TOX/2022/48

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

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

Introduction

1. In 2022, the Department for Environment, Food and Rural Affairs (DEFRA) held a consultation on the Bread and Flour Regulation (BFR) 1998 review. DEFRA has asked whether the consultees agree 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 will 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) guidance level on safe levels and upper levels (UL) and assess whether there is a potential risk from fortification of thiamin (vitamin B1) and increased fortification levels of the following nutrients: calcium carbonate, iron and nicotinic acid (vitamin B3) in non-wholemeal wheat flour.

This is a paper for discussion. This does not represent the views of the Committee and should not be cited.

Background

3. The BFR 1998 stipulates the levels of calcium carbonate, iron, thiamin (vitamin B1) and nicotinic acid that must be present in flour. Calcium is added in the form of calcium carbonate and niacin can be added to flour using either nicotinic acid or nicotinamide. 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.

4. The existing BFR has set a minimum fortification level for thiamin (vitamin B1) at 19%, whilst calcium, iron and niacin have been set at 15% of the nutrient reference value (NRV) supplied by 100 g as stated in point 1 of Part A of Annex XIII of regulation EC No. 1169/2011. The minimum amount (added/present in the flour) which is required in the legislation (0.24 mg) is for thamin hydrochloride, this is equivalent of 0.21 mg of thamin and 19% of the NRV. In practise, foods are not currently fortified at these respective levels, but industry are looking to increase fortification to the minimum levels. The respective NRVs are presented in Table 1.

Table 1: Daily NRVs of calcium, iron, niacin and thiamin (vitamin B1).

Mineral	**NRV* (mg)**
Calcium (calcium carbonate)	800
Iron	14
Niacin (nicotinic acid or nicotinamide)	16
Thiamin (Vitamin B1)	1.1

*NRV values taken from point 1 of Part A of Annex XIII of regulation EC No. 1169/201.

Toxicity

5. The toxicity and potential adverse effects of calcium, iron, niacin and thamin are discussed below.

Calcium

6. High intakes of calcium carbonate of around 4,000 mg/day (equivalent to 1,600 mg calcium) via calcium containing medication with or without vitamin D 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).

7. Calcium supplements have been administered to people with colonic polyps or people who are at risk of colonic polyps. Gastrointestinal effects were reported in a small number of patients receiving 1,600 or 2,000 mg/day of calcium (EVM, 2003).

8. High calcium diets can affect the bioavailability of other minerals such as iron, zinc, magnesium and phosphorous by inhibiting the absorption of iron salts and heme-iron and zinc, reducing magnesium absorption and excretion, and the binding of calcium aceteate and calcium carbonate to phosphate in the intestinal lumen (EFSA, 2006).

Iron

9. 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).

10. 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

11. Symptoms of acute toxicity from nicotinic acid include: flushing, itchy skin, nausea, vomiting and gastrointestinal issues (such as diarrhoea and constipation). Long term intakes of 3,000 mg/day of nicotinic acid have been reported to cause jaundice, hyperglycaemia and abdominal pain. In addition to elevated serum bilirubin, increased alakaline 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 nicotinic acid therapy (EVM, 2003).

12. Patients with hypercholesterolaemia that have been treated with nicotinic acid at 3-9 g/day over a period of months to years showed symptoms of severe liver dysfunction and potentially life-threatening hepatotoxicity that may require liver transplantation (EFSA, 2006).

Thiamin

13. Thiamin is considered to be of very low oral 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).

14. However, a small number of cases were associated with adverse effects such as muscle tremors, rapid pulse and nerve hyperirritability at low daily doses of 17 mg/day of thiamine hydrochloride. In one case, a patient consuming thiamin at 100mg/day for a period of 15 days, 2 months prior to consumption of a single oral dose of thaimin of 100mg, experienced 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

15. A tolerable upper level (TUL) or safe upper level (UL) for calcium, iron, nicotinic acid and thiamin have not been established by the Expert Group on Vitamins and Minerals (EVM) (2003) due to the lack of insufficient animal and human data.

16. 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). The Scientific Committee on Food (SCF) established a TUL of 2,500 mg/day for calcium in 2003 which was endorsed by EFSA (EFSA, 2012). A brief literature search did not provide any new information or data indicating that levels of calcium above 1,500 mg/day could be used as a safe UL.

17. The EVM proposed that a supplemental intake of 17 mg/day (0.28 mg/kg bw day for a 60 kg adult) 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 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 14-18 years (Institute of Medicine, 2001). However, moderate symptoms of iron toxicity have been reported to occur from 20 mg/kg bw/day (Madiwale and Liebelt, 2006).

18. The EVM proposed that a guidance level of 17mg/day (0.28 mg/kg bw/day in a 60 kg adult) for 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 nicotinic acid seem to be related to acute, bolus intakes of nicotinic acid. Adverse effects from long term exposure of nicotinic acid in food would be less likely as free nicotinic acid levels in food are low. Additionally, the EVM noted that the guidance level is based on intakes of conventional formulations of nicotinic acid. This would not be applicable to sustained release preparations and nicotinic acid 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 nicotinic acid based on flushing of skin (EFSA, 2014). 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.

19. The EVM proposed a guidance level for thiamin of 100 mg/day (equivalent to 10.7 mg/kg for a 60 kg adult) of supplemental thiamin and would not be expected to result in adverse effects. The EVM noted that this guidance level was only applicable to the water-soluble forms of thamin. Furthermore, the study by Gokhale et al. (1999) used to derive the guidance level was conducted in young women (EVM, 2003). EFSA noted that 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

20. Exposure assessments for calcium, iron, niacin and thiamin in non-wholemeal flour were performed.

21. Exposure to calcium, iron, niacin and thiamin were determined using 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 were those currently allowed by legislation: Annex XIII of regulation EC No. 1169/2011). 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.

Table 2. Concentration data used to derive exposure to calcium, iron, niacin and thiamin.

Nutrient	Nutrient reference value (mg)	Minimum levels based on current legislation (mg/100 g))	Level based on fortification at 15% (mg/100 g)
Calcium	800	94	120
Iron	14	1.65	2.1
Niacin	16	1.6	2.4
Thiamin	1.1	0.24	NA*

* A change in fortification level has not been proposed.

22. The assessments were carried out in CRÈME, the software used by the FSA to interrogate dietary datasets and calculate exposure. The mean and 97.5th percentile exposure estimates have been provided in Tables 3-6.

Methodology for estimating current and proposed intakes from non-wholemeal flour

23. Intake 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 was interrogated to identify foods containing non-wholemeal flour (n=1835). A selected number of food groups containing more than 20 foods are shown in Table A1 of Annex A.

24. The amount of non-wholemeal flour in these foods was used to derive intakes of calcium, iron, niacin and thiamin using the current regulatory allowance (Table 2). As the fortification level for thiamin is not expected to change, intake from the proposed increases were calculated for calcium, iron, and niacin only.

25. Intakes of these nutrients from supplements were also considered. Data for supplements were obtained from market sources (e.g. websites of major retailers). Tables 7-12 give ranges of exposures in adults and children.

Intake from the entire diet and from flour at the current and proposed fortification levels

26. Intake of 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 A. All food groups including the foods containing non-wholemeal flour are detailed in paragraph 23). The levels of the nutrient for each of the foods included were derived from the nutrient databank from the NDNS.

27. Intake of calcium, iron, niacin and thiamin in the entire diet and from flour fortification at current and proposed levels are shown in

28.

29. Table 3-5.

30. Among all age groups, the maximum mean & 97.5th percentile exposures of calcium at the current level of fortification are 68 and 140 mg/person/day respectively. The maximum mean and 97.5th percentile exposures at the proposed level of fortification are both at 87 mg/person/day.

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.

31. Among all age groups, the maximum mean & 97.5th percentile exposures of iron at the current level of fortification are 1.2 and 2.5 mg/person/day, respectively. The maximum mean and 97.5th 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 97.5th percentile levels, respectively.

32. Among all age groups, the maximum mean & 97.5th percentile exposures of niacin at the current level of fortification are 1.2 and 2.4 mg/person/day, respectively. The maximum mean and 97.5th 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 mean and 97.5th percentile levels respectively.

33. Among all age groups, the maximum mean and 97.5th percentile exposures of thamin at the current level of fortification are 0.17 and 0.36 mg/person/day. The maximum exposure to thiamin from the entire diet are1.5 and 2.8 mg/person/day at mean and 97.5th percentile levels, respectively.

Table 3: Chronic and acute intake of calcium in the diet and from flour fortification at current and proposed levels (15% of the nutrient reference value supplied by 100g flour) levels.

Age groups	Category	Chronic intake of calcium (mg/person/day) Mean	97.5th Percentile	Acute intake of calcium (mg/person/day)* Mean	97.5th Percentile
Infants (4-18 months)	Entire diet	680	1200	840	1500
Infants (4-18 months)	Current levels in flour	15	48	26	75
Infants (4-18 months)	Proposed levels in flour	19	61	33	96
1.5-3 years	Entire diet	740	1300	1000	1800
1.5-3 years	Current levels in flour	34	78	55	120
1.5-3 years	Proposed levels in flour	43	99	70	150
4 - 10 years	Entire diet	760	1400	1000	1900
4 - 10 years	Current levels in flour	55	110	87	170
4 - 10 years	Proposed levels in flour	71	140	110	220
11 – 18 years	Entire diet	770	1500	1100	2200
11 – 18 years	Current levels in flour	68	140	110	230
11 – 18 years	Proposed levels in flour	87	180	140	300
19 – 64 years	Entire diet	810	1600	1100	2300
19 – 64 years	Current levels in flour	58	140	99	240
19 – 64 years	Proposed levels in flour	74	180	130	300
65 + years	Entire diet	820	1500	1100	2000
65 + years	Current levels in flour in flour	49	120	76	170
65 + years	Proposed levels	62	150	98	220

*Rounded to 2 s.f.

Table 4: Chronic and acute intake of iron in the diet and from flour fortification at current and proposed (15% of the nutrient reference value supplied by 100g flour) levels.

Age groups	Category	Chronic intake of iron (mg/person/day)* Mean	97.5th Percentile	Acute intake of iron (mg/person/day)* Mean	97.5th Percentile
Infants (4-18 months)	Entire diet	6.8	12	8.4	15
Infants (4-18 months)	Current levels in flour	0.27	0.84	0.46	1.3
Infants (4-18 months)	Proposed levels in flour	0.34	1.1	0.58	1.7
1.5-3years	Entire diet	6	10	7.9	14
1.5-3years	Current levels in flour	0.6	1.4	0.96	2
1.5-3years	Proposed levels in flour	0.76	1.7	1.2	2.6
4 - 10 years	Entire diet	8.1	14	10	18
4 - 10 years	Current levels in flour	0.97	1.9	1.5	3
4 - 10 years	Proposed levels in flour	1.2	2.4	1.9	3.8
11 – 18 years	Entire diet	9.3	17	12	22
11 – 18 years	Current levels in flour	1.2	2.5	2	4.1
11 – 18 years	Proposed levels in flour	1.5	3.2	2.5	5.2
19 - 64 years	Entire diet	10	19	14	28
19 - 64 years	Current levels in flour	1	2.4	1.7	4.2
19 - 64 years	Proposed levels in flour	1.3	3.1	2.2	5.3
65 + years	Entire diet	9.7	17	13	22

65 + years	Current levels in flour	0.85	2.1	1.3	3
65 + years	Proposed levels in flour	1.1	2.6	1.7	3.8

*Rounded to 2.sf.

Table 5: Chronic and acute intake of niacin equivalent in the diet and from flour fortification at current and proposed (15% of the nutrient reference value supplied by 100g flour) levels.

Age Groups	Category	Chronic intake of niacin (mg/person/day)* Mean	97.5th Percentile	Acute intake of niacin (mg/person/day)* Mean	97.5th Percentile
Infants (4-18 months)	Entire diet	14	25	17	34
Infants (4-18 months)	Current levels in flour	0.26	0.81	0.45	1.3
Infants (4-18 months)	Proposed levels in flour	0.39	1.2	0.67	1.9
1.5-3years	Entire diet	18	28	24	42
1.5-3years	Current levels in flour	0.58	1.3	0.93	2
1.5-3years	Proposed levels in flour	0.87	2	1.4	3
4 - 10 years	Entire diet	25	39	32	55
4 - 10 years	Current levels in flour	0.94	1.9	1.5	2.9
4 - 10 years	Proposed levels in flour	1.4	2.8	2.2	4.3
11 - 18years	Entire diet	31	55	44	86
11 - 18years	Current levels in flour	1.2	2.4	1.9	4
11 - 18years	Proposed levels in flour	1.7	3.6	2.9	6
19 - 64 years	Entire diet	36	68	50	99
19 - 64 years	Current levels in flour	0.98	2.4	1.7	4
19 - 64 years	Proposed levels in flour	1.5	3.6	2.5	6
65 + years	Entire diet	31	52	41	73
65 + years	Current levels in flour	0.83	2	1.3	2.9

65 + years	Proposed levels in flour	1.2	3	2	4.4

*Rounded to 2.sf.

Table 6: Chronic and acute intake of 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.

Age groups	Category	Chronic intake of thiamine (mg/person/day)* Mean	97.5th Percentile	Acute intake of thiamine (mg/person/day)* Mean	97.5th Percentile
Infants (4-18 months)	Entire diet	0.81	1.3	0.99	1.7
Infants (4-18 months)	Current levels in flour	0.039	0.12	0.067	0.19
1.5-3years	Entire diet	1	1.8	1.3	2.5
1.5-3years	Current levels in flour	0.087	0.2	0.13	0.3
4 - 10 years	Entire diet	1.3	2.3	1.7	3.1
4 - 10 years	Current levels in flour	0.14	0.28	0.22	0.43
11 - 18years	Entire diet	1.4	2.8	2.1	4
11 - 18years	Current levels in flour	0.17	0.36	0.29	0.6
19 - 64 years	Entire diet	1.5	2.8	2.2	4.3
19 - 64 years	Current levels in flour	0.15	0.36	0.25	0.6
65 + years	Entire diet	1.5	2.7	2	3.8
65 + years	Current levels in flour	0.12	0.3	0.2	0.44

* Rounded to 2.s.f.

Intake from supplements

34. Intakes from supplemental calcium, iron, niacin and thiamin are presented in tables A3-A6 of Annex A.

35. Among all age groups the upper intakes of supplemental calcium are up to 1,200 mg/day. This exposure from calcium supplements accounts up to 60% and 43% of mean and 97.5th percentile calcium levels in entire diet (which includes supplements and diet).

36. Among all age groups the upper intakes of supplemental iron are up to 28 mg/day. This exposure from iron supplements accounts up to 74% and 60% of mean and 97.5th percentile calcium levels in the entire diet.

37. Among all age groups the upper intakes of supplemental niacin are up to 1000 mg/day. This exposure from niacin supplements accounts up to 100% and 91% of mean and 97.5th percentile niacin levels in the entire diet.

38. Among all age groups the upper intakes of supplemental thamin are up to 500 mg/day. This exposure from thamin supplements accounts up to 100% of both mean and 97.5th percentile thamin levels in the entire diet.

Table 7: Daily exposure to supplements in adults and children based on online sources.

Supplement	**Daily dosage in adults (mg)**	**Exposure in adults (mg/kg bw/day)***	**Daily dosage in children(mg)**	**Exposure in children (mg/kg bw/day)***
Calcium (adults)	200-1200	2.5-15	80-450	3-17
Iron	14-28	0.18-0.36	2.8-7.5	0.1-0.27
Niacin	50-1000	0.64-13	4.8-20	0.18-0.74
Thiamin	100-500	1.3-6.4	0.7-5	0.026-0.18

*Rounded to 2 significant figures and exposure values were calculated based on average bodyweights in NDNS (adults – 78.6 kg and children – 27.1 kg).

Risk characterisation

Intakes from food

39. Chronic intake of calcium at the current and proposed fortification levels (Table 2) do not exceed the guidance levels of 1,500 mg/day (EVM, 2003) and 2,500 mg/day (EFSA, 20212) across all age groups. Acute intakes of calcium at the current and proposed levels were below 2,000mg (supplementation studies have failed to show adverse effects at this level) (EVM, 2003).

40. Chronic intake levels of iron at the current and proposed fortification levels (Table 3) do 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 (Madiwale and Liebelt, 2006). This level was not exceeded by the acute intake levels of iron at the current and proposed fortification levels.

41. Chronic intake levels of niacin equivalents (Table 4) at the current and proposed fortification levels do not exceed the guidance level for nicotinic acid of 17 mg/day (EVM, 2003) across all age groups. The acute intake levels of niacin equivalents (Table 4) at the current and proposed fortification levels were below levels at which adverse effects start to occur (i.e., 50 mg).

42. Chronic intake levels of thamin at the current and proposed fortification levels (Table 5) did not exceed the current guidance level of 100 mg (EVM, 2003). Acute intake levels of thamin at the current and proposed fortification were below levels that could cause adverse effects (i.e. ≥7,000 mg of thamin hydrochloride).

Intake from supplements

43. Daily exposure to calcium supplements (Table 7, Table A2) do not exceed the guidance level of 1,500 mg/day (EVM, 2003) or the SCF guidance level of 2,500 mg/day in adults and children. However, consumption of iron, niacin and thamin (supplements may result in exceedances. Exposure to higher dosage iron supplements (i.e., 28 mg/day) can exceed the guidance level (17 mg/day) up to 1.6-fold in adults (Table A3). Daily exposure to niacin supplements would result in exceedance of guidance level of 17mg/day (EVM, 2003) between 3 and 60-fold higher than the guidance level (Table A4). As for thamin supplements, daily exposure could lead to a 5-fold exceedance of the guidance level (100mg/day) (Table A5) (Table 7).

Intake from supplements and food

44. Mean and 97.5th percentile calcium intake from food and supplements (Table A3) did not exceed the guidance level of 1,500mg/day (EVM, 2003) at the current and proposed fortification levels at any of the age groups.

45. Mean and 97.5th percentile iron intake from food and supplements (Table A4) did not exceed the guidance level of 17 mg/day (EVM, 2003) in the 4-18 months, 1.5-3, 4-10- and 11-18-years age group. However, in the 19-64 years age group mean and 97.5th percentile iron intakes exceeded the guidance level of 17 mg/day at current and proposed fortification levels up to 1.8-fold and 1.7-fold, respectively. In the 65+ years age group mean and 97.5th percentile iron exceeded the guidance level up to 1.8-fold at both the current and proposed fortification levels.

46. Mean and 97.5th percentile niacin intake from food and supplements exceed the guidance level of 17 mg/day (EVM, 2003) across all age groups. Current and proposed fortification levels both exceeded the guidance level up to 1.2-fold in the 4-18 months age group. In the 1.5-3 years age group current and proposed fortification levels exceeded the guidance level up to 1.2-fold and 1.4-fold, respectively. In the 4-10 years group, current and proposed fortification levels were up to 1.3-fold and 1.4-fold, respectively. In the 19-64 years and 65+ years age group current and proposed fortification levels both exceeded the guidance level up to 59-fold.

47. Mean and 97.5th percentile intakes from food and supplements only exceed the guidance level for thamin of 100 mg/day (EVM, 2003) in the 19-64 years and 65+ years age group. Current and proposed fortification levels in these age groups both exceeded the guidance level by 5-fold. Exposures for all other age groups are below the guidance level.

Conclusion

48. Chronic intakes of calcium, iron, niacin and thamin from food at the current and proposed fortification levels did not exceed the guidance level. Acute intakes of calcium, iron, niacin and thamin at current and proposed fortification levels did not exceed levels known to cause adverse effects and therefore exposure from flour fortification is not of toxicological concern.

49. 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.

50. Calcium intake from food and supplements at the current and proposed did not exceed the guidance level. However, iron, niacin intakes from food and supplements exceeded guidance level in some age groups. There may be toxicological concern for the relevant age groups that consume supplements and have background exposure from their diet.

51. Mean chronic exposure to calcium from the entire diet was highest in the elderly, and represents 55% of the guidance level of 1500mg/day (EVM, 2003). Intake of iron for the highest exposed group (adults) was 59% of the guidance level of 17mg/day (EVM, 2003). However, chronic intake of calcium and iron for adults at the 97.5th percentile exceeds their guidance levels. Mean chronic intake of niacin and thiamin were highest for adults and represents 4% and 1.5% of the TULs respectively.

52. For calcium supplements taken into account at the upper range for children (450mg/day), there are no exceedances for the average consumer, however exceedances can be observed for high consumers. For adults, exceedances can be observed from supplements and the diet even when proposed increases have not been taken into account. Similarly for iron, exceedances of the guidance values are not observed in children, for the average consumer. However, exceedances can be observed at 97.5th

percentile for children, and both mean and 97.5th percentile for adults even before the proposed increases are taken into account. With regards to niacin and thiamin, exceedances are observed for adults when supplements are combined with intake from food and no exceedances are observed for children.

53. The proposed increases of calcium, iron and thiam are unlikely to lead to chronic exceedances of their guidance levels. However, increases of the level of niacin in non-wholemeal flour would result in exceedance of the guidance level across all ages groups. The largest exceedances occurred amongst 19-64 year olds at chronic and acute intake levels that were up to 4 and 6-fold, respectively.

Questions on which the views of the Committee are sought

Members are invited to consider the following questions:

i) Do the Committee think that there is an increased risk to the UK population if the calcium, iron, niacin and thiamin (Vitamin B1) levels in non-wholemeal flour were to increase to proposed fortification levels?

ii) Do members have any further comments?

Secretariat
October 2022

List of Abbreviations and Technical terms

BFR	Bread and Flour Regulations
COT	Committee on Toxicity Chemicals in Food, Consumer Products and the Environment.
DEFRA	Department for Environment, Food and Rural Affairs
DHSC	Department of Health and Social Care
EVM	Expert Group on Vitamins and Minerals
SCF	Scientific Committee on Food
TUL	Tolerable Upper Level
NRV	Nutrient reference Value

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TOX/2022/48 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.

Food group	Number of foods assessed in the group
1% Milk (60R)	5
Alcoholic soft drinks (Alcopops) (49E)	4
Apples and pears not canned (40A)	27
Artificial sweeteners (55R)	11
Baked beans (37C)	8
Bananas (40C)	5
Beans and pulses (including ready meal & homemade dishes) (37I)	72
Beers and lagers (49A)	29
Beverages dry weight (50A)	44

Biscuits (homemade) (7B)	15
Biscuits (manufactured/retail) (7A)	153
Block margarine (20A)	2
Bottled water still or carbonated (51D)	11
Brown, granary and wheatgerm bread (59R)	42
Buns cakes and pastries (homemade) (8E)	132
Buns cakes and pastries (manufactured) (8D)	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 (homemade) (9D)	26
Cereal based milk puddings (manufactured) (9C)	40
Cheddar cheese (14B)	9
Chips purchased including takeaway (38A)	42
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 (including with vitamins A,D,E) (54N)	47
Coffee (made up weight) (51A)	25
Commercial toddlers drinks (52A)	9

Commercial toddlers foods (52R)	131
Cottage cheese (14A)	5
Cream (including imitation cream) (13B)	41
Crisps and savoury snacks (42R)	43
Dairy desserts (homemade) (15D)	11
Evening primrose oil and other plant oils (54B)	18
Folic acid (54D)	2
Fortified wine (48B)	10
Fromage frais and other dairy desserts (manufactured) (15C)	51
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 (49B)	9
Low alcohol & alcohol free cider & perry (49D)	3
Low alcohol and alcohol free wine (48C)	4
Low fat spread not polyunsaturated (19R)	7

Manufactured beef products (including ready meals) (23A)	49
Manufactured canned tuna products (including ready meals) (34G)	8
Manufactured chicken products (including ready meals) (27A) - 79 foods.	79
Manufactured coated chicken/turkey products (26A)	34
Manufactured egg products including ready meals (16C)	18
Manufactured lamb products (including ready meals) (24A)	11
Manufactured oily fish products (including ready meals) (35A)	45
Manufactured pork products (including ready meals) (25A)	9
Manufactured shellfish products (including ready meals) (34E)	17
Manufactured white fish products (including ready meals) (34C)	8
Meat alternatives (including ready meals and homemade dishes) (37K)	41
Meat pies and pastries (homemade) (31B)	39
Meat pies and pastries (manufactured) (31A)	38
Minerals (two or more including multiminerals) no vitamins (54H)	4
Multivitamins and/or minerals with omega (54P)	30

Non-nutrient supplements (including herbal) (54J)	46
Nutrition powders and drinks (50E)	62
Nuts and seeds (56R)	53
Other bacon and ham (including homemade dishes) (22B)	66
Other beef & veal (including homemade recipe dishes) (23B)	135
Other bread (4R)	17
Other breakfast cereals (not high fibre) (6R)	70
Other canned tuna (including homemade dishes) (34H)	7
Other cereal based puddings (homemade) (9H)	58
Other cereal based puddings (manufactured) (9G)	23
Other cereals (1R)	106
Other cheese (14R)	80
Other chicken/turkey (including homemade recipe dishes) (27B)	146
Other cooking fats and oils not polyunsaturated (20C	28
Other eggs and egg dishes including homemade (16D) -	98
Other fried/roast potatoes (including homemade dishes) (38D) -	55
Other fruit not canned (40R)	193
Other lamb (including homemade recipe dishes) (24B)	80
Other manufactured potato products fried/baked (38C)	20

Other manufactured vegetable products (including ready meals) (37L)	49
ther meat (including homemade recipe dishes) (32B)	66
Other meat products (manufactured including ready meals) (32A)	34
Other milk (13R)	72
Other nutrient supplements (54K)	55
Other oily fish (including homemade dishes) (35B) - 71 foods.	71
Other pork (including homemade recipe dishes) (25B)	69
Other potato products and dishes (manufactured) (39A)	20
Other potatoes (including homemade dishes) (39B)	50
Other sausages (including homemade dishes) (30B)	46
Other shellfish (including homemade dishes) (34F)	45
Other vegetables (including homemade dishes) (37M)	217
Other white fish (including homemade dishes) (34D)	83
Pasta (manufactured products and ready meals) (1D)	39
Pasta (other, including homemade dishes) (1E)	36
Peas not raw (37A)	20
Pizza (1C)	12
lyunsaturated 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 bacon and ham (22A)	3
Reduced fat spread (not polyunsaturated) (21B)	16
Reduced fat spread (polyunsaturated) (21A)	9
Rice (manufactured products and ready meals) (1F)	9
ice (other, including homemade dishes) (1G)	53
Salad and other raw vegetables (36B)	93
Savoury sauces pickles gravies & condiments (50R)	203
Semi-skimmed milk (11R)	9
Single vitamins/minerals not Folic acid, iron, calcium or vitamin C (54M)	61
Skimmed milk (12R)	11
Smoothies (61R)	10
Soft drinks low calorie carbonated (58B)	24
Soft drinks low calorie concentrated (58A)	13
Soft drinks low calorie, ready to drink, still (58C)	26
Soft drinks not low calorie carbonated (57B)	39
Soft drinks not low calorie concentrated (57A)	23

Soft drinks not low calorie, ready to drink, still (57C)	43
Soft margarine not polyunsaturated (20B)	3
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 multiseed bread) (2R)	58
White fish coated or fried (33R)	139
Whole milk (10R)	11
Wholemeal bread (3R)	31
Wine (48A)	16
Yogurt (15B)	82

Table A3: Calcium intake from foods and supplements.

` Age group	Category	Chronic intake of calcium from food (mg/person/day)* Mean	97.5th Percentile	Calcium from supplements, upper range (mg)	Intake from supplements and diet (mean)	Intake from supplements and diet (97.5th percentile)
Infants (4-18 months)	Entire diet	680	1200	450	1100	1700
Infants (4-18 months)	Current levels in flour	15	48	450	470	500
Infants (4-18 months)	Proposed levels in flour	19	61	450	470	500
1.5-3years	Entire diet	740	1300	450	1200	1800
1.5-3years	Current levels in flour	34	78	450	490	530
1.5-3years	Proposed levels in flour	43	99	450	490	550
4 - 10 years	Entire diet	760	1400	450	1200	1900
4 - 10 years	Current levels in flour	55	110	450	510	560
4 - 10 years	Proposed levels in flour	71	140	450	520	590
11 - 18years	Entire diet	770	1500	450	1200	2000
11 - 18years	Current levels in flour	68	140	450	520	590
11 - 18years	Proposed levels in flour	87	180	450	540	630
19 - 64 years	Entire diet	810	1600	1200	2000	2800
19 - 64 years	Current levels in flour	58	140	1200	1300	1300
19 - 64 years	Proposed levels in flour	74	180	1200	1300	1400
65 + years	Entire diet	820	1500	1200	2000	2700
65 + years	Current levels in flour	49	120	1200	1200	1300
65 + years	Proposed levels in flour	62	150	1200	1300	1400

Table A4: Iron intake from food and supplements.

Age group	Category	Chronic intake of iron (mg/person/day)* Mean	97.5th Percentile	Iron from supplements, upper range (mg)	Intake from supplements and diet (mean)	Intake from supplements and diet (97.5th percentile)
Infants (4-18 months)	Entire diet	6.8	12	7.5	14.0	20
Infants (4-18 months)	Current levels in flour	0.27	0.84	7.5	7.8	8.3
Infants (4-18 months)	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
1.5-3years	Current levels in flour	0.6	1.4	7.5	8.1	8.9
1.5-3years	Proposed levels	0.76	1.7	7.5	8.3	9.2
4 - 10 years	Entire diet	8.1	14	7.5	16	22
4 - 10 years	Current levels in flour	0.97	1.9	7.5	8.5	9.4
4 - 10 years	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
11 - 18years	Current levels in flour	1.2	2.5	7.5	8.7	10
11 - 18years	Proposed levels in flour	1.5	3.2	7.5	9	11
19 - 64 years	Entire diet	10	19	28	38	47
19 - 64 years	Current levels in flour	1	2.4	28	29	30
19 - 64 years	Proposed levels in flour	1.3	3.1	28	29	31

65 + years	Entire diet	9.7	17	28	38	45
65 + years	Current levels in flour	0.85	2.1	28	29	30
65 + years	Proposed levels in flour	1.1	2.6	28	29	31

Table A5: Intake of niacin from food and supplements.

Age Groups	Category	Chronic intake of niacin (mg/person/day)* Mean	97.5th Percentile	Niacin from supplements, upper range (mg)	Intake from supplements and diet (mean)	Intake from supplements and diet (97.5th percentile)
Infants (4-18 months)	Entire diet	14	25	20	34	45
Infants (4-18 months)	Current levels in flour	0.26	0.81	20	20	21
Infants (4-18 months)	Proposed levels in flour	0.39	1.2	20	20	21
1.5-3 years	Entire diet	18	28	20	38	48
1.5-3 years	Current levels in flour	0.58	1.3	20	21	21
1.5-3 years	Proposed levels in flour	0.87	2	20	21	22
4 - 10 years	Entire diet	25	39	20	45	59
4 - 10 year	Current levels in flour	0.94	1.9	20	21	22
4 - 10 year	Proposed levels in flour	1.4	2.8	20	21	23
11 - 18 years	Entire diet	31	55	20	51	75
11 - 18 years	Current levels in flour	1.2	2.4	20	21	22
11 - 18 years	Proposed levels in flour	1.7	3.6	20	22	24
19 - 64 years	Entire diet	36	68	1000	1000	1100
19 - 64 years	Current levels in flour	0.98	2.4	1000	1000	1000

19 - 64 years	Proposed levels in flour	1.5	3.6	1000	1000	1000
65 + years	Entire diet	31	52	1000	1000	1100
65 + years	Current levels in flour	0.83	2	1000	1000	1000
65 + years	Proposed levels in flour	1.2	3	1000	1000	1000

Table A6: Intake of thiamin from food and supplements.

Age groups	Category	Chronic intake of thiamine (mg/person/day)* Mean	97.5th Percentile	Intake of thiamin from supplements, upper range (mg)	Intake from supplements and diet (mean)	Intake from supplements and diet (97.5th percentile)
Infants (4-18 months)	Entire diet	0.81	1.3	5	5.9	6.3
Infants (4-18 months)	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
1.5-3years	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
4 - 10 years	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
11 - 18years	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
19 - 64 years	Current levels in flour	0.15	0.36	500	500	500
65 + years	Entire diet	1.5	2.7	500	500	500
65 + years	Current levels in flour	0.12	0.3	500	500	500

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