TOX/2023/03

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

## First draft statement on the guidance levels for the fortificants in the bread and flour regulations

### Introduction

- 1. In 2022, the Department for Environment, Food and Rural Affairs (Defra) held a consultation on the Bread and Flour Regulations (BFR) 1998 to increase the fortification level to allow harmonisation with EU retained Regulation (EU) No 1169/2011. Defra asked whether the consultees agreed with the proposal to raise the minimum levels of calcium carbonate, iron and niacin added to non-wholemeal flour to 15% of the nutrient reference values (NRV). The minimum amount of thiamin required to be present in non-wholemeal wheat flour would remain the same at 19% of the NRV. NRVs are established guidelines for the recommended daily energy and nutrient consumption.
- 2. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) have been asked by the Department of Health and Social Care (DHSC) to provide an assessment on the dietary exposure of calcium carbonate, iron, nicotinic acid and thiamin (Vitamin B1) at current and proposed fortification levels. The exposure assessment should provide a comparison to the UK Expert Group on Vitamins and Minerals (EVM) safe levels and upper levels (UL) and assess whether there is a potential risk to human health from the proposed increased fortification in non-wholemeal wheat flour.
- 3. A paper (TOX/2022/48) was brought to the Committee in October. DHSC have requested that a statement be published with the conclusions of

the Committee. Annex A contains the first draft statement for the consideration of the Committee.

### Questions on which the views of the Committee are sought

Members are invited to consider the following questions:

- i). Do the Members have any comments on the structure and content of the first draft statement?
- ii). Do Members have any further comments?

**Secretariat** 

February 2023

TOX/2023/03 Annex A

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

First draft statement on the guidance levels for fortificants in the bread and flour regulations (BFR)

### **Background**

- 1. In 2022, the Department for Environment, Food and Rural Affairs (Defra) held a consultation on the Bread and Flour Regulations (BFRs) 1998 to increase the fortification level to allow harmonisation with EU retained Regulation (EU) No 1169/2011. Defra asked whether the consultees agreed with the proposal to raise the minimum levels of calcium carbonate, iron and niacin added to non-wholemeal flour to 15% of the nutrient reference values (NRV). The minimum amount of thiamin required to be present in non-wholemeal wheat flour would remain the same at 19% of the NRV. NRVs are established guidelines for the recommended daily energy and nutrient consumption.
- 2. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) have been asked by the Department of Health and Social Care (DHSC) to provide an assessment on the dietary exposure of calcium carbonate, iron, niacin (nicotinic acid) and thiamin (Vitamin B1) at current and proposed fortification levels. The exposure assessment should provide a comparison to the UK Expert Group on Vitamins and Minerals (EVM) safe levels and upper levels (UL) and assess whether there is a

potential risk to human health from the proposed increased fortification in nonwholemeal wheat flour.

### Introduction

- 3. The BFR 1998 stipulates the levels of calcium carbonate, iron, thiamin (vitamin B1) and niacin (nicotinic acid) that are required to be present in all wheat flour other than wholemeal (i.e. non-wholemeal flour). Calcium is added in the form of calcium carbonate. Natural calcium found in food would not be present in the form of calcium carbonate. Therefore, exposure to calcium from fortified food can be distinguished from natural or supplementary sources when analysed. Niacin is added to flour using either nicotinic acid or nicotinamide.
- 4. The existing BFRs (1998) set a minimum fortification level for thiamin (vitamin B1) of 0.24 mg for thiamin hydrochloride, which is equivalent to 0.21 mg of thiamin or 19% of the NRV. The minimum fortification levels of calcium, iron and niacin have been set at 15% of the nutrient reference value (NRV) as stated in Annex XIII of regulation EC No. 1169/2011 (in point 1 of Part A). In practise, foods are not currently fortified at these respective levels, but industry are looking to increase fortification to the set minimum levels. The Daily NRVs for calcium carbonate, iron, niacin and thiamin (Vitamin B1) are 800, 14, 16 and 1.1 mg, respectively.

### **Toxicity**

### **Calcium**

5. High intakes of calcium carbonate of around 4,000 mg/day (equivalent to 1,600 mg calcium) can result in a condition called milk-alkali syndrome in people with underlying medical conditions such as peptic ulcers (EFSA, 2006). This condition is characterised by hypercalcaemia, alkalosis and renal impairment, which is associated with symptoms of hypertension, neurological problems, abdominal pain and tissue calcification (EVM, 2003).

- 6. Calcium supplements have been administered to people with colonic polyps or people who are at risk of colonic polyps. Gastrointestinal (GI) effects were reported in a small number of patients receiving 1,600 or 2,000 mg/day of calcium (EVM, 2003).
- 7. High calcium diets can affect the bioavailability of other minerals such as iron, zinc, magnesium and phosphorous by inhibiting the absorption of iron salts, haem-iron and zinc, reducing magnesium absorption and excretion, and the binding of calcium acetate and calcium carbonate to phosphate in the intestinal lumen (EFSA, 2006).

### Iron

- 8. Iron toxicity is particularly hazardous in children and most poisoning cases are reported in children consuming iron supplements intended for adults. Symptoms in infants include gastrointestinal irritation at acute doses of around 20 mg/kg bw and other systemic effects which occur at doses <60 mg/kg bw. The lethal dose in children is between 200-300 mg/kg bw (EVM, 2003).
- 9. In adults, gastrointestinal effects such as constipation, nausea, vomiting and diarrhoea have been reported at therapeutic doses of 50-220 mg/day (EFSA, 2006). Iron toxicity can lead to inflammation and perforation of the gastrointestinal tract and iron disrupts the cellular metabolism in the central nervous system, liver and heart. Free iron in the serum, enters and concentrates in the mitochondria where it forms free radicals, which can impair energy metabolism and can eventually lead to cell death (Baranwal and Singhi, 2003; Yuen and Becker, 2022). However, iron poisoning in adults is rare, individual case reports suggest a lethal dose of 1,400 mg/kg bw (EVM, 2003)

### Niacin (nicotinic acid/vitamin B3)

- 10. Symptoms of acute toxicity from niacin include flushing, itchy skin, nausea, vomiting and gastrointestinal issues (such as diarrhoea and constipation). Long term intakes of 3,000 mg/day of niacin have been reported to cause jaundice, hyperglycaemia and abdominal pain. In addition to elevated serum bilirubin, increased alkaline phosphatase and aminotransferase levels have been reported in a small number of cases. Anorexia, ophthalmological effects, skin hyperpigmentation and precipitation of incipient psychosis have also been reported as side effects of niacin therapy (EVM, 2003).
- 11. Patients with hypercholesterolaemia that have been treated with niacin at 3-9 g/day over a period of months to years showed symptoms of severe liver dysfunction which has the potential to be life threatening and may require liver transplantation (EFSA, 2006).

### **Thiamin**

- 12. Thiamin is considered to be of very low toxicity with symptoms such as headache, nausea, irritability, insomnia, rapid pulse and weakness being seen at high oral doses of ≥7,000 mg thiamin hydrochloride (EVM, 2003).
- 13. However, a small number of case reports have shown association with adverse effects such as muscle tremors, rapid pulse and nerve hyperirritability at low daily doses of 17 mg/day of thiamin hydrochloride. In one case, a patient consuming thiamin at 100 mg/day for a period of 15 days, 2 months prior to consumption of a single oral dose of thiamin of 100 mg, experienced an anaphylactic reaction followed by death. In another case, a patient experienced exacerbated eczema after receiving an oral dose of 200 mg of thiamin in an experimental provocation (EVM, 2003).

### Health based guidance values

- 14. Tolerable upper levels (TUL) nor safe upper levels (UL) have been established for calcium, iron, niacin (nicotinic acid) and thiamin by the Expert Group on Vitamins and Minerals (EVM) due to the lack of insufficient animal and human data (EVM, 2003).
- 15. However, the EVM stated that "1,500 mg/day of supplemental calcium would not be expected to result in any adverse effect, but that higher doses could result in adverse gastrointestinal symptoms in a few people" (EVM, 2003). Literature publicly available at the time of the COTs assessment (EVM, 2003) did not provide any new information or data indicating that any other level of calcium should be used as a safe UL. The Scientific Committee on Food (SCF) established a TUL of 2,500 mg/day for calcium in 2003 (SCF, 2003). This TUL was based on different long duration intervention studies in which total daily calcium intakes of 2,500 mg from both diet and supplements were tolerated without adverse effects and was endorsed by EFSA in 2012 (EFSA, 2012).
- 16. The EVM proposed that a supplemental intake of 17 mg/day for iron would not be expected to produce adverse effects in the majority of individuals. However, this guidance value does not apply to individuals who have an increased susceptibility to iron overload, a condition which is associated with a homozygous haemochromatosis genotype (with an estimated prevalence of up to 0.4% in the Caucasian population). An UL for iron has not been established by EFSA. The National Institutes of Health Office of Dietary Supplements in the United States have advised safe ULs of 40 mg/day for individuals aged 0 months to 13 years and 45 mg/day for individuals aged 14 years and over (Institute of Medicine, 2001). However, moderate symptoms of iron toxicity have been reported from 20 mg/kg bw/day (Madiwale and Liebelt, 2006). However, Madiwale and Liebelt (2006) reported

that ingestion <20 mg/kg is non-toxic and moderate symptoms of iron toxicity can occur between 20 to 60 mg/kg.

- 17. The EVM proposed that a guidance level of 17 mg/day for niacin (nicotinic acid) would not be expected to result in any adverse effects. However, it was noted by the EVM that this guidance level is for supplementation only, as adverse effects from niacin seem to be related to acute, bolus intakes. Adverse effects from long term exposure of niacin in food would be less likely as free niacin levels in food are low. Additionally, the EVM noted that the guidance level is based on intakes of conventional formulations of niacin. This would not be applicable to sustained release preparations and niacin contained in dietary supplements is not in the sustained release form (EVM, 2003). In 2002, the SCF set an UL of 10 mg/day for niacin based on flushing of skin (EFSA, 2014).
- 18. The EVM proposed a guidance level for supplemental thiamin of 100 mg/day which would not be expected to result in adverse effects. The EVM noted however that this guidance level was only applicable to the watersoluble forms of thamin. Furthermore, the study by Gokhale *et al.* (1999), used to derive the guidance level, was conducted in young women (EVM, 2003). An UL for thiamin was not established by the SCF due to limited data on adverse effects in humans and lack of dose-response studies (EFSA, 2016). Whilst there is a lack of evidence of toxicity from a high intake of thamin from food or supplements (Martel *et al.*, 2021), symptoms such as headache, nausea, irritability, insomnia, rapid pulse and weakness have been seen at high oral doses of ≥7,000 mg/day thiamin hydrochloride (EVM, 2003).

### **Exposure assessment**

19. Exposures to calcium, iron, niacin and thiamin were determined using consumption data from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) and the National Diet and Nutrition Survey (NDNS). Levels of these nutrients in the entire diet were obtained from the nutrient

databank (Bates *et al.*, 2014, 2016, 2020; Roberts *et al.*, 2018). Levels of nutrients in non-wholemeal flour used in the exposure assessment were those currently in use by industry. Exposure to the nutrients based on the proposed increases were also determined, except for thiamin, where no increases have been proposed. Table 2 provides information about current and proposed fortification levels for each nutrient where applicable. Exposure to these nutrients were calculated in Crème Global, the software that the FSA uses to interrogate dietary data and calculate exposure. Exposure estimates were derived by multiplying food consumption amounts by the levels of the nutrients in the foods. Chronic exposure or intake of these nutrients are presented. Chronic intake is derived from the average amount of flour consumed over the survey days multiplied by the levels of nutrients. Chronic exposure or intake is calculated for each consumer. The mean and P97.5 are then computed.

Table 1. Concentration data used to derive exposure to calcium, iron, niacin and thiamin

Nutrient	Nutrient reference value (mg/person/day)	Current minimum levels(mg/100 g non- wholemeal flour)	Level based on fortification at 15% (mg/100 g non- wholemeal flour)
Calcium	800	94	120
Iron	14	1.65	2.1
Niacin	16	1.6	2.4
Thiamin	1.1	0.24	NA*

<sup>\*</sup> A change in fortification level has not been proposed.

### Methodology for estimating current and proposed exposures from nonwholemeal flour

20. Exposures based on current and proposed levels were calculated from foods containing non-wholemeal flour. This by definition is wheat flour without whole grain wheat. The recipe database associated with the NDNS food groupings identified foods containing non-wholemeal flour (n=1835). A

selection of food groups (foods with non-wholemeal flour), each containing more than 20 foods are shown in Table A1 in Annex A.

- 21. The fortification level for thiamin remains unchanged, therefore exposures at the proposed fortification levels were only calculated for calcium, iron, and niacin.
- 22. Exposures to these nutrients from supplements were also considered. Data for supplements were obtained from market sources (e.g., websites of major retailers). Concentrations of calcium supplements ranged from 200-1200 mg for adults and 80-450 mg for children. Whereas concentrations of iron supplements ranged from 14-28 mg in adults and 2.8-7.5 mg in children. Concentrations of niacin supplements ranged from 50-1000 mg in adults and 4.8-20 mg in children. Ultimately, concentrations of thiamin supplements ranged from 100-500 mg for adults and 0.7-5 mg for children

### Exposures from the entire diet and from flour at the current and proposed fortification levels

- 23. Exposure to the nutrients from the entire diet was estimated using all food groups from NDNS years 1-11, which are presented in Table A2 of Annex B. All food groups including the foods containing non-wholemeal flour are detailed in paragraph 20. The levels of the nutrient for each of the foods included were derived from the nutrient databank from the NDNS.
- 24. Exposure to calcium, iron, niacin and thiamin from the entire diet and from flour fortification at current and proposed levels are shown in Table 2-5.
- 25. For calcium, across all age groups (4 months to 65+ years), the maximum mean and maximum 97.5<sup>th</sup> percentile exposures at the current level of fortification were 68 and 140 mg/person/day, respectively. The maximum mean and 97.5<sup>th</sup> percentile exposures at the proposed level of fortification are 87 and 180 mg/person/day, respectively. The maximum exposures to calcium

from the entire diet are 820 and 1,600 mg/person/day at mean and 97.5 the percentile levels respectively (Table 3).

- 26. For iron, across all age groups (4 months to 65+ years), the maximum mean and maximum 97.5<sup>th</sup> percentile exposures at the current level of fortification are 1.2 and 2.5 mg/person/day respectively. The maximum mean and 97.5<sup>th</sup> percentile exposures at the proposed level of fortification are 1.5 and 3.2 mg/person/day respectively. The maximum exposures to iron from the entire diet are 10 and 19 mg/person/day at mean and 97.5<sup>th</sup> percentile levels respectively (Table 4).
- 27. For nicacin, across all age groups (4 months to 65+ years), the maximum mean and maximum 97.5<sup>th</sup> percentile exposures at the current level of fortification are 1.2 and 2.4 mg/person/day respectively. The maximum mean and 97.5<sup>th</sup> percentile exposures at the proposed level of fortification are 1.7 and 3.6 mg/person/day respectively. The maximum exposure to niacin from the entire diet are 36 and 68 at the mean and 97.5<sup>th</sup> percentile, respectively (Table 5).
- 28. For thiamin, across all age groups (4 months to 65+ years), the maximum mean and maximum 97.5<sup>th</sup> percentile exposures at the current level of fortification are 0.17 and 0.36 mg/person/day. The maximum exposure to thiamin from the entire diet are 1.5 and 2.8 mg/person/day at the mean and 97.5<sup>th</sup> percentile, respectively (Table 6).

Table 2. Chronic exposures to calcium from the diet and from flour fortification at current and proposed levels (15% of the nutrient reference value supplied by 100 g flour) levels

Ago		exposure to calcium (mg/person/day)  Mean	97.5th
Age group	Category	Weari	Percentile

Entire diet	680	1200	
		10	
Current levels in flour	15	48	
Proposed levels in	19	61	
Entire diet	740	1300	
Current levels in flour	34	78	
Proposed levels in flour	43	99	
Entire diet	760	1400	
Current levels in flour	55	110	
Proposed levels in flour	71	140	
Entire diet	770	1500	
Current levels in flour	68	140	_
Proposed levels in flour	87	180	3
Entire diet	810	1600	
Current levels in flour	58	140	
Proposed levels in flour	74	180	
Entire diet	820	1500	
Current levels in flour in flour	49	120	
Proposed levels	62	150	
	Current levels in flour Proposed levels in flour Entire diet  Current levels in flour Proposed levels in flour Entire diet  Current levels in flour Proposed levels in flour Proposed levels in flour Entire diet  Current levels in flour Entire diet  Current levels in flour Proposed levels in flour Entire diet  Current levels in flour Entire diet  Current levels in flour Entire diet  Current levels in flour Entire diet	Current levels in flour Proposed levels in flour Entire diet 740  Current levels in flour Proposed levels in flour Entire diet 760  Current levels in flour Entire diet 755  Current levels in flour Proposed levels in flour Entire diet 770  Current levels in flour Entire diet 770  Current levels in flour Proposed levels in flour Proposed levels in flour Entire diet 810  Current levels in flour Entire diet 820  Current levels in flour Entire diet 820  Current levels in flour	Current levels in flour         15         48           Proposed levels in flour         19         61           Entire diet         740         1300           Current levels in flour         34         78           Proposed levels in flour         43         99           Entire diet         760         1400           Current levels in flour         55         110           Proposed levels in flour         71         140           Entire diet         770         1500           Current levels in flour         68         140           Proposed levels in flour         87         180           Current levels in flour         58         140           Proposed levels in flour         58         140           Entire diet         820         1500           Current levels in flour         49         120           Current levels in flour in flour         49         120

Table

Chronic exposures to iron from the diet and from flour fortification at current and proposed (15% of the nutrient reference value supplied by 100 g flour) levels

		Chronic exposure to iron (mg/person/day)*	
Age group	Category	Mean	97.5th Percentile

lu fauta	Fusing dist	0.0	40
Infants	Entire diet	6.8	12
(4-18			
months)	-		
	Current levels in flour	0.27	0.84
	Proposed levels in	0.34	1.1
	flour		
1.5-	Entire diet	6	10
3years			
	Current levels in flour	0.6	1.4
	Proposed levels in	0.76	1.7
	flour	0.7.0	
4 - 10	Entire diet	8.1	14
years		0.1	
ycars	Current levels in flour	0.97	1.9
	Proposed levels in	1.2	2.4
	flour	1.2	2.4
11 – 18	Entire diet	9.3	17
years	Ermio diot	0.0	17
yeare	Current levels in flour	1.2	2.5
	Proposed levels in	1.5	3.2
	flour	1.0	5.2
19 - 64	Entire diet	10	19
	Entire diet	10	19
years	Cummant layeda in flaum	1	2.4
	Current levels in flour		2.4
	Proposed levels in	1.3	3.1
	flour		
65 +	Entire diet	9.7	17
years			
	Current levels in flour	0.85	2.1
	Proposed levels in	1.1	2.6
	flour		

Table 4. Chronic exposures to niacin equivalents from the diet and from flour fortification at current and proposed (15% of the nutrient reference value supplied by 100 g flour) levels

		Chronic exposures to niacin (mg/person/day)*	
	Category	Mean	97.5th Percentile
Infants (4- 18 months)	Entire diet	14	25
	Current levels in flour	0.26	0.81

	Proposed levels in flour	0.39	1.2
1.5-3years	Entire diet	18	28
	Current levels in flour	0.58	1.3
	Proposed levels in flour	0.87	2
4 - 10 years	Entire diet	25	39
	Current levels in flour	0.94	1.9
	Proposed levels in flour	1.4	2.8
11 -	Entire diet	31	55
18years			
	Current levels in flour	1.2	2.4
	Proposed levels in flour	1.7	3.6
19 - 64 years	Entire diet	36	68
	Current levels in flour	0.98	2.4
	Proposed levels in flour	1.5	3.6
65 + years	Entire diet	31	52
	Current levels in flour	0.83	2
	Proposed levels in flour	1.2	3

Table 5: Chronic exposures to thiamin in the diet and from flour fortification at current (19% of the nutrient reference value supplied by 100g flour; there is no proposed increase to thiamin) levels

		Chronic intake of thiamine (mg/person/day)*	
Age group	Category	Mean	97.5th Percentile
Infants (4-18 months)	Entire diet	0.81	1.3
	Current levels in flour	0.039	0.12
1.5-3years	Entire diet	1	1.8
	Current levels in flour	0.087	0.2

4 - 10 years	Entire diet	1.3	2.3
	Current levels in flour	0.14	0.28
11 - 18years	Entire diet	1.4	2.8
	Current levels in flour	0.17	0.36
19 - 64 years	Entire diet	1.5	2.8
	Current levels in flour	0.15	0.36
65 + years	Entire diet	1.5	2.7
	Current levels in flour	0.12	0.3

<sup>\*</sup> Rounded to 2.s.f

### **Exposure from supplements**

- 29. It should be noted that supplements data were derived from various online sources in Tables A5-A8 in Annex A. The exact consumption by the population was unknown therefore exposures were calculated based on recommended serving sizes.
- 30. Across all age groups (4 months to 65+ years) the upper exposures of supplemental calcium were up to 1,200 mg/day. In adults aged over 19 years, this exposure is equivalent to 1.48- and 0.75-fold the mean and 97.5<sup>th</sup> percentile calcium exposures from the entire diet (which includes all food groups including non-wholemeal flour), respectively.
- 31. Across all age groups (4 months to 65+ years) the upper exposures of supplemental iron were up to 28 mg/day. In adults aged over 19 years, this exposure is equivalent to 3- and 1.6-fold the mean and 97.5<sup>th</sup> percentile calcium exposures from the entire diet, respectively.
- 32. Across all age groups (4 months to 65+ years) the upper exposures of supplemental niacin were up to 1,000 mg/day. In adults aged over 19 years this exposure is equivalent of up to 32- and 19-fold of the mean and 97.5th percentile niacin exposures from the entire diet, respectively.
- 33. Across all age groups (4 months to 65+ years) the upper exposures of supplemental thiamin were up to 500 mg/day. In adults aged over 19 years,

this exposure is equivalent to 330- and 185-fold the mean and 97.5<sup>th</sup> percentile thamin exposures from the entire diet.

### **Risk characterisation**

### **Exposures from food**

- 34. Chronic exposure of calcium at the current and proposed fortification levels (Table 3) did not exceed the guidance levels of 1,500 mg/day (EVM, 2003) and 2,500 mg/day (EFSA, 2012) across all age groups. Exposures from the entire diet were up to 1,600 mg/person day which although it exceeds the EVM guidance level, marginally, is below the SCF TUL of 2,500 mg/day
- 35. Chronic exposures to iron at the current and proposed fortification levels (Table 4) did not exceed the guidance levels of 17 mg/day (EVM, 2003) across all ages. However, it is important to note that the guidance level is based on supplemental intake and does not apply to the population who have an increased susceptibility to iron overload. Moderate symptoms of iron toxicity have been reported to occur from 20 mg/kg bw per day (Madiwale and Liebelt, 2006). Exposures from the entire diet were up to 19 mg/person/day, which would result in marginal exceedance of the EVM guidance level but not the level reported to cause moderate symptoms of iron toxicity. It is not anticipated that there would be a risk to health from iron exposures in the entire diet to most of the population. However, the EVM guidance value does not apply to individuals who have an increased susceptibility to iron overload, a condition which is associated with a homozygous haemochromatosis genotype.
- 36. Chronic exposures to niacin equivalents (Table 5) at the current and proposed fortification levels did not exceed the guidance level for niacin of 17 mg/day (EVM, 2003) across all age groups. Exposures to niacin from the entire diet were up to 68 mg/person/day, which exceeds the EVM guidance level up to 4-fold. However, the EVM guidance level is for supplementation only, as adverse effects from niacin seem to be related to acute, bolus

intakes. Adverse effects from long term exposure to niacin in food would be less likely as free niacin levels in food are low. It is unlikely that there would be a risk of adverse health effects at these exposures although there is some uncertainty because of the data used to establish the EVM guidance level: that it is intended for supplements, is based on a bolus intake and that the levels of free niacin in food are low.

37. Chronic exposures to thiamin at the current and proposed fortification levels (Table 6) did not exceed the current guidance level of 100 mg/day (EVM, 2003). Exposures to thiamin from the entire diet were up to 2.8 mg/person/day which were also below the EVM guidance level and it is unlikely that there would be a risk of adverse health effects.

### **Exposure from supplements**

38. Daily exposure to calcium supplements did not exceed the EVM guidance level of 1,500 mg/day (EVM, 2003) or the SCF guidance level of 2,500 mg/day in adults and children (SCF, 2003). Exposure to higher dosage iron supplements (i.e., 28 mg/day) can exceed the guidance level of 17 mg/day (EVM, 2003) by up to 1.6-fold in adults. Daily exposure to niacin supplements could result in exceedances of the guidance level of 17 mg/day (EVM, 2003), by between 3- and 60-fold. For thiamin supplements, daily exposure could lead to up to a 5-fold exceedance of the guidance level of 100 mg/day (EVM, 2003).

### **Exposure from supplements and food**

39. Mean calcium exposures from food (the entire diet and flour at the current and proposed fortification levels) and supplements (Table A3) were up to 2,000 mg/person/day, respectively and below either the EVM guidance level and/or the SCF TUL. Exposures associated with 97.5<sup>th</sup> percentile consumption were between 1,700 and 2,800 mg/person/day. For population groups below 19 years of age, the exposures are below the SCF TUL and it is unlikely that there would be a risk of adverse health effects. Population groups

for 19 years and over marginally exceeded the SCF TUL and it is unlikely that there would be a risk of adverse health effects in humans at these exposures.

- 40. Mean and 97.5<sup>th</sup> percentile iron exposures from food and supplements were up to 20 mg/person/day which were either below or a minor exceedance of the guidance level of 17 mg/day (EVM, 2003) in those aged upto 18 years. There is unlikely to be a risk of adverse health effects in these populations due to exposures from iron. However, in the 19-64 and 65+ years age groups, mean and 97.5<sup>th</sup> percentile iron exposures were up to 38 and 47 mg/person/day which were exceedances of up to 2.2-fold and 2.8-fold, respectively. It is unlikely that there is a risk of adverse health effects. The EVM guidance value does not apply to individuals who have an increased susceptibility to iron overload, a condition which is associated with a homozygous haemochromatosis genotype.
- 41. Mean and 97.5<sup>th</sup> percentile niacin exposure from food (entire diet) and supplements exceeded the guidance level of 17 mg/day (EVM, 2003) across all age groups. In those aged up to 18 years exceedances of the 17 mg/day guidance level were up to 3- and 4.4-fold for mean and 97.5<sup>th</sup> percentile consumption, respectively. In individuals aged up to 3 years the exceedances were approximately half of these (up to 2.2- and .8-fold for mean and 97.5<sup>th</sup> percentile consumers, respectively). In those aged over 19 years the exceedances of the 17 mg/day guidance level were up to 59- and 65-fold for mean and 97.5<sup>th</sup> percentile consumers, respectively. Most of this exceedance comes from the consumption of supplements containing niacin at 1,000 mg.
- 42. As indicated in paragraph 36, the EVM guidance level is for supplementation only, as adverse effects from niacin seem to be related to acute, bolus intakes. Adverse effects from long term exposure to niacin in food would be less likely as free niacin levels in food are low. It is unlikely that there would be a risk of adverse health effects at the exposures from the entire diet, although there is some uncertainty because of the data used to establish the EVM guidance level. It is intended for supplements and is more

considered for a bolus intake. It should also be noted that the levels of free niacin in food are low. Exposures from consumption of supplements containing high levels of niacin e.g. 1,000 mg could be at increased risk of adverse health effects, especially when consumed consistently over a prolonged period of time.

43. Exposures to thiamin for all age groups below 18 years of age are below the guidance level of 100 mg/day (EVM, 2003). Mean and 97.5<sup>th</sup> percentile intakes from food and supplements only exceeded the guidance level for thiamin of 100 mg/day (EVM, 2003) in the 19-64 years and 65+ years age groups. In these age groups both exceeded the guidance level by 5-fold. This was predominantly from consumption of supplements which may contain up to 500 mg. It is unlikely that these exposures would cause adverse health effects.

### Conclusion

- 44. Chronic exposures of calcium, iron, niacin and thamin from non-wholemeal flour at the current and proposed fortification levels did not exceed the guidance level. For each of the nutrients, the difference in exposure between current and proposed levels of fortification is very small, especially when compared to exposures form the entire diet and from supplements. Therefore, the change to the proposed levels of fortification would not increase the risk to adverse health effects when taken in consideration of the entire diet and consumption of supplements.
- 45. Intakes of calcium from supplements alone did not exceed the guidance level. Consumption of higher dosage iron, niacin and thamin supplements may result in exceedances of the guidance level. However, it is important to note that not all members of the population will consume supplements.
- 46. Calcium exposure from food and supplements only exceeded the guidance level EFSA TUL of 2,500 mg/day marginally and only in 97.5<sup>th</sup>

percentile consumers in those aged over 19 years. There is unlikely to be a risk of adverse health effects based on these exposures.

- 47. Iron exposures from food and supplements exceeded the guidance levels in some age groups, up to a maximum of 2.8-fold the 17 mg/day guidance level. There is unlikely to be a risk of adverse health effects based on these exposures. However, the EVM guidance value does not apply to individuals who have an increased susceptibility to iron overload, a condition which is associated with a homozygous haemochromatosis genotype.
- 48. In those aged up to 18 years niacin exceedances of the 17 mg/day guidance level (EVM, 2003) were up to 3- and 4.4-fold for mean and 97.5<sup>th</sup> percentile consumption, respectively. In those aged over 19 years the exceedances of the 17 mg/day guidance level were up to 59- and 65-fold for mean and 97.5<sup>th</sup> percentile consumers, respectively. Most of this exceedance comes from the consumption of supplements containing niacin at 1,000 mg. Adverse effects from long term exposure to niacin in food would be less likely as free niacin levels in food are low. However, there is some uncertainty because of the data used to establish the EVM guidance level. It is intended for supplements and is more considered for a bolus intake. Exposures from consumption of supplements containing high levels of niacin e.g. 1,000 mg could lead to increased risk of adverse health effects, especially when consumed consistently over a prolonged period of time.
- 49. Exposures to thiamin for all age groups below 18 years of age are below the guidance level of 100 mg/day (EVM, 2003). Mean and 97.5<sup>th</sup> percentile intakes from food and supplements only exceeded the guidance level for thiamin in consumers aged over 19, by a maximum of upto 5-fold. This was predominantly from consumption of supplements which may contain up to 500 mg. It is unlikely that these exposures would cause adverse health effects.

- 50. The <u>NHS</u> states that "most people do not need to take vitamin supplements and can get all the vitamins and minerals they need by eating a healthy, balanced diet".
- 51. While the Committee noted that there would be a possible exceedance in individuals that consume supplements, the COT overall concluded that an increase in the minimum fortification level of calcium, iron and niacin to 15% of the NRV would not result in any additional risk when compared to current fortification levels.

**Secretariat** 

February 2023

### **List of Abbreviations and Technical terms**

BFR	Bread and Flour Regulations	
СОТ	Committee on Toxicity Chemicals in	
	Food, Consumer Products and the	
	Environment.	
DHSC	Department of Health and Social	
	Care	
SCF	Scientific Committee on Food	
TUL	Tolerable Upper Level	
NRV	Nutrient reference Value	

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### Secretariat

February 2023

### TOX/2022/XX ANNEX A

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

# Review of the guidance levels for fortificants in the bread and flour regulations (BFR)

Table A1: A selection of food groups containing foods with non-wholemeal flour

Food group	Number of foods assessed in the group
Biscuits (manufactured/retail)	105
Brown, granary and wheatgerm bread	25
Buns cakes and pastries (homemade)	118
Buns cakes and pastries (manufactured)	103
Burgers and kebabs purchased	24
Fruit pies (homemade)	20
Manufactured coated chicken/turkey products	34
Meat pies and pastries (homemade)	39
Meat pies and pastries (manufactured)	38
Other breakfast cereals (not high fibre)	24
Other cereal based puddings (homemade)	40
Other cereals	41
Other manufactured vegetable products (including ready meals)	21
Other sausages (including homemade dishes)	30

Pasta (manufactured products and ready meals)	26
Savoury sauces pickles gravies & condiments	31
White bread (not high fibre, not multiseed bread)	56
White fish coated or fried	112

Table A2: All food groups from the NDNS used to estimate the intake of nutrients from the entire diet

group
5
4
27
11
8
5
72
29
44
15
153
2
11
42
132
113

Burgers and kebabs purchased (29R)	31
Butter (17R)	6
Calcium only or with vitamin D (54F)	17
Canned fruit in juice (40D)	24
Canned fruit in syrup (40E)	41
Carrots (raw) (36A)	4
Carrots not raw (37E)	11
Cereal based milk puddings	26
(homemade) (9D)	
Cereal based milk puddings	40
(manufactured) (9C)	
Cheddar cheese (14B)	9
Chips purchased including takeaway	42
(38A)	
Chocolate confectionery (44R)	53
Cider and perry (49C)	7
Citrus fruit not canned (40B)	12
Cod liver oil and other fish oils (54A)	1
Cod liver oil and other fish oils	47
(including with vitamins A,D,E) (54N)	
Coffee (made up weight) (51A)	25
Commercial toddlers drinks (52A)	9
Commercial toddlers foods (52R)	131
Cottage cheese (14A)	5
Cream (including imitation cream)	41
(13B)	
Crisps and savoury snacks (42R)	43
Dairy desserts (homemade) (15D)	11
Evening primrose oil and other plant	18
oils (54B)	
Folic acid (54D)	2
Fortified wine (48B)	10

Fromage frais and other dairy desserts	51
(manufactured) (15C)	
Fruit juice (45R)	45
Fruit pies (homemade) (8C)	24
Fruit pies (manufactured) (8B)	7
Green beans not raw (37B)	8
Herbal tea (made up) (51C)	3
High fibre breakfast cereals (5R)	128
Ice cream (53R)	40
Infant formula (13A)	82
Iron only or with vitamin C (54E)	11
Leafy green vegetables not raw (37D)	28
Liqueurs (47A)	9
Liver and dishes (28R)	36
Low alcohol & alcohol free beer & lager	9
(49B)	
Low alcohol & alcohol free cider &	3
perry (49D)	
Low alcohol and alcohol free wine	4
(48C)	
Low fat spread not polyunsaturated	7
(19R)	
Manufactured beef products (including	49
ready meals) (23A)	
Manufactured canned tuna products	8
(including ready meals) (34G)	
Manufactured chicken products	79
(including ready meals) (27A) - 79	
foods.	
Manufactured coated chicken/turkey	34
products (26A)	

Manufactured egg products including	18
ready meals (16C)	
Manufactured lamb products (including	11
ready meals) (24A)	
Manufactured oily fish products	45
(including ready meals) (35A)	
Manufactured pork products (including	9
ready meals) (25A)	
Manufactured shellfish products	17
(including ready meals) (34E)	
Manufactured white fish products	8
(including ready meals) (34C)	
Meat alternatives (including ready	41
meals and homemade dishes) (37K)	
Meat pies and pastries (homemade)	39
(31B)	
Meat pies and pastries (manufactured)	38
(31A)	
Minerals (two or more including	4
multiminerals) no vitamins (54H)	
Multivitamins and/or minerals with	30
omega (54P)	
Non-nutrient supplements (including	46
herbal) (54J)	
Nutrition powders and drinks (50E)	62
Nuts and seeds (56R)	53
Other bacon and ham (including	66
homemade dishes) (22B)	
Other beef & veal (including	135
homemade recipe dishes) (23B)	
Other bread (4R)	17

Other breakfast cereals (not high fibre)	70
(6R)	
Other canned tuna (including	7
homemade dishes) (34H)	
Other cereal based puddings	58
(homemade) (9H)	
Other cereal based puddings	23
(manufactured) (9G)	
Other cereals (1R)	106
Other cheese (14R)	80
Other chicken/turkey (including	146
homemade recipe dishes) (27B)	
Other cooking fats and oils not	28
polyunsaturated (20C	
Other eggs and egg dishes including	98
homemade (16D) -	
Other fried/roast potatoes (including	55
homemade dishes) (38D) -	
Other fruit not canned (40R)	193
Other lamb (including homemade	80
recipe dishes) (24B)	
Other manufactured potato products	20
fried/baked (38C)	
Other manufactured vegetable	49
products (including ready meals) (37L)	
ther meat (including homemade recipe	66
dishes) (32B)	
Other meat products (manufactured	34
including ready meals) (32A)	
Other milk (13R)	72
Other nutrient supplements (54K)	55

Other oily fish (including homemade	71
dishes) (35B) - 71 foods.	
Other pork (including homemade recipe	69
dishes) (25B)	
Other potato products and dishes	20
(manufactured) (39A)	
Other potatoes (including homemade	50
dishes) (39B)	
Other sausages (including homemade	46
dishes) (30B)	
Other shellfish (including homemade	45
dishes) (34F)	
Other vegetables (including homemade	217
dishes) (37M)	
Other white fish (including homemade	83
dishes) (34D)	
Pasta (manufactured products and	39
ready meals) (1D)	
Pasta (other, including homemade	36
dishes) (1E)	
Peas not raw (37A)	20
Pizza (1C)	12
Iyunsaturated low fat spread (19A)	10
Polyunsaturated margarine (18A)	1
Polyunsaturated oils (18B)	7
Preserves (41B)	22
Ready meals based on sausages (30A)	2
Ready meals/meal centres based on	3
bacon and ham (22A)	
Reduced fat spread (not	16
polyunsaturated) (21B)	

Reduced fat spread (polyunsaturated)	9
(21A)	
Rice (manufactured products and ready	9
meals) (1F)	
ice (other, including homemade dishes)	53
(1G)	
Salad and other raw vegetables (36B)	93
Savoury sauces pickles gravies &	203
condiments (50R)	
Semi-skimmed milk (11R)	9
Single vitamins/minerals not Folic acid,	61
iron, calcium or vitamin C (54M)	
Skimmed milk (12R)	11
Smoothies (61R)	10
Soft drinks low calorie carbonated	24
(58B)	
Soft drinks low calorie concentrated	13
(58A)	
Soft drinks low calorie, ready to drink,	26
still (58C)	
Soft drinks not low calorie carbonated	39
(57B)	
Soft drinks not low calorie concentrated	23
(57A)	
Soft drinks not low calorie, ready to	43
drink, still (57C)	
Soft margarine not polyunsaturated	3
(20B)	
Soup (homemade) (50D)	39
Soup (manufactured/retail) (50C)	48
Spirits (47B)	1
Sponge puddings (homemade) (9F)	10

Sponge puddings (manufactured) (9E)	9
Sugar (41A)	15
Sugar confectionery (43R)	54
Sweet spreads fillings and icing (41R)	23
Tap water only (51R) -	2
Tea (made up) (51B) -	9
Tomatoes not raw (37F	14
Tomatoes raw (36C)	3
White bread (not high fibre, not	58
multiseed bread) (2R)	
White fish coated or fried (33R)	139
Whole milk (10R)	11
Wholemeal bread (3R)	31
Wine (48A)	16
Yogurt (15B)	82

Table A3: Calcium exposure from foods and supplements

		Chronic exposure of calcium from food (mg/person/day)*		Calcium exposure from supplements, upper range (mg/person/day)	Calcium exposure from supplements and diet (mean) (mg/person/day)	Calcium exposure from supplements and diet (97.5 <sup>th</sup> percentile) (mg/person/day)
Age group	Category	Mean	97.5th Percentile			
Infants (4-18 months)	Entire diet	680	1200	450	1100	1700
	Current levels in flour	15	48	450	470	500
	Proposed levels in flour	19	61	450	470	500
1.5- 3years	Entire diet	740	1300	450	1200	1800
	Current levels in flour	34	78	450	490	530
	Proposed levels in flour	43	99	450	490	550
4 - 10 years	Entire diet	760	1400	450	1200	1900
	Current levels in flour	55	110	450	510	560

	Proposed levels in flour	71	140	450	520	590
11 - 18years	Entire diet	770	1500	450	1200	2000
	Current levels in flour	68	140	450	520	590
	Proposed levels in flour	87	180	450	540	630
19 - 64 years	Entire diet	810	1600	1200	2000	2800
	Current levels in flour	58	140	1200	1300	1300
	Proposed levels in flour	74	180	1200	1300	1400
65 + years	Entire diet	820	1500	1200	2000	2700
	Current levels in flour	49	120	1200	1200	1300
	Proposed levels in flour	62	150	1200	1300	1400

Table A4: Iron exposure from food and supplements

		Chronic exposure to iron (mg/person/day)*		Iron exposure from supplements, upper range (mg/person/day)	Iron exposure from supplements and diet (mean) (mg/person/day)	Iron exposure from supplements and diet (97.5 <sup>th</sup> percentile) (mg/person/day)
Age group	Category	Mean	97.5th Percentile			
Infants (4-18 months)	Entire diet	6.8	12	7.5	14.0	20
	Current levels in flour	0.27	0.84	7.5	7.8	8.3
	Proposed levels in flour	0.34	1.1	7.5	7.8	8.6
1.5- 3years	Entire diet	6	10	7.5	14	18
	Current levels in flour	0.6	1.4	7.5	8.1	8.9
	Proposed levels	0.76	1.7	7.5	8.3	9.2
4 - 10 years	Entire diet	8.1	14	7.5	16	22

	Current levels in	0.97	1.9	7.5	8.5	9.4
	flour					
	Proposed levels in flour	1.2	2.4	7.5	8.7	9.9
11 - 18years	Entire diet	9.3	17	7.5	17	25
	Current levels in flour	1.2	2.5	7.5	8.7	10
	Proposed levels in flour	1.5	3.2	7.5	9	11
19 - 64 years	Entire diet	10	19	28	38	47
	Current levels in flour	1	2.4	28	29	30
	Proposed levels in flour	1.3	3.1	28	29	31
65 + years	Entire diet	9.7	17	28	38	45
	Current levels in flour	0.85	2.1	28	29	30

Proposed	1.1	2.6	28	29	31
levels in					
flour					

Table A5: Exposure to niacin from food and supplements

		Chronic exposure to niacin (mg/person/day)*		Niacin exposure from supplements, upper range (mg/person/dy)	Niacin exposure from supplements and diet (mean) (mg/person/day)	Nacin exposure from supplements and diet (97.5 <sup>th</sup> percentile) (mg/person/day)
	Category	Mean	97.5th Percentile			
Infants (4-18 months)	Entire diet	14	25	20	34	45
	Current levels in flour	0.26	0.81	20	20	21
	Proposed levels in flour	0.39	1.2	20	20	21
1.5-3 years	Entire diet	18	28	20	38	48
	Current levels in flour	0.58	1.3	20	21	21
	Proposed levels in flour	0.87	2	20	21	22
4 - 10 years	Entire diet	25	39	20	45	59

	Current levels in flour	0.94	1.9	20	21	22
	Proposed levels in flour	1.4	2.8	20	21	23
11 - 18 years	Entire diet	31	55	20	51	75
	Current levels in flour	1.2	2.4	20	21	22
	Proposed levels in flour	1.7	3.6	20	22	24
19 - 64 years	Entire diet	36	68	1000	1000	1100
	Current levels in flour	0.98	2.4	1000	1000	1000
	Proposed levels in flour	1.5	3.6	1000	1000	1000
65 + years	Entire diet	31	52	1000	1000	1100
	Current levels in flour	0.83	2	1000	1000	1000

Proposed	1.2	3	1000	1000	1000
levels in					
flour					

Table A6: Exposure to thiamin from food and supplements

		Chronic		Evacoure of	Thiamin	Thiamin
		exposure to thiamin (mg/person/day)*		Exposure of thiamin from supplements, upper range (mg/person/day)	expsoure from supplements and diet (mean) (mg/person/day)	exosure from supplements and diet (97.5 <sup>th</sup> percentile) (mg/person/day)
Age group	Category	Mean	97.5th Percentile			
Infants (4-18 months)	Entire diet	0.81	1.3	5	5.9	6.3
	Current levels in flour	0.039	0.12	5	5.0	5.1
1.5- 3years	Entire diet	1	1.8	5	6	6.8
	Current levels in flour	0.087	0.2	5	5.1	5.2
4 - 10 years	Entire diet	1.3	2.3	5	6.3	7.3
	Current levels in flour	0.14	0.28	5	5.1	5.3
11 - 18years	Entire diet	1.4	2.8	5	6.4	7.8
	Current levels in flour	0.17	0.36	5	5.2	5.4
19 - 64 years	Entire diet	1.5	2.8	500	500	500

	Current levels	0.15	0.36	500	500	500
	in flour					
65 +	Entire diet	1.5	2.7	500	500	500
years						
	Current levels	0.12	0.3	500	500	500
	in flour					

Table A5. Online sources for iron supplement data

Supplement	Iron dosage	Link	Notes
	per day (mg)		
Sainsbury's Health Multivitamins &	14	Sainsbury's Health Multivitamins & Iron Tablets 1 a	1 tablet per day
Iron Tablets 1 a Day x60		Day x60   Sainsbury's (sainsburys.co.uk)	
Feroglobin Capsules	17	Feroglobin® Capsules   Iron Supplement   Vitabiotics	Iron (as fumerate) 1 tablet
			per day
Ultra Iron	14	Ultra Iron   Iron Tablets   Vitabiotics	1 tablet per day
Holland & Barrett Gentle Iron	20	Holland & Barrett Gentle Iron 20mg 90 Capsules :	1 tablet per day
20mg 90 Capsules		Amazon.co.uk: Health & Personal Care	
Iron Complex 90 Capsules	14	Iron Complex 90 Capsules   BioCare	1 tablet per day
Iron & Folic Acid Tablets	14	Iron & Folic Acid Tablets   MYPROTEIN™	1 tablet per day

Nature's Bounty Gentle Iron	17	Nature's Bounty Gentle Iron Complex with Vitamins	Iron (as Ferrous
Complex with Vitamins B12 and C		B12 and C Capsules x100   Sainsbury's	Bisglycinate) 1 tablet per
Capsules x100		(sainsburys.co.uk)	day
Solgar® Gentle Iron (Iron	20	Solgar® Gentle Iron (Iron Bisglycinate) 20 mg	1 tablet per day
Bisglycinate) 20 mg Vegetable		Vegetable Capsules - Pack of 90 : Amazon.co.uk:	
Capsules - Pack of 90		Health & Personal Care	
Iron 14mg	28	Iron Tablets 14mg   Simply Supplements	1-2 tablet per day
Iron (Ferrous Bisglycinate)	20	Iron Capsules (K-Pure)   Ferrous Bisglycinate	1 tablet per day
Capsules (K-Pure®) 20mg		Bulk™	
Nature's Bounty, Gentle Iron, 28	28	Nature's Bounty, Gentle Iron, 28 mg, 90 Capsules	1 tablet per day
mg, 90 Capsules		(iherb.com)	
Range	14-28		
Supplement	Iron dosage	Link	Notes
	per day (mg)		
Holland and Barrett Kids Multivits	7.5	Holland and Barrett Kids Multivits & Iron Tablets	
& Iron Tablets   Holland & Barrett		Holland & Barrett	
Tasty Chews, A Chewable	2.8	Children's Chewable Multivitamins   Nature's Best	
Multivitamin and Mineral For		(naturesbest.co.uk)	
Children 4-14 years			

Wellkid Smart Chewable	7	Wellkid® Smart Chewable By Vitabiotics   Vitamins	1 tablet per day children
		<u>For Kids</u>	aged 4-12 years
Solgar Kangavites Tropical	5	Solgar Kangavites Tropical Vitamins for Children -	Children 3-5 years 1 tablet
Vitamins for Children - 120		120 Chewables   bodykind	per day children 6+ years 2
Chewables			per day

Table A6. Online sources for calcium supplement data

Supplement	Calcium	Link	Notes
	dosage per		
	day (mg)		
Calcium & Magnesium Tablets	800	Calcium & Magnesium Tablets	3 tablets per day
MYPROTEIN™		MYPROTEIN™	
Osteocare Original	800	Osteocare® Original   Bone Health	2 tablets per day The
		Tablets   Vitabiotics	UK's No.1 calcium
			formula for women
			and men of all ages.

Numark Chewable Calcium & Vitamin D - 30	800	Numark Chewable Calcium & Vitamin	1 tablet per day
x 400mg Tablets		D - 30 x 400mg Tablets   Chemist 4 U	Numark Vitamin D
		(chemist-4-u.com)	and Calcium Tablets
			are not suitable for
			children under the
			age of 12.
OsteoGuard®, High Strength Calcium and	1000	Osteoguard® Calcium & Magnesium	1-2 tablets per day
Magnesium Formula		Tablets   Nature's Best	This product is
		(naturesbest.co.uk)	suitable for all adults.
Natures Aid Chewable Calcium with Vitamin	800	Natures Aid Chewable Calcium with	1-2 tablets per day
D - 60 Tablets		Vitamin D - 60 Tablets   bodykind	
Calcium + Vitamin D3 + Vitamin K1 Capsules	200	Calcium + Vitamin D3 + Vitamin K1	1 tablet per day
1000mg		Supplement   Bulk™	
Super Calcium	780	Super Calcium   Higher Nature	1-3 tablets per day
Nature's Bounty, Calcium Plus Vitamin D3,	1200	Nature's Bounty, Calcium Plus	2 per day For adults,
600 mg, 220 Rapid Release Softgels		Vitamin D3, 600 mg, 220 Rapid	take two (2) softgels
		Release Softgels (iherb.com)	daily, preferably with
			meals.

Alive! Calcium Gummies with Vitamin D3   60	500	Alive! Calcium Gummies with Vitamin	2 soft gels per day
Chewable Gummies   Specially Formulated		D3   60 Chewable Gummies	13+ years
for Adults and Children From 3 Years.		Specially Formulated for Adults and	
		Children From 3 Years. :	
		Amazon.co.uk: Health & Personal	
		<u>Care</u>	
Range	200-1200		
Supplement	Calcium	Link	Notes
	dosage per		
	day (mg)		
	day (mg)		
Children's Chewable Multivitamins   Nature's	80	Children's Chewable Multivitamins	
Children's Chewable Multivitamins   Nature's Best (naturesbest.co.uk)		Children's Chewable Multivitamins   Nature's Best (naturesbest.co.uk)	
			Children 2+ years
Best (naturesbest.co.uk)	80	Nature's Best (naturesbest.co.uk)	Children 2+ years take 1 gummy per
Best (naturesbest.co.uk)	80	Nature's Best (naturesbest.co.uk)	
Best (naturesbest.co.uk)	80	Nature's Best (naturesbest.co.uk)	take 1 gummy per
Best (naturesbest.co.uk)  CALCI-YUMMIES	150	Nature's Best (naturesbest.co.uk)  Calci-YUMMies   1st Phorm	take 1 gummy per day

		Amazon.co.uk: Health & Personal	
		Care	
NaturesPlus Animal Parade Source of Life	250	NaturesPlus Animal Parade Source of	2+ years 2 gummies
Calcium Children's Chewable - Natural		Life Calcium Children's Chewable -	per day
Vanilla Sundae Flavour - 90 Chewable		Natural Vanilla Sundae Flavour - 90	
Animal Shaped Tablets - Gluten Free - 90		Chewable Animal Shaped Tablets -	
Servings : Amazon.co.uk: Health & Personal		Gluten Free - 90 Servings :	
Care		Amazon.co.uk: Health & Personal	
		Care	
Wellkid Calcium Liquid	300-450	Wellkid® Calcium Liquid By	10ml (300mg)
		Vitabiotics   Vitamins For Kids	children aged 4-6
			years and 15 ml (450
			mg) for children aged
			7-12 years
Calcium and Vitamin D softies 30	280	Haliborange Kids Calcium and	1-2 softies per day
		Vitamin D softies 30 : Amazon.co.uk:	Recommended for
		Health & Personal Care	children

Alive! Calcium Gummies with Vitamin D3   60	250	Alive! Calcium Gummies with Vitamin	1 soft gel per day for
Chewable Gummies   Specially Formulated		D3   60 Chewable Gummies	children aged 3-12
for Adults and Children From 3 Years.		Specially Formulated for Adults and	years
		Children From 3 Years. :	
		Amazon.co.uk: Health & Personal	
		<u>Care</u>	
Solgar Kangavites Tropical Vitamins for	128	Solgar Kangavites Tropical Vitamins	Children 3-5 years 1
Children - 120 Chewables		for Children - 120 Chewables	tablet per day children
		<u>bodykind</u>	6+ years 2 per day

Table A7. Online sources for Niacin supplement data

Supplement	Niacin	Link	Notes
	dosage per		
	day (mg)		
Vitamin B3 Niacin/Nicotinic Acid (Flush	50	Vitamin B3 Niacin/Nicotinic Acid (Flush Effect)	1 tablet per day
Effect) 50mg, Magnesium Stearate Free		50mg, Magnesium Stearate Free & No Nasty	
& No Nasty Additives, Made in Wales		Additives, Made in Wales (180 Capsules):	
(180 Capsules)		Amazon.co.uk: Health & Personal Care	

NOW Foods, Niacin, 500 mg, 250	500	NOW Foods, Niacin, 500 mg, 250 Tablets	1 tablet per day
Tablets		(iherb.com)	
Solgar Niacin (Vitamin B3) 500 Mg	500	Solgar Niacin (Vitamin B3) 500 mg Vegetable	1 tablet per day
Vegetable Capsules - Pack Of 100		Capsules - Pack of 100 - Your Health Store	
		(healthstoreexpress.co.uk)	
Solgar Niacin 100mg Tablets 100	100	Solgar Niacin 100mg Tablets 100   Landys	1 tablet per day
		<u>Chemist</u>	
Swanson Niacin, 100mg - 250 tablets	100	Swanson Niacin, 100mg - 250 tablets	1 tablet per day
		(lifestylehealthstore.co.uk)	
Niacin, 100 mg, 300 Tablet	100	Niacin, 100 mg, 300 Tablets   PipingRock Health	1 tablet per day
		<u>Products</u>	
Niacin, 1000 mg, 100 Quick Release	1000	Niacin 1000 mg 2 x 100 Capsules   Niacin 1000	1 tablet per day
Capsules, 2 Bottles	1	Tablets   PipingRock Health Products	
Vitamin B3 250mg (Niacin), Contributes	250	Vitamin B3 & Niacin Tablets   Nature's Best	1 tablet per day
to the Normal Function Of The Nervous		(naturesbest.co.uk)	
System			
Source Naturals, Niacin, 100 mg, 250	100	Source Naturals, Niacin, 100 mg, 250 Tablets	1 tablet per day
Tablets		(iherb.com)	

Nature's Way, Niacin, Vitamin B3, 100	100	Nature's Way, Niacin, Vitamin B3, 100 mg, 100	1 tablet per day
mg, 100 Capsules		Capsules (iherb.com)	
Range	50-1000		
Supplement	Niacin	Link	Notes
	dosage per		
	day (mg)		
Holland and Barrett Kids Multivits & Iron	13.5	Holland and Barrett Kids Multivits & Iron Tablets	1 tablet per day
Tablets   Holland & Barrett		Holland & Barrett	suitbale for 4+
			years
Children's Chewable Multivitamins	9	Children's Chewable Multivitamins   Nature's	
Nature's Best (naturesbest.co.uk)		Best (naturesbest.co.uk)	
Wellkid Peppa Pig Multi-vits	4.8	Wellkid® Peppa Pig Multi Vitamins By Vitabiotics	2 jellies per day
			children 3+ NE
Wellkid Smart Chewable	9	Wellkid® Smart Chewable By Vitabiotics	1 tablet per day
		<u>Vitamins For Kids</u>	children aged 4-
			12 years
Kids Multivitamin Gummies	8.2	Kids Multivitamin Gummies   MYPROTEIN™	1 gummy per day
Solgar Kangavites Tropical Vitamins for	20	Solgar Kangavites Tropical Vitamins for Children	Children 3-5
Children - 120 Chewables		- 120 Chewables   bodykind	years 1 tablet per

	day children 6+
	years 2 per day

Table A8. Online sources for thiamin supplement data

Supplement	Thiamin	Link	Notes
	dosage per		
	day (mg)		
Solgar Vitamin B1 (Thiamin) 500 mg	500	Solgar Vitamin B1 (Thiamin) 500 mg Tablets -	1 tablet per
Tablets - Pack of 100 - Supports Energy		Pack of 100 - Supports Energy Metabolism and	day
Metabolism and Nervous System - Vegan		Nervous System - Vegan : Amazon.co.uk: Health	
		<u>&amp; Personal Care</u>	
Natures Aid Vitamin B1 Thiamin - 90 x	100	Natures Aid Vitamin B1 Thiamin - 90 x 100mg	1 tablet per
100mg Tablets		Tablets   bodykind	day
Vitamed Thiamine 100mg 100 Tablets	107	Vitamed Thiamine 100mg 100 Tablets:	1 tablet per
		Amazon.co.uk: Health & Personal Care	day
Vitamin B1 100mg (Thiamin) 180 Tablets	100	Vitamin B1 100mg (Thiamin) 180 Tablets Suitable	1 tablet per
Suitable for Vegans and Vegetarians Made		for Vegans and Vegetarians Made in UK by	day

in UK by Futurevits 6 Month Supply,		Futurevits 6 Month Supply, Premium Grade only.:	
Premium Grade only.		Amazon.co.uk: Health & Personal Care	
B-1 (Thiamin), 100 mg, 250 Tablets	100	B-1 (Thiamin), 100 mg, 250 Tablets   PipingRock	1 tablet per
PipingRock Health Products		Health Products	day
HealthAid Vitamin B1 (Thiamin) 100mg -	100	HealthAid Vitamin B1 (Thiamin) 100mg - Prolong	1 tablet per
Prolong Release - 90 Tablets		Release - 90 Tablets : Amazon.co.uk: Health &	day
		Personal Care	
Source Naturals, B-1, Thiamin, 100 mg, 100	100	Source Naturals, B-1, Thiamin, 100 mg, 100	1 tablet per
Tablets		Tablets (iherb.com)	day
Holland & Barrett Vitamin B1 + Thiamine	100	Holland & Barrett Vitamin B1 + Thiamine 100mg	1 tablet per
100mg 120 Tablets		120 Tablets   Holland & Barrett	day
		(hollandandbarrett.com)	
Lindens Vitamin B1 Thiamine Tablets - 100	100	<u>Lindens Vitamin B1 Thiamine Tablets - 100 Pack -</u>	1 tablet per
Pack - for Heart, Immune and Psychological		for Heart, Immune and Psychological Function &	day
Function & Energy Release - UK		Energy Release - UK Manufacturer, Letterbox	
Manufacturer, Letterbox Friendly		Friendly: Amazon.co.uk: Health & Personal Care	
Vitamin B1 (Thiamin) 100mg 180 Vegan	100	Vitamin B1 (Thiamin) 100mg 180 Vegan Tablets :	1 tablet per
Tablets		Amazon.co.uk: Health & Personal Care	day
Range	100-500		

Supplement	Thiamin	Link	Notes
	dosage per		
	day (mg)		
Wellkid Peppa Pig Multi-vits	0.7	Wellkid® Peppa Pig Multi Vitamins By Vitabiotics	2 jellies per
			day children
			3+
Wellkid Smart Chewable	0.9	Wellkid® Smart Chewable By Vitabiotics   Vitamins	1 tablet per
		<u>For Kids</u>	day children
			aged 4-12
			years
Centrum Kids Multivitamins & Minerals, 30	0.5	Centrum Kids Multivitamins & Minerals, 30 Tablets	
Tablets		: Amazon.co.uk: Health & Personal Care	
[New] Creekside Naturals Mighty Eyes, Eye	5	[New] Creekside Naturals Mighty Eyes, Eye	1 tablet per
Vitamin and Mineral Supplement for		Vitamin and Mineral Supplement for Children with	day
Children with Lutein, Zeaxanthin, Thiamine,		Lutein, Zeaxanthin, Thiamine, and Zinc, Vegan,	
and Zinc, Vegan, Zero Sugar, 30 Soft		Zero Sugar, 30 Soft Chewables : Amazon.co.uk:	
Chewables		Health & Personal Care	
Solgar Kangavites Tropical Vitamins for	1.5	Solgar Kangavites Tropical Vitamins for Children -	Children 3-5
Children - 120 Chewables		120 Chewables   bodykind	years 1 tablet

	per day
	children 6+
	years 2 per
	day