TOX/2022/01

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Matters arising: exposure assessment of vitamin D in infant formula and food

Background

1. In 2006, the European Commission established a minimum vitamin D content for infant- and follow-on formulae of 1 µg per 100 kcal (Directive 2006/141/EC). Subsequently in 2016, in Commission Delegated Regulation 2016/127, this was doubled to 2 µg per 100 kcal (the rationale for this change was not included in this document). This new regulation became applicable in Great Britain from the 1st of January 2021. EU legislation on nutrition continues to be directly applicable in Northern Ireland.

2. In order to inform discussion across the four nations on whether existing advice around vitamin D supplements remained appropriate or needed updating, in light of the increase in the minimum vitamin D content of infant- and follow-on formulae, the FSA conducted an exposure assessment to determine whether this increase could result in infants (0 – 12-month-olds) exceeding the tolerable upper level (TUL) (with and without additional exposure from vitamin D supplements).

3. On the basis of the information presented to the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) on the 7th of December 2021, estimates of vitamin D exposure (from infant formulae and supplements combined) were not considered to be excessive, as only slight exceedances of the TUL occurred in infants. The Committee was reassured that this exceedance (which only occurs when infants consume ≥1000 ml of infant formula per day in addition to vitamin D supplements) goes against current NHS advice (that "babies fed infant formula should not be given a vitamin D supplement if they're consuming more than 500ml (about a pint) of infant formula a day").

4. However, the Committee noted that the exposure assessment did not account for other dietary sources of vitamin D. It was noted that this is important for infants over the age of 4 months, a proportion of whom would be eating solid foods. Therefore, this paper presents revised estimates of infant exposures to vitamin D, with consideration of other dietary sources of vitamin D.

Tolerable upper levels (TULs) for vitamin D

5. In 2012, the European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA) established tolerable upper levels (TULs) for vitamin D (EFSA, 2012), based on a risk assessment conducted in 2003 by the Scientific Committee on Food (SCF, 2003). The SCF risk assessment used hypercalcaemia as the adverse effect induced by excessive vitamin D exposure. The TULs established by EFSA in 2012 were as follows:

- For infants (birth to 1 year of age), the TUL is 25 µg per person, per day.
- For children aged 1 to 4 years, the TUL is 50 µg per person, per day.

6. In 2014, the COT published a statement on the adverse effects of high levels of vitamin D, in which they agreed with the TULs set by EFSA in 2012 (COT, 2014).

7. However, in 2018, based on the overall evidence, the EFSA NDA Panel kept the TUL of 25 µg/day for infants up to 6 months old, and set a new UL of 35 µg/day for infants aged 6-12 months (EFSA, 2018). The TUL for toddlers above 1 year of age (50 µg per person, per day) was not changed in EFSA's 2018 assessment following its original establishment in 2003 and confirmation in 2012.

Exposure assessment

8. An exposure assessment was conducted to estimate chronic infant exposures to vitamin D from the background diet. In terms of the occurrence data used for this exposure assessment, Table 1 below gives an overview of the vitamin D levels present in a variety of different solid foods (known to contain higher levels of vitamin D) that could be consumed by an infant. These levels are largely based on a report published by SACN (SACN, 2016). The consumption data used for exposure assessment come from the 2011 Diet and Nutrition Survey of Infants and Young

Children (DNSIYC) (DH, 2013) and the rolling National Dietary and Nutrition surveys (NDNS) years 1-11 (Bates *et al.,* 2014, 2016, 2020; Roberts *et al*., 2018). Maximum consumption rates have been included to help estimate a worst-case scenario.

9. Further details on the derivation of the vitamin D levels in specific food groups, as well as the consumption rates used for the exposure assessment are provided below.

Occurrence and consumption data

Mushrooms

10. Wild mushrooms are a natural source of vitamin D. However, cultivated and UV treated mushrooms can also contain vitamin D. A search within the recipes database of the NDNS (Bates *et al*., 2014, 2016; Roberts *et al*., 2018) was conducted to retrieve mushrooms and recipes containing mushrooms which had been recorded in the survey. The chronic consumption estimates for mushrooms are presented in Table 1. It is important to consider that these estimates are based on all types of cultivated mushrooms, as there are no consumption data on wild mushrooms, and it is uncertain if any of those reported in the NDNS had been treated with UV (Bates et al., 2014, 2016; Roberts et al., 2018).

11. Exposure estimates of vitamin D in mushrooms were calculated using consumption data from NDNS and DNSIYC, and occurrence data from online sources. The minimum and maximum estimated vitamin D_2 levels for mushrooms (cultivated and UV treated) were 2.1 µg/kg (84 IU/kg) and 100 µg/kg (4,000 IU/kg) (Cardwell et al., 2018). These were used to calculate the exposure estimates presented in Table 1. It is important to note that UV-treated mushrooms tend to have a slightly higher retail price, though consumption estimates are assumed to be similar to cultivated mushrooms.

Egg yolk

12. Natural sources of Vitamin D include egg yolk. Chronic consumption estimates of egg yolk are presented in Table 1. It is important to note that whole egg consumption from the NDNS database was considered in order to ensure that all egg yolk consumers were included. On average, the egg yolk makes up 29.3 % of the edible portion of a medium egg, and 28.7 % of a large egg. The NDNS database does not specify the use of large or medium eggs, so the figure was rounded to 29 %

for this paper (DH, 2013). The factor of 29 % was then applied to whole eggs foods to give estimates for consumption specifically of egg yolks, and foods containing solely egg whites were removed from the assessment. Exposure estimates of vitamin D in egg yolk, using chronic consumption data and estimated vitamin D levels of 126 µg/kg (5,040 IU) (SACN, 2016), are presented in Table 1.

Oily fish

13. Oily fish such as salmon, mackerel, herring and sardines are good sources of vitamin D. Estimates for chronic exposure to vitamin D in fish are presented in Table 1. Estimated minimum and maximum vitamin D levels of 50 and 160 µg/kg (2,000 and 6,400 IU) (SACN, 2016) were used to derive exposure.

Animal meat and fat

14. Further sources of vitamin D are animal meat and fat. Exposure from chicken, beef, pork and turkey were considered and are presented in Table 1. Consumption of meat and fat were considered together as fat is likely to be consumed alongside meat. Additionally, the number of consumers of animal fat alone would be very low. Exposure estimates of vitamin D were derived using chronic consumption data and estimated minimum and maximum vitamin D levels of 1 and 15 µg/kg (40 and 600 IU), respectively (SACN, 2016).

Animal offal

15. Consumption estimates of animal liver and kidney are based on overall animal offal consumption. Consumption was based on all animal offal, as liver and kidney were given as examples of offal that contain vitamin D in the 2016 SACN report and other types of offal were not specified (SACN, 2016). Exposure estimates of vitamin D_3 in animal liver and kidney were derived using chronic consumption data and estimated minimum and maximum vitamin D_3 levels of 1 and 15 µg/kg (40 and 600 IU/kg), respectively (SACN, 2016).

Exposure estimates from food products voluntarily fortified with vitamin D

16. Foods such as margarines and fat spreads, breakfast cereals, dried and evaporated milk and plant-based drinks are voluntarily fortified with vitamin D. The estimated minimum and maximum vitamin D occurrence levels in these food products were obtained from supermarket label information. Estimates of

consumption rates for these food products are presented in Table 1, in addition to estimates of corresponding vitamin D exposure.

17. It is important to note that consumption estimates of plant-based drinks are based on cow's milk due to the low number of consumers of plant-based drinks recorded in the NDNS. Additionally, the consumption estimates are based on consumption of cow's milk on its own, in breakfast cereals and in beverages.

18. Estimated minimum and maximum vitamin D levels for margarine and fat spreads were 50 and 75 µg/kg (2,000-3,000 IU), respectively (Sainsbury's, Tesco, 2020). For breakfast cereals, estimated minimum and maximum vitamin D levels were 25 and 84 µg/kg (1,000 and 3,360 IU), respectively (Sainsbury's 2020). As for dried milk, estimated minimum and maximum vitamin D levels were 1.5 and 46 µg/kg (60 and 1,840 IU), respectively. For evaporated milk, estimated vitamin D levels were 26 and 29 µg/kg. Additionally, plant-based drinks had estimated minimum and maximum vitamin D levels of 7.5 and 18 µg/kg (300-720 IU), respectively. More specifically soya, coconut and almond milk alternatives had vitamin D levels of 7.5 µg/kg (300 IU). Oat milk alternatives had estimated minimum and maximum vitamin D levels of 7.5 and 18 µg/kg (300-720 IU), respectively (Sainsbury's, Tesco, 2020).

19. As noted above, the form of vitamin D that these foods were fortified with was not specified. However, their exposures are compared to the TUL of 25 µg/day which is protective of both forms of vitamin D (D_2 and D_3).

Table 1: Estimates of chronic exposure of infants (aged 4 to 12 months) to vitamin D from consumption of some foods.

Food type (number of consumers)	Mean consumption (g/day)	97.5th percentile consumption (g/day)	Estimated vitamin D concentration (µg/kg)	Mean exposure (µg/person/day)*	97.5th percentile exposure (µg/person/day)*	Max exposure (µg/person/day)*
Mushrooms (298)	2.7	13	Min: 2.1	0.0057	0.028	0.041

Mushrooms (298)	2.7	13	Max: 100	0.27	1.3	2.0
Eggs (292)	3.7	14	126	0.47	1.7	3.1
Oily fish (167)	7.3	24	Min: 50	0.37	1.2	2.2
Oily fish (167)	7.3	24	Max: 160	1.2	3.9	7.0
Chicken (930)	7.6	27	Min:1	0.0076	0.027	0.063
Chicken (930)	7.6	27	Max: 15	0.11	0.41	0.95
Beef (847)	7.7	30	Min:1	0.0077	0.030	0.051
Beef (847)	7.7	30	Max: 15	0.11	0.45	0.77
Pork (451)	7.1	27	Min: 1	0.0071	0.027	0.053
Pork (451)	7.1	27	Max: 15	0.11	0.40	0.80
Turkey (60)	6.0	17	Min:1	0.0060	0.017	0.020
Turkey (60)	6.0	17	Max:15	0.091	0.26	0.30
Offal- liver and kidney (17)*	5.9	19	Min:1	0.0059	0.019	0.36
Offal- liver and kidney (17)*	5.9	19	Max:15	0.089	0.28	0.36
Margarine and spreads (426)	2.8	9.6	Min: 50	0.14	0.48	1.0
Margarine and	2.8	9.6	Max: 75	0.21	0.72	1.5

spreads (426)						
Breakfast cereals (519)	13	56	Min: 25	0.31	1.4	5.3
Breakfast cereals (519)	13	56	Max: 84	1.1	4.7	18
Dried milk (464)	1.6	10	Min: 1.5	0.0024	0.015	0.077
Dried milk (464)	1.6	10	Max: 46	0.074	0.46	2.4
Evaporated milk (2*)	1.2	1.3	Min: 26	0.032	0.033	0.033
Evaporated milk (2*)	1.2	1.3	Max: 29	0.035	0.037	0.038
Plant-based drinks (750)**	79	532	Min: 7.5	0.59	4.0	8.4
Plant-based drinks (750)**	79	532	Max: 18	1.4	9.6	20

*Consumption or exposure estimates made with a small number of consumers may not be accurate. The number of consumers is less than 60, this should be treated with caution and may not be representative for a large number of consumers.

** Cow's milk has been used as a proxy for plant-based drinks. Cow's milk contains very low amounts of vitamin D (approx. 1µg/kg). As such, the exposure may be overestimated as it is expected that only a low number of infants and toddlers would consume plant-based drinks in place of cow's milk.

20. The tables below provide estimates of chronic exposure to vitamin D from

consumption of infant formula/follow-on milk and the diet, which are based on the new regulation (Table 2) or based on vitamin D levels in milk products available on the UK market (Table 3). The ranges of vitamin D exposure in Tables 2 and 3 were estimated by taking account of the following:

- the estimated range of concentrations of vitamin D in infant formula;
- the estimated rates of consumption; and,
- minimum and maximum vitamin D levels in various other food products as described above.

Table 2: Estimates of chronic infant exposure to vitamin D from consumption of food and infant formula/follow-on milk (based on new regulation).

Age group	Number of consumers	Mean chronic exposure to vitamin D (µg/person/day)*	97.5th percentile chronic exposure to vitamin D (µg/person/day)*	Maximum chronic exposure to vitamin D (µg/person/day)*
4 - <6 months	104	7.5 - 9.5	14 -17	15 -19
6- <12 months	1274	5.1 – 8.5	12 -18	20 - 30
4 -<12 months	1378	5.3 – 8.7	12 - 19	20 - 30

* Uses a minimum of 1.34 µg /100ml and a maximum of 2.01 µg /100ml (i.e. 2 – 3 µg /100 kcal) vitamin D in infant formula/follow-on milk.

Table 3: Estimates of chronic exposure to vitamin D from consumption of food and infant formula/follow-on milk (based on vitamin D levels in milk products available on UK market).

Age group	Concentration used (µg/100kcal)	Number of consumers	Mean chronic exposure to vitamin D (µg/person/day)*	97.5th percentile chronic exposure to vitamin D	Maximum chronic exposure to vitamin D

				(µg/person/day)*	(µg/person/day)*
4 - <6 months	2.20 – 2.5	104	8.1 – 9.6	15 - 17	17 - 20
6 - <12 months	2.54	1274	6.3- 7.5	15 - 16	25 - 26
12 - <18 months	1.64 - 5.0	1271	3.7 – 9.8	8.3 – 24	13 - 38
18 - <48 months	1.64 – 6.27	1156	2.9 – 7.4	7.1 - 18	12 - 33
4 - <12 months	2.20 – 2.54	1378	5.7 – 7.6	13 - 16	22 - 26

* Uses a minimum of 1.34 µg /100ml and a maximum of 2.01 µg /100ml (i.e. 2 – 3 µg /100kcal) vitamin D.

21. Based on Tables 2 and 3 (which show estimates of vitamin D exposure in infants from consumption of food and infant formula/follow-on milk), the mean and 97.5th percentile values are all below the TUL of 25 µg/day. If an additional vitamin D intake of 10 µg/day is added (highest recommended intake from a vitamin D supplement) (data not shown), there would be a minor exceedance of the TUL of 25 µg/day in infants (ages 4 - <6 months and 6 - <12 months), but only at the 97.5th percentile - i.e. infants consuming foods at the 97.5th percentile, including maximum vitamin D concentrations permitted in infant formula.

Summary and conclusions

22. As shown in Table 2 for infants, the estimated mean and 97.5th percentile levels of chronic exposure to vitamin D (from consumption of food and infant formula/follow-on milk only) are below the TUL of 25 µg/day, indicating no health concern. However, there are some minor exceedances of the TUL at the maximum estimated exposure levels when additional intake from vitamin D supplements is

considered.

23. It is unlikely that for those infant groups where an exceedance is calculated that there would be exceedances on a daily basis as it is likely that the diet of an individual (excepting formula and supplements) would vary. Furthermore, the exceedances of the TUL where they do occur are minor and are unlikely to cause any health effects in infants.

Questions for the Committee

1. Does the Committee consider that the new minimum vitamin D content in infant formulae leads to excessive vitamin D exposure in infants?

2. If so, does the Committee consider that the current UK government guidance on vitamin D supplementation for infants needs updating?

Secretariat

January 2022

Abbreviations

DNSIYC	Diet And Nutrition Survey of Infants and Young Children
EFSA	European Food Safety Authority
kcal	kilocalories
NDNS	National Dietary and Nutrition survey
NHS	UK National Health Service
NLCS	Nutrition Labelling, Composition and Standards
SACN	Scientific Advisory Committee on Nutrition
SCF	Scientific Committee on Food
TUL	tolerable upper level

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