**97.5th**	
UK Children	1.14	2.43	mg/day	**5.7**	**12.2**	mg/day
UK Young people	1.5	2.88	mg/day	**7.5**	**14.4**	mg/day
UK Female teenagers	1.39	2.72	mg/day	**6.95**	**13.6**	mg/day
UK Male teenagers	1.85	3.87	mg/day	**9.25**	**19.4**	mg/day
UK Female adults	0.95	2.25	mg/day	**4.75**	**11.3**	mg/day
UK Male adults	1.02	2.55	mg/day	**5.1**	**12.8**	mg/day
UK Children	0.08	0.17	mg/kg bw/day	**0.4**	**0.85**	mg/kg bw/day
UK Young people	0.06	0.12	mg/kg bw/day	**0.3**	**0.6**	mg/kg bw/day
UK Female teenagers	0.03	0.06	mg/kg bw/day	**0.15**	**0.3**	mg/kg bw/day
UK Male teenagers	0.03	0.08	mg/kg bw/day	**0.15**	**0.4**	mg/kg bw/day
UK Female adults	0.02	0.04	mg/kg bw/day	**0.1**	**0.2**	mg/kg bw/day
UK Male adults	0.01	0.04	mg/kg bw/day	**0.05**	**0.2**	mg/kg bw/day

Use of zeaxanthin as a food ingredient would result in intakes of lignosulfonate ranging up to 20 mg/day (male teenagers) or 0.9 mg/kg bw/day (UK children).

Proposed use of zeaxanthin as a food supplement at up to 4 - 20 mg/day would result in lignosulfonate intakes of 20 - 100 mg/day.

Intakes of lignosulfonate from use as a carrier for zeaxanthin could result in intakes ranging from less than 10 to 100 mg/day, depending on the application and dose. Like other carotenoids, not all zeaxanthin products will be in the water dispersible form. If the proportion of product supplied in such forms (approximately 50%) is taken into account in the intake estimates, then high level lignosulfonate intakes would range up to about 50 mg/day.

4.3 Lutein

In 2004 DSM Nutritional Products and Kemin Foods submitted a dossier[10] to the JECFA that contained information about potential intakes of lutein from its use as a food ingredient in the USA. Information was provided for average consumers and for the 90th percentile to represent high level consumers.

It is proposed that lignosulfonate should be used as a carrier for lutein in a ratio of one unit of lutein to five units of lignosulfonate. This would give rise to intakes of lignosulfonate in the following ranges (Table 5):

Table 5. Potential intakes of lignosulfonate resulting from use as a carrier for lutein in food

	Lutein Intake range			API:LS = 1 : 5 LS Intakes		
Population group	**Mean**	**90th**		**Mean**	**90th**	
US Infants	4.2	8.4	mg/day	**21**	**42**	mg/day
US Children	6.6	11.1	mg/day	**33**	**55.5**	mg/day
US Female teenagers	7.9	13.3	mg/day	**39.5**	**66.5**	mg/day
US Male teenagers	10.7	18.6	mg/day	**53.5**	**93**	mg/day
US Female adults	6.2	11.5	mg/day	**31**	**57.5**	mg/day
US Male adults	8	15.2	mg/day	**40**	**76**	mg/day
US Total population	7.1	13.4	mg/day	**35.5**	**67**	mg/day
US Infants	0.37	0.73	mg/kg bw/day	**1.85**	**3.65**	mg/kg bw/day
US Children	0.27	0.47	mg/kg bw/day	**1.35**	**2.35**	mg/kg bw/day
US Female teenagers	0.15	0.25	mg/kg bw/day	**0.75**	**1.25**	mg/kg bw/day
US Male teenagers	0.17	0.3	mg/kg bw/day	**0.85**	**1.5**	mg/kg bw/day
US Female adults	0.09	0.18	mg/kg bw/day	**0.45**	**0.9**	mg/kg bw/day
US Male adults	0.1	0.19	mg/kg bw/day	**0.5**	**0.95**	mg/kg bw/day
US Total population	0.14	0.28	mg/kg bw/day	**0.7**	**1.4**	mg/kg bw/day

Use of lutein as a food ingredient would result in intakes of lignosulfonate ranging up to 93 mg/day (US male teenagers) or 3.7 mg/kg bw/day (US infants) at the 90th percentile of intake.

Proposed use of lutein as a food supplement at up to 6 mg/day would result in lignosulfonate intakes of 30 mg/day.

Intakes of lignosulfonate from use as a carrier for lutein could result in intakes ranging from less than 10 to 95 mg/day, depending on the application and dose. Not all lutein products are in the water dispersible form. More realistically, if the proportion of product supplied in the water dispersible form (approximately 50%) is taken into account in the intake estimates, then high level lignosulfonate intakes would range up to about 45 mg/day.

4.4 Lycopene

In 2005 DSM Nutritional Products submitted an information dossier to the JECFA that contained information about potential intakes of lycopene from its use as a food colour and

[10] Estimated Dietary Intakes for Lutein from use as a Food Ingredient (2004). For consideration by the Joint FAO/WHO Expert Committee on Food Additives, 63rd Meeting, Geneva, 8-17 June 2004. DSM Nutritional Products, Basel, Switzerland and Kemin Foods, Des Moines,USA.

as a nutrient in the EU[11]. Information was provided for average consumers and for the 97.5th percentile to represent high level consumers.

It is proposed that lignosulfonate could be used as a carrier for lycopene in a ratio of one unit of lycopene to five units of lignosulfonate. This would give rise to intakes of lignosulfonate in the following ranges (Table 6):

Table 6. Potential intakes of lignosulfonate resulting from use as a carrier for lycopene in food

		Lycopene Intake range			API:LS = 1 : 5 LS Intakes		
	Population group	**Mean**	**97.5th**		**Mean**	**97.5th**	
Food colour	France, households	2.19	3.33	mg/day	**11**	**16.7**	mg/day
	Germany	1.97	3.28	mg/day	**9.85**	**16.4**	mg/day
	UK Pre-school children	3.64	8.44	mg/day	**18.2**	**42.2**	mg/day
	UK Schoolchildren	5.61	12.4	mg/day	**28.1**	**62.2**	mg/day
	UK Adults	3.38	9.36	mg/day	**16.9**	**46.8**	mg/day
	UK Elderly	2.02	6.57	mg/day	**10.1**	**32.9**	mg/day
	UK Pre-school children	0.26	0.61	mg/kg bw/day	**1.3**	**3.05**	mg/kg bw/day
	UK Schoolchildren	0.16	0.42	mg/kg bw/day	**0.8**	**2.1**	mg/kg bw/day
	UK Adults	0.05	0.13	mg/kg bw/day	**0.25**	**0.65**	mg/kg bw/day
Fortification	France, households	3.37	4.05	mg/day	**16.9**	**20.3**	mg/day
	UK Pre-school children	4.32	9.97	mg/day	**21.6**	**49.9**	mg/day
	UK Schoolchildren	5.53	13	mg/day	**27.7**	**65**	mg/day
	UK Adults	4.7	13.5	mg/day	**23.5**	**67.7**	mg/day
	UK Elderly	4.22	12.6	mg/day	**21.1**	**63.1**	mg/day

Use of lycopene as a food colour or nutrient would result in intakes of lignosulfonate ranging up to 68 mg/day (UK adults) or 3.1 mg/kg bw/day (UK pre-school children) at the 97.5th percentile of intake.

The use of lycopene as a food supplement between 1 and 25 mg/day would result in lignosulfonate intakes of 5 to 125 mg/day.

Intakes of lignosulfonate from use as a carrier for lycopene could result in intakes ranging from less than 10 to 125 mg/day, depending on the application and dose. Not all lycopene products are in the water dispersible form. If the proportion of product supplied in the water dispersible form (approximately 50%) is taken into account in the intake estimates, then high level lignosulfonate intakes would range up to about 63 mg/day. The JECFA ADI for lycopene (synthetic and derived from *Blakeslea trispora*) is 0 – 0.5 mg/kg bw/day[12]. This would represent an intake of lignosulfonate of 0 – 2.5 mg/kg bw/day or 150 mg/day for a 60 kg adult. This would be 125 mg/day if lignosulfonate was present in all water dispersible form products.

[11] Intakes of lycopene from its use as a food colour, as a fortifying agent and from natural sources (2006). Prepared for DSM Nutritional Products Ltd, Basel, Switzerland. D R Tennant, Food Chemical Risk Analysis, Brighton, UK.

[12] Joint FAO/WHO Expert Committee on Food Additives. Sixty-seventh meeting Rome, 20-29 June 2006. Summary and Conclusions

4.5 Canthaxanthin

European uses of canthaxanthin as a food colour are presently limited to Saucisses de Strasbourg[13]. Given the extremely restricted application, intakes are likely to be of no significance.

4.6 Beta-apo-8'-carotenal

No intake data are available for beta-apo-8'-carotenal. However, in Europe use as a food colour is subject to the same limitations as for lycopene and lutein, which are subject to quantitative limits, unlike beta-carotene[7]. Beta-apo-8'-carotenal has no uses as a supplement or food ingredient. Intakes from use of lignosulfonate as a carrier of beta-apo-8'-carotenal as a food colour are therefore likely to be much less than for beta-carotene, lycopene or lutein.

4.7 Summary of potential lignosulfonate intakes resulting from proposed use as a carrier for carotenoids.

To be effective as a carrier for carotenoids lignosulfonate would need to be used in a ratio of five units of lignosulfonate to one unit of carotenoid. Use of beta carotene as a colour, food supplement and fortificant would result in high level intakes of lignosulfonate of up to 10, 100 and 25 mg/day, respectively. The use of zeaxanthin as a food ingredient would result in intakes of lignosulfonate of less than 20 mg/day or 1 mg/kg bw/day. However, the use of zeaxanthin as a supplement could result in intakes up to 100 mg/day. The use of lutein as a food ingredient or supplement would result in intakes of lignosulfonate of less than 100 mg/day or 3 mg/kg bw/day. The use of lycopene as a food colour or food ingredient would result in intakes of lignosulfonate of less than 70 mg/day or 4 mg/kg bw/day. However, use of lycopene as a supplement could result in intakes up to 125 mg/day. The use of canthaxanthin is very restricted and unlikely to give rise to significant intakes of lignosulfonate. The use of beta-apo-8'-carotenal as a food colour would be unlikely to result intakes of lignosulfonate higher than for the other carotenoids.

Carotenoids are unlikely to be used in combinations because their technological and nutritional properties are very similar. As a consequence high level intakes of lignosulfonate resulting from its use as a carrier for carotenoids are unlikely to exceed about 100 mg/day or 4 mg/kg bw/day. These estimates are likely to be conservative because lignosulfonate will only be used mainly as a carrier in water dispersible formulations, which occupy about one half of the market. If the proportion of product supplied in the water dispersible form is taken into account in the intake estimates, then high level lignosulfonate intakes would range up to about 50 mg/day or 2 mg/kg bw/day. Furthermore, lignosulfonate is highly unlikely to replace all water dispersible carriers presently used. As a consequence intake estimates should be regarded as 'upper bound' and unlikely to be achieved in reality.

[13] European Parliament and Council Directive 94/36/EC of 30 June 1994 on colours for use in foodstuffs. OJ No. L237, pp13 – 29.

5. Lignosulfonate intakes based on fat soluble vitamin intakes.

Several national and international bodies have recommended tolerable upper nutrient intake levels (ULs) that are designed to prevent possible adverse effects from excessively high intakes. These recommendations are based on toxicological studies and are not designed to represent actual levels of use. Furthermore, tolerable upper levels include vitamin intakes from all sources including that naturally present in food. Therefore they do not necessarily represent upper level intakes from fortification or supplementation, where the use of lignosulfonate as a carrier might be adopted. Nevertheless, tolerable upper levels provide a useful risk management datum because intakes are unlikely to be sustained above this level. The SCF has established Reference Labeling Values RLVs[14] for vitamins and minerals. These can be used to make predictions of more typical levels of intake where the vitamin is added to food.

Some regulatory bodies have provided data about dose levels for dietary supplements. Where such data are available they will also be used to predict potential upper intake levels for lignosulfonate.

5.1 Vitamin A

In 2002 the EU Scientific Committee for Food (SCF) identified tolerable upper levels of intake for vitamin A[15]. It is proposed that lignosulfonate should be used as a carrier for vitamin A in a ratio of one unit of vitamin A to four units of lignosulfonate. Consumption of vitamin A from supplements at SCF recommended tolerable upper levels would give rise to the theoretical intake of lignosulfonate given in Table 7.

The Food and Nutrition Board of the US National Academy of Sciences has also defined tolerable upper intake levels, which are the highest total level of a nutrient (diet plus supplements) that can be consumed safely on a daily basis by adults without being likely to cause adverse health effects to almost all individuals in the population[16]. Their recommended UL for vitamin A is 3000 µg per day and if this was all made up of dietary supplements then the intake of lignosulfonate would be 12 mg/day. The tolerable upper intake level for vitamin A in Japan is 1,500 µg/day[17].

The UK expert group on vitamins and minerals (EVM)[18] investigated intakes of vitamin A and found intakes from its natural occurrence in food to range from 520 µg to 6059 µg per day. However, this would not be associated with lignosulfonate intake. Intakes of vitamin A from supplements were estimated to be up to 2400 µg/day. Since lignosulfonate would be used as a carrier for vitamin A in supplements in a ratio of one unit of vitamin A to four units of lignosulfonate, intakes of lignosulfonate could be up to 9.6 mg/day, also assuming that all commercial formulations used would contain lignosulfonate at the proposed 1:4 ratio mentioned

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[14] Scientific Committee on Food (2003). Opinion of the Scientific Committee on Food on the revision of reference values for nutrition labeling. SCF/CS/NUT/GEN/18 Final 6 March 2003.

[15] Scientific Committee on Food (2002). Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Preformed Vitamin A (retinol and retinyl esters). SCF/CS/NUT/UPPLEV/24 Final. 7 October 2002 (expressed on 26 September 2002)

[16] Mason, P. (2003). Upper safety limits for vitamins – why have different authorities set different guidance? The Pharmaceutical Journal. 271, p55 – 57.

[17] Hathcock, J. N. (2004). Vitamin and Mineral Safety 2nd Edition. Council for Responsible Nutrition (CRN).

[18] Expert Group on Vitamins and Minerals (2003). Safe Upper Levels for Vitamins and Minerals. Food Standards Agency, UK. ISBN 1-904026-11-7

Table 7. Theoretical intakes of lignosulfonate resulting from use as a carrier for vitamin A

				API:LS = 1 : 4	
Source	**Population group**			**LS Intakes**	
SCF RLV	Adult	800	micrograms/day	**3.2**	mg/day
SCF RLV	Children	400	micrograms/day	**1.6**	mg/day
EU SCF UL	1 - 3 yrs	800	micrograms/day	**3.2**	mg/day
EU SCF UL	4 - 6 yrs	1100	micrograms/day	**4.4**	mg/day
EU SCF UL	7 - 10 yrs	1500	micrograms/day	**6**	mg/day
EU SCF UL	11 - 14 yrs	2000	micrograms/day	**8**	mg/day
EU SCF UL	15 - 17 yrs	2600	micrograms/day	**10.4**	mg/day
EU SCF UL	Adults	3000	micrograms/day	**12**	mg/day
US FNB UL	US Population	3000	micrograms/day	**12**	mg/day
Japan UL		1500	micrograms/day	**6**	mg/day
UK EVM	Supplement users	2400	micrograms/day	**9.6**	mg/day

Intakes of lignosulfonate resulting from its use as a carrier for vitamin A would range from about 2 to 12 mg/day. If the proportion of vitamin A product supplied in the water dispersible form (45%) is taken into account in the intake estimates then high level lignosulfonate intakes would range up to about 5.4 mg/day.

5.2 Vitamin D

In 2002 the EU Scientific Committee for Food identified tolerable upper levels of intake for vitamin D[19]. It is proposed that lignosulfonate should be used as a carrier for vitamin D in a ratio of one unit of vitamin D to 200 units of lignosulfonate. Consumption of vitamin D from supplements at SCF recommended tolerable upper levels would give rise to the levels of intake of lignosulfonate given in Table 8.

The Food and Nutrition Board (FNB) of the US National Academy of Sciences has defined tolerable upper intake levels, which are the highest total level of a nutrient (diet plus supplements) that can be consumed safely on a daily basis by adults without being likely to cause adverse health effects to almost all individuals in the population[20]. Their recommended UL for vitamin D is 50 µg per day and if this was all made up of dietary supplements then the intake of lignosulfonate would be 10 mg/day. The tolerable upper intake level for vitamin D in Japan is 50 µg/day[21].

The UK expert group on vitamins and minerals[22] investigated intakes of vitamin D and found intakes from food to range from 0.003 mg/day to 0.009 mg/day. However, this would not necessarily be associated with lignosulfonate intake. Intakes from supplements were estimated to be up to 0.0125 mg/day. Since lignosulfonate would be used as a carrier for vitamin D in supplements in a ratio of one unit of vitamin A to 200 units of lignosulfonate, intakes could be up to 2.5 mg/day.

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[19] Scientific Committee on Food (2002). Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Vitamin D. SCF/CS/NUT/UPPLEV/38 Final. 16 December 2002.

[20] Mason, P. (2003). Upper safety limits for vitamins – why have different authorities set different guidance? The Pharmaceutical Journal. 271, p55 – 57.

[21] Hathcock, J. N. (2004). Vitamin and Mineral Safety 2nd Edition. Council for Responsible Nutrition (CRN).

[22] Expert Group on Vitamins and Minerals (2003). Safe Upper Levels for Vitamins and Minerals. Food Standards Agency, UK. ISBN 1-904026-11-7

Table 8. Theoretical intakes of lignosulfonate resulting from use as a carrier for Vitamin D

				API:LS = 1 : 200 LS Intakes	
Source	**Population group**				
SCF RLV	Adults	5	micrograms/day	**1**	mg/day
SCF RLV	Children	7	micrograms/day	**1.4**	mg/day
EU SCF UL	0 - 2 yrs	25	micrograms/day	**5**	mg/day
EU SCF UL	3 - 10 yrs	25	micrograms/day	**5**	mg/day
EU SCF UL	11 - 17yrs	50	micrograms/day	**10**	mg/day
EU SCF UL	Adults	50	micrograms/day	**10**	mg/day
US FNB UL	US Population	50	micrograms/day	**10**	mg/day
Japan UL		50	micrograms/day	**10**	mg/day
UK EVM	Supplement users	0.0125	mg/day	**2.5**	mg/day

Intakes of lignosulfonate resulting from its use as a carrier for vitamin D would range from about 1 to 10 mg/day. If the proportion of vitamin D product supplied in the water dispersible form (65%) is taken into account in the intake estimates then high level lignosulfonate intakes would range up to about 6.5 mg/day.

5.3 Vitamin E

It is proposed that lignosulfonate should be used as a carrier for vitamin E (alpha tocopherol acetate) in food supplements. Lignosulfonate would be used as a carrier for vitamin E in supplements in a ratio of one unit of vitamin E to 1 unit of lignosulfonate.

In 2005 a multi-sponsor survey of vitamin supplement consumptions by 788 adult men and women drawn from a national online panel was conducted in the USA[23]. In the US the RDA for Vitamin E is 30 IU and mostly all multivitamin tablets contained this level. A few multivitamin tablets products contained 45 IU but not more than 100 IU. The results of the survey and resulting intakes of lignosulfonate are summarised in Table 9. In a similar study conducted in Germany in 2004[24], 240 persons consuming one supplement per day had an average intake of 87 mg vitamin E and an intake of 268 at the 90th percentile. In the same study 23 persons consuming more than one supplement per day had an average intake of 154 mg vitamin E and an intake of 336 at the 90th percentile. The use of lignosulfonate as a carrier in these products would result in similar levels of intake.

In tablets, vitamin E powder can only be used up to a level of 200 to 400 IU (upper level less likely). Capsules and tablets containing dosages higher than 400 IU are made using an oil-based formulation of vitamin E, which would not contain lignosulfonate. As a consequence intakes of lignosulfonate from use in single dose vitamin E supplements are unlikely to exceed 268 mg/day.

[23] Multi-sponsor Surveys Inc (2005). The 2005 Gallup Study of Vitamin Use in the United States. (Confidential).

[24] Beitz, R, Mensink, G B, Rams, S and Doring A (2004). Use of vitamin and mineral supplements in Germany. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 47(11):1057-65.

Table 9. Potential intakes of lignosulfonate relating to survey of Vitamin E supplement consumption in USA.

Product	% consuming	Vitamin E intake		API:LS = 1 : 1 **LS Intakes**	
Multivitamins <100 IU		<67	mg/day	**<67**	mg/day
Less than 100 I.U.	9%	<67	mg/day	**<67**	mg/day
100 I.U.	8%	67	mg/day	**67**	mg/day
200 I.U.	11%	134	mg/day	**134**	mg/day
400 I.U.	42%	268	mg/day	**268**	mg/day
800 I.U.	12%	536	mg/day	**n.a.***	mg/day
1200 I.U.	4%	804	mg/day	**n.a.***	mg/day
1600 I.U.	<0.05%	1072	mg/day	**n.a.***	mg/day
More than 1600 I.U.	0%	>1072	mg/day	**n.a.***	mg/day

* water dispersible form not applicable at this dose level

In 2002 the EU Scientific Committee for Food identified tolerable upper levels of intake for vitamin E[25]. Consumption of vitamin E from supplements at SCF recommended tolerable upper levels would give rise to the levels of intake of lignosulfonate given in Table 10.

The Food and Nutrition Board of the US National Academy of Sciences has also defined tolerable upper intake levels[26]. Their recommended UL for vitamin E is 1000 mg per day and if this was all made up of dietary supplements then the intake of lignosulfonate would be 1000 mg/day. The tolerable upper intake level for vitamin E in Japan is 600 mg/day[27]. However, since lignosulphonate can be used only as a carrier for the water dispersible form of vitamin E product and this is limited to 400 IU per day, neither of these upper limits is relevant.

The UK expert group on vitamins and minerals[28] reported that vitamin E is present in a variety of dietary supplements at doses of up to 268 mg/day in multi-constituent products and 670 mg/day in single constituent products. Since lignosulfonate would be used as a carrier for vitamin E in supplements in a ratio of one unit of vitamin E to 1 unit of lignosulfonate, intakes could be up to 670mg/day. Again, because lignosulfonate can be used only as a carrier for the water dispersible form of vitamin E product and this is limited to 400 IU per day, the upper level is not relevant.

[25] Scientific Committee on Food (2003). Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Vitamin E. SCF/CS/NUT/UPPLEV/31 Final 23 April 2003 (expressed on 4 April 2003).

[26] Mason, P. (2003). Upper safety limits for vitamins – why have different authorities set different guidance? The Pharmaceutical Journal. 271, 55 – 57.

[27] Hathcock, J. N. (2004). Vitamin and Mineral Safety 2nd Edition. Council for Responsible Nutrition (CRN).

[28] Expert Group on Vitamins and Minerals (2003). Safe Upper Levels for Vitamins and Minerals. Food Standards Agency, UK. ISBN 1-904026-11-7

Table 10. Hypothetical intakes of lignosulfonate resulting from use as a carrier for Vitamin E

				API:LS = 1 : 1 LS Intakes	
Source	**Population group**				
SCF RLV	Adults	12	mg/day	**12**	mg/day
SCF RLV	Children	5	mg/day	**5**	mg/day
EU SCF UL	1 - 3 yrs	100	mg/day	**100**	mg/day
EU SCF UL	4 - 6 yrs	120	mg/day	**120**	mg/day
EU SCF UL	7 - 10 yrs	160	mg/day	**160**	mg/day
EU SCF UL	11 - 14 yrs	220	mg/day	**220**	mg/day
EU SCF UL	15 - 17 yrs	260	mg/day	**260**	mg/day
EU SCF UL	Adults	300	mg/day	**300**	mg/day
US FNB UL	Adults	1000	mg/day	**n.a.***	mg/day
Japan UL		600	mg/day	**n.a.***	mg/day
UKEVM	Multi-vitamin supplements	268	mg/day	**268**	mg/day
UKEVM	Single vitamin supplements	670	mg/day	**n.a.***	mg/day

* water dispersible form not applicable at this dose level

Intakes of lignosulfonate resulting from its use as a carrier for vitamin E could range from less than 10 to about 300 mg/day. If the proportion of vitamin E product supplied in the water dispersible form (50%) is taken into account in the intake estimate then high level lignosulfonate intakes would range up to about 150 mg/day.

5.4 Vitamin K

In 2003 the EU Scientific Committee for Food was unable to determine tolerable upper levels of intake for vitamin K[29]. The UK expert group on vitamins and minerals[30] reported that food supplements may contain up to 0.045 mg vitamin K (either as K1 or K2) for general consumption and 0.20 mg in supplements intended for women from pre-conception to nursing (Table 11). The tolerable upper intake level for vitamin K in Japan is 30 mg/day[31].

Table 11. Potential intakes of lignosulfonate resulting from use as a carrier for Vitamin K

				API:LS = 1 : 18 LS Intakes	
Source	**Population group**				
SCF RLV	Adults	75	µg/day	**1.35**	mg/day
SCF RLV	Children	12	µg/day	**0.22**	mg/day
UK EVM	Supplement users	0.045	mg/day	**0.81**	mg/day
UK EVM	Mothers	0.2	mg/day	**3.6**	mg/day
Japan	Upper limit	30	mg/day	**n.a.***	mg/day

* not related to doses actually consumed

[29] Scientific Committee on Food (2003). Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Vitamin K. SCF/CS/NUT/UPPLEV/32 Final. 24 April 2003. (expressed on 4 April 2003).

[30] Expert Group on Vitamins and Minerals (2003). Safe Upper Levels for Vitamins and Minerals. Food Standards Agency, UK. ISBN 1-904026-11-7

[31] Hathcock, J. N. (2004). Vitamin and Mineral Safety 2nd Edition. Council for Responsible Nutrition (CRN).

Intakes of lignosulfonate resulting from its use as a carrier for vitamin K could range from about less than 1 to over 500 mg/day. However, the upper level is related to the Japanese upper safe level for vitamin K, which will not necessarily be reached in reality. Maximum intakes probably would not exceed 10 mg/day in practice.

5.5 Summary of potential lignosulfonate intakes resulting from proposed use as a carrier for vitamins.

The use of lignosulfonate as a carrier for vitamin A would result in maximum intakes of lignosulfonate of less than 12 mg/day if all of the vitamin A was consumed as supplements at the tolerable upper intake level. The use of lignosulfonate as a carrier for vitamin D would result in maximum intakes of lignosulfonate of less than 10 mg/day if all of the vitamin D was consumed as supplements at the tolerable upper intake level. The use of lignosulfonate as a carrier for vitamin E could result in maximum intakes of lignosulfonate of up to about 300 mg/day. The use of lignosulfonate as a carrier for vitamin K would result in maximum intakes of lignosulfonate of less than 10 mg/day if all of the vitamin K was in supplement form.

Approximately 50% of vitamin supplement products contain vitamins that are suspended in oil and lignosulfonate would not be used in these products. Furthermore, lignosulfonate is unlikely to replace all carriers presently used. If consumption reflects the market share then intakes of lignosulfonate would be unlikely to exceed half the values provided above.

Vitamins can be used in combination but the amounts of individual vitamins in such multi-vitamin products tend to be lower than in single vitamin products. Intakes resulting from vitamin E use in multi-vitamin products could result in lignosulfonate intakes up to 300 mg/day. Adding vitamins A, D and K at highest supplement levels would result in a total intake of lignosulfonate of less than 350 mg/day or 175 mg/day if the proportion in water dispersible form is taken into account.

6. Potential intakes of lignosulfonate – overall summary and conclusions

Intakes of lignosulfonate resulting from its use as a carrier for carotenoids are unlikely to exceed 100 mg/day or 4 mg/kg bw/day for the highest intake groups (90^{th}, 97.5^{th} percentiles). The carotenoids are not likely to be used together because they share similar technological and nutritional properties and therefore substitute for each other.

Intakes of lignosulfonate resulting from its use as a carrier for vitamins would generally result in maximum intakes of lignosulfonate of less than 20 mg/day except for vitamin E, where intakes could approach 300 mg/day. In multi-vitamin supplements the maximum lignosulfonate intake would not be expected to exceed 350 mg/day.

A consumer who consumed foods fortified or coloured with carotenoids would have a maximal intake of lignosulfonate from this source of 100 mg/day. If he also took a multivitamin supplement he could obtain up to 350mg from that source. However, the total intake is unlikely to reach 450 mg/day because of limited market share and the fact that lignosulfonate would be used mainly in water dispersible products, which make up approximately 50% of the total market.