

**OPTIONS FOR IMPROVING FOLATE INTAKES OF WOMEN OF REPRODUCTIVE AGE AND PREVENTING NEURAL TUBE DEFECTS**

*[Revised version incorporating changes to paragraph 36 reporting the advice of the Committee on Carcinogenicity]*

**Executive Summary**

1. Neural tube defects (NTDs) occur in the early stages of foetal life and can result in miscarriage, neonatal death or life long disability. In the UK there are approximately 700-900 NTD-affected pregnancies per year not including miscarriages.
2. The Board is asked to agree advice to UK Health Ministers on folic acid fortification and NTD-prevention. Ministers will make a decision on implementation.
3. The paper sets out the current position in the UK; independent advice from the Scientific Advisory Committee on Nutrition (SACN); practical and technical issues which need to be taken into account; the findings of consumer research; the views of consultation respondents; and a view on the associated ethical issues.
4. It analyses four options on the basis of these considerations:
  - maintaining current efforts (Option1);
  - increasing efforts to encourage more women to take folic acid as recommended (Option 2);
  - further encouragement of voluntary fortification by industry (Option 3); and
  - mandatory fortification of wheat flour or bread (Option 4) with or without controls on voluntary fortification.
5. The primary decisions to be made are:
  - whether to support mandatory fortification; and if so
  - what food or foods should be fortified;
  - whether the folic acid should be labelled;
  - whether controls on voluntary fortification and advice on use of supplements should be introduced to manage high intakes of folic acid; and



## OPTIONS FOR IMPROVING FOLATE INTAKES OF WOMEN OF REPRODUCTIVE AGE AND PREVENTING NEURAL TUBE DEFECTS

### Issue

1. To agree advice to UK Health Ministers on folic acid fortification and neural tube defects (NTDs). Ministers will consider the issue and agree a decision on implementation.

### Strategic Aim

2. To help reduce diet-related diseases.

### Background

3. Low intake of the vitamin folate is an established cause of NTD-affected pregnancies, which can result in miscarriage, neonatal death and lifelong disability<sup>1</sup>. The Agency has estimated the economic costs associated with all NTDs at almost £136 million per annum (Annex 1, Table 1).
4. In 2000, the Committee on the Medical Aspects of Food Policy (COMA)<sup>1</sup> advised that universal fortification of flour with folic acid (a synthetic folate) would have a significant effect in preventing NTD-affected conceptions and births. After consideration, the Board<sup>2</sup> agreed not to recommend this, to UK Health Ministers, at that time, due to concerns about risks to the elderly and the issue of limiting freedom to choose unfortified foods. UK Health Ministers agreed with this assessment. In 2004 the Scientific Advisory Committee on Nutrition (SACN) agreed that there was sufficient evidence to justify updating the earlier advice from COMA. Health Departments and the Agency agreed this should be done and UK Health Ministers wrote to confirm they were waiting for Agency advice on this matter. In 2006, the Board<sup>3</sup> received SACN's draft updated advice and agreed to carry out a consultation on options for improving folate intake of young women. UK Health Ministers will make a decision on implementation once they have received advice from the Agency.

### *NTD-affected Pregnancies in the UK*

5. In the UK women are offered, during antenatal care, diagnostic screening for NTDs. There are approximately 700-900 NTD-affected pregnancies per year, not

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<sup>1</sup> Department of Health. Folic acid and the prevention of disease. Report on health and social subjects 50. London: TSO 2000.

<sup>2</sup> 2002 Board paper – (FSA 02/05/02)

<sup>3</sup> 2006 Board paper – (FSA 06/04/05)

taking into account miscarriages that occur as a result of the condition<sup>4</sup>. Most women who are diagnosed opt for an abortion, which is available in all countries except Northern Ireland. The incidence of NTD-affected births varies between England, Wales, Scotland and Northern Ireland with the latter having the highest incidence; there are about 160 NTD births per year in the UK overall (Annex 1, Table 2 and 3 ).

6. As well as low folate intake, NTD risk is increased by low socio-economic status, obesity<sup>5</sup> and diabetes<sup>6</sup> and is influenced by genetic factors (including ethnicity with those of North European and South Asian descent having the highest prevalence<sup>1</sup>). There have been a number of clinical trials around the world including a large-scale trial in the UK (MRC Vitamin Study Research Group, 1999) which showed that improving folate intake and status reduced the risk of an NTD-affected pregnancy by 70%<sup>7</sup>.

#### *Current Policy on Folic Acid and NTD Prevention*

7. The B vitamin folate is essential for everyone's health and there UK dietary recommendations for all age groups; adults are advised to consume 200 micrograms of folate / day<sup>8</sup>. Intakes below this level, over a sustained period of time, increase the risk of folate deficiency. The vitamin is required for normal cell division so deficiency impairs, amongst other things, growth and red blood cell production causing anaemia.
8. In the UK women who could become pregnant or are planning a pregnancy are advised to take an additional 400 micrograms of folic acid / day (making a total of 600 micrograms of folate / day) as a supplement from before conception until the 12<sup>th</sup> week of pregnancy (Department of Health 1992). They are also advised to eat more foods naturally rich in folate, and foods fortified with folic acid, especially breakfast cereals (Department of Health 2000). Similar advice to this is given across the UK through, for example, Primary Care Trusts, family planning clinics and NHS Direct.

#### *Folate Consumption*

9. National diet and nutrition surveys (NDNS) data show that overall 23% of the population, 34% of women of child bearing age and 37% of those aged over 65

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<sup>4</sup> National data on NTDs are incomplete; these figures take include reported terminations and some estimates of underreporting for England and Wales.

<sup>5</sup> Werler MM, Louik C, Shapiro S & Mitchell AA. Pre-pregnant weight in relation to risk of neural tube defects. *JAMA*. 1996, 275:1089-1092.

<sup>6</sup> Bercera JE, Khoury MJ, Cordero JF & Erikson JD. Diabetes mellitus during pregnancy and the risks for specific birth defects: a population based case control study. *Paediatrics*. 1990. 85(1): 1-9.

<sup>7</sup> MRC Vitamin Study Research Group. Prevention of neural tube defects; results of the Medical Research Council Vitamin Study. *Lancet*. 1991; 338:131-137.

<sup>8</sup> This is the reference nutrient intake (RNI) for adults. The RNI is the amount of a nutrient that is considered sufficient to meet requirements of 97.5% of the population.

years have folate intakes below the recommended levels of 200 micrograms / day. Women with low folate intakes are often but not always in low socio-economic groups (Annex 2, Table 1).

10. Later this year, the Agency will publish findings from the Low Income Diet and Nutrition Survey (LIDNS; a UK survey of 3700 low income children and adults). The proportion of the women in LIDNS with folate intakes below recommended levels was greater than that seen in NDNS in 2000/1 (Annex 2, Table 2).
11. Since 1992 voluntary fortification of cereal products with folic acid has been encouraged by the UK Government. Folic acid is currently added to a large number of foods on a voluntary basis but overall only low fat spreads and breakfast cereals make notable contributions to UK dietary intakes; about a third of reduced and low-fat spreads and two-thirds of breakfast cereals consumed are fortified. The contribution that these foods and also supplements make to the folate intake of women of reproductive age has been estimated using NDNS data. This shows that fortified breakfast cereals contribute 5% to the folate intakes of the bottom 20% of folate consumers; low-fat spreads make no contribution to the bottom 60% of folate consumers; and supplements make a 2% or less contribution to the bottom 80% of folate consumers (Annex 2, Table 3).
12. A number of fortified breads have been tried on the market but currently there are only a small number on sale and these tend to be premium products.
13. Flour and bread are the most commonly used vehicle in countries that have adopted mandatory fortification in order to improve folate intakes (paragraphs 18-23). The vast majority of flour consumed in the UK is as wheat bread; other products containing wheat flour such as cakes and biscuits account for a lower proportion of the flour consumption (Annex 2, Table 4).
14. According to NDNS data, most (over 90%) women with low folate intakes consume wheat bread (Annex 2, Table 1) which also gives other dietary characteristics of this group. Women in the LIDNS consumed similar quantities of bread as those in NDNS (Annex 2, Table 2). The amount of wheat flour and bread consumed by adults is relatively uniform when analysed by age, gender and income (Annex 2, Tables 4 and 5) which also shows the amount of flour-containing products other than bread consumed. Further details of flour-containing products consumed are given in Annex 2, Tables 6 and 7.
15. Data on the use of folic acid supplements indicate that about a quarter of women take folic acid as recommended, i.e. before and after conception<sup>9</sup>. This relatively low rate of usage is in part due to only about half of pregnancies being planned<sup>9</sup>.

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<sup>9</sup> Scientific Advisory Committee on Nutrition. Folate and Disease Prevention. TSO, 2006.

Women of low socioeconomic status are least likely to plan their pregnancies<sup>9</sup> and to follow advice on folic acid<sup>9</sup>; they also have the poorest folate status.<sup>10</sup>

### *Influencing Women to follow advice on Folic Acid and the effect of Advice on NTD Rates*

16. The number of NTD-affected pregnancies in the UK has been relatively stable since the 1990s. A campaign on folic acid was run across the UK from 1995/1998 by the then Health Education Authority (HEA) that aimed to increase the pre-pregnancy and early pregnancy use of folic acid supplements (Annex 3). There has been no formal analysis of the impact of this campaign on numbers of NTD cases; however an analysis of trend data on NTD-affected pregnancies for England and Wales found no detectable effects of the 1992 recommendation to women to take folic acid supplements<sup>11</sup>. This is despite active encouragement of voluntary fortification of cereals products with folic acid since 1992 and the HEA campaign.
17. A literature review, commissioned by the Agency, on the effectiveness of folic acid campaigns from a number of countries (including the HEA campaign) and other behavioural change interventions (including studies on supplements and also studies on other health behaviours such as use of contraception) found limited evidence on how to achieve higher uptakes of folic acid supplements pre-pregnancy and in early pregnancy. The author of the review concluded that even the best quality and most sustained campaigns had very limited impact, particularly for women from socio-economically deprived backgrounds. A major barrier to success was seen as the high rate of unplanned pregnancies. For women who plan their pregnancies, however, there is some evidence, from studies not specifically addressing use of folic acid supplements, that compliance with advice might be improved by some types of interventions, for example by offering pre-pregnancy care to women routinely (this is not currently done in the NHS), by working with families and by using peer support approaches (Annex 3).

### *Experiences from other Countries*

18. Annex 4 (Table 1) gives examples of folic acid food fortification strategies around the world. Mandatory fortification has been introduced in a number of countries, including the USA, Canada and Chile. Since 2002, these three countries have assessed the impact of mandatory fortification and have reported reductions in

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<sup>10</sup> Henderson L, Gregory J, Irving K & Swan G. The National Diet and Nutrition Survey: adults aged 19-64 years. London TSO, 2003

<sup>11</sup> Botto LD, Lisis A, Robert-Gnansia E, Erickson JD, Vollset SE, Mastroiacovo P, Botting B, Cocchi G, de Vigan C, de Walle H, Feijoo M, Irgens LM, McDonnell B, Merlob P, Ritvanen A, Scarano G, Siffel C, Metneki J, Stoll C, Smithells R & Goujard J. International retrospective cohort study of neural tube defects in relation to folic acid recommendations: are the recommendations working? *BMJ* 2005, 330:571.

NTD incidence of 27% to over 50%. To date, the preferred vehicle for mandatory fortification has been wheat and other cereal products.

19. In 2006, the Republic of Ireland agreed to mandatory fortification of all breads (with the exception of some minor products) and is currently developing an implementation strategy and legislation. Initially it was anticipated that fortification would take place in the bakery, however, significant practical difficulties have been found in controlling the level of folic acid being added and achieving uniform levels in bread. The option of adding folic acid to bread making flour in the flour mill is now being explored.
20. It is not possible to make a straightforward comparison of the impact of mandatory fortification on NTD incidence in different countries as this is affected by how much the population's folic acid intakes are increased, baseline NTD incidence and baseline folate intakes and status. These factors were taken into account by SACN when they modelled the effects of introducing mandatory fortification in the UK (paragraphs 33 and 34). They also help explain why mandatory fortification had a greater impact in Chile where a 47% reduction in NTD incidence was reported, compared to the USA where a 27% reduction was reported; Chile had a higher pre-fortification NTD incidence and probably a lower folate status.
21. Another difficulty with comparing the impacts of different mandatory fortification regimes on folic acid intakes of populations is that countries have used / will use a range of different approaches. Different foods are fortified (e.g. flour, bread, pasta and rice in the USA and bread in the Republic of Ireland) with varying levels of folic acid and also different countries may have different consumption patterns of fortified foods. It has, however, been estimated that mandatory fortification in the USA increased the average folic acid intakes of the population by between 215 and 240 micrograms / day, whereas Ireland estimate that their plans will increase the folic acid intake of women by 110 micrograms / day. (Estimates cannot be made for Canada and Chile as no nationally representative data has been published). For the UK, SACN have estimated that mandatory fortification of white and brown flour (excluding wholemeal flour), with no voluntary fortification, at a dose of 300 micrograms / 100 grams flour, will increase the average folic acid intake of the population by about 78 micrograms / day (paragraph 34).
22. The Swedish Government has recently commissioned an assessment on folic acid fortification. The draft report does not recommend mandatory fortification at this stage. This is due to uncertainties about the risk of cancer, although they were unable to undertake a full risk assessment of this<sup>12</sup>.

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<sup>12</sup> The Swedish Council on Technology. Benefits of fortifying flour with folic acid with the aim of reducing the risk of neural tube defects. 2007.

23. Annex 4 (Table 2) gives more details of the implementation and experiences (including information on labelling and trade) of mandatory fortification in the USA and Canada.

### **Policy Options for the UK**

24. The policy options were developed taking into account the views of stakeholders, advice from SACN and information from other countries. A UK wide consultation was published in December 2006 requesting views on the following:

- Option 1 - continue with the current policy of advice to women;
- Option 2 - increase the effort to encourage young women to take folic acid supplements and make changes to diet to increase the consumption of folate rich foods;
- Option 3 - encourage industry to fortify more foods with folic acid on a voluntary basis;
- Option 4 - recommend the mandatory fortification of bread or flour with folic acid.

25. Views were also sought on the need for controls on voluntary fortification with folic acid.

### **Advice from the Scientific Advisory Committee on Nutrition (SACN)**

26. In 2006, SACN published the report *Folate and Disease Prevention*<sup>9</sup> after assessing the evidence on the possible benefits and risks of mandatory fortification of flour with folic acid (Annex 5).

27. SACN concluded that mandatory fortification would improve the folate status of women most at risk of NTD-affected pregnancies. In addition, it would also improve the folate status of those (including many elderly people) who are also at risk of poor status. If wholemeal flour is excluded, mandatory fortification (with strict controls on voluntary fortification of breakfast cereals and fat spreads) at a dose of 300 micrograms of folic acid / 100 grams of white and brown wheat flour (actual level of 225 micrograms / 100 grams food after processing losses), would mean an average increase in folic acid intake of 78 micrograms / day. This would prevent 11-18% of NTDs (77-162 cases / year) and would also reduce the proportion of the general UK population not achieving dietary recommendations for folic acid from 23% to 5% (see Annex 6, Table 1 for a further assessment of fortification scenarios).

28. SACN considered a range of postulated risks of increased folic acid intake. The key concerns considered by SACN were delaying the diagnosis of vitamin B12

deficiency in the elderly and progression of pre-cancerous polyps to bowel cancer. In view of the latter concern, the Committee on Carcinogenesis (CoC) were asked to examine the data on folic acid and cancer from animal studies, an unpublished trial in humans, as well as cancer trend information from the USA and Canada.

29. SACN also explored the potential effect of mandatory fortification of flour with folic acid on the number of people (including children) who might be exposed to high intakes of folic acid. In the USA and Europe, the tolerable upper intake level (UL<sup>13</sup>) for folic acid for adults is 1 milligram / day. Lower ULs were set for children on the basis of body weight. In the UK, a Guidance Level<sup>14</sup> (GL) of 1 milligram / day for adults has been agreed as the evidence on risks of folic acid was not considered to be sufficiently robust to set a Safe Upper Level<sup>15</sup>. GLs were not set for children in the UK as there were no data reporting harmful effects of folic acid in children. Therefore the ULs set for children and adults in Europe were used to explore high intakes.
30. SACN confirmed that no data were found to suggest that folic acid at doses up to 1 milligram / day (GL for adults) would delay the diagnosis of vitamin B12 deficiency and there has been no increase in reported cases of severe manifestation of vitamin B12 deficiency in the USA since mandatory fortification was introduced. SACN has recommended that UK Health Ministers should develop a clinical strategy to manage vitamin B12 deficiency irrespective of a decision on folic acid fortification.
31. With regard to cancer, SACN concluded that the evidence for a link between folic acid and increased or reduced risk of cancers in humans is equivocal. As there were insufficient data for a full assessment of folic acid intake levels in relation to cancer risk, SACN recommended that, as a precaution, there should not be a substantial increase in average population intakes of folic acid or in the numbers consuming intakes above the GL/UL.
32. After reviewing worldwide data, SACN found insufficient evidence to conclude that mandatory fortification would have any positive or negative effects on other chronic diseases.
33. In the UK, voluntary fortification and supplements containing folic acid currently benefit a range of consumers. Without the contribution of folic acid in breakfast cereals and low fat spreads NTD-affected pregnancies would increase by 10%

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<sup>13</sup> The UL represents the highest level of a nutrient that is likely to pose no risk of adverse health effects.

<sup>14</sup> The Guidance Level (GL) is based on limited data and represents an approximate indication of intakes that would not be expected to cause any adverse effects, was set by The expert Group of Vitamins and Minerals (EVM).

<sup>15</sup> The Safe Upper Levels were set by the EVM when supported by adequate data and represent intakes that can be consumed over a lifetime without significant risk to health.

and the percentage of the general UK population not meeting dietary recommendations would increase from 23 to 36% (Annex 6, Table 1). Without folic acid in breakfast cereals, low fat spreads and supplements containing folic acid, NTD-affected pregnancies would increase by 13% and the number of people not meeting dietary recommendations would increase from 23% to 38% (Annex 6, Table 1).

34. However, it is estimated that there are currently 127,000 people (adults and children) with folic acid intakes exceeding the GL/UL for folic acid due to consuming fortified foods or supplements containing folic acid. SACN have therefore recommended that action is taken to address the current risk of people consuming folic acid in excess of the GL/UL. Stopping all voluntary fortification and introducing mandatory fortification of white and brown wheat flour at a dose of 300 micrograms / 100 grams would lead to a redistribution of folic acid intakes without increasing the number of people with folic acid intakes above the GL/UL, while the numbers with intakes of folic acid below dietary recommendations would be reduced from about 13 million to about 3 million. Mean folic acid intakes of the UK population would increase by 78 micrograms / day.
35. SACN recommendations on mandatory fortification are compared with those of other countries in Annex 6, paragraphs 22-29.
36. SACN therefore recommends the mandatory fortification of wheat flour, with controls on voluntary fortification and advice on the use of supplements. **This recommendation is consistent with advice from the CoC for a precautionary approach in considering mandatory fortification of flour with folic acid.** SACN's recommendation for mandatory fortification includes the proviso that the folic acid intakes and status of the UK population and postulated risks, including cancer, are carefully monitored and that the data on the benefits and possible risks are reviewed five years after the introduction of mandatory fortification.

### **Technical and Implementation Issues**

37. A food that is considered an appropriate vehicle for folic acid fortification in order to increase the folic acid intakes in women most at risk of NTD-affected pregnancies must be consumed by a very high proportion of women of reproductive age regularly, and in relatively uniform amounts; it must also be consumed by women who currently have low folate intakes. The candidate food must also not be consumed by others (particularly children) in large volumes as this would increase the risk of exceeding guidance levels (GL/UL). Folic acid must be relatively stable in the food; details of losses of folic acid from different bakery products are given in Annex 7.

### *Choice of Foods for Fortification with Folic Acid*

38. Annex 7 shows a range of foods considered by the Agency and a summary is below.

#### *(i) Wheat bread/flour*

39. Wheat bread would be a suitable vehicle for mandatory fortification as it is consumed almost universally and in relatively equal amounts across all population groups (paragraph 14). Fortification would therefore increase folic acid consumption evenly across the population (Annex 6, Table 1). Mandatory fortification of wheat flour has advantages over fortification of bread itself for reasons set out in Annex 7, including the fact that white and brown wheat flour in the UK already has four nutrients added on a mandatory basis and mandatory folic acid fortification could be implemented through the same legal instrument<sup>16</sup> (see Annex 7, paragraph 6). The regulation is not applied to imported flours. The Republic of Ireland is exploring limiting fortification to bread making flour only but we have been advised that this would be more difficult in the UK (Annex 7, paragraph 8).

40. There are some groups who would not benefit from the fortification of wheat flour. Women with coeliac disease avoid wheat products (UK prevalence, 1%<sup>17</sup>). This group, however, do not benefit from any of the nutrients currently added to flour as the regulations are for wheat flours only, unless manufacturers add the nutrients on a voluntary basis; some gluten free flours and flour products, such as breads, are fortified to a similar extent as white and brown wheat flour currently. The nutrition issues for those with coeliac disease may be broader than the issue here of folic acid fortification.

#### *(ii) Soft drinks and milk*

41. Soft drinks and milk are unsuitable vehicles for fortification as consumption can vary greatly and they can be consumed in large volumes, particularly by children; also folic acid is degraded in acidic foods, such as carbonated drinks and fruit juices.

#### *(iii) Chewing gum*

42. Chewing gum is also unsuitable as it is only consumed by less than a quarter of any age group of women<sup>10</sup>.

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<sup>16</sup> The Bread and Flour Regulations 1998 requires thiamine, nicotinic acid, iron and calcium to be added to white and brown flour (see Annex 7 for details)

<sup>17</sup> Ciclitira PJ, Johnson MW, Dewar DH, Ellis HJ (2005) The pathogenesis of coeliac disease. *Mol Aspects Med.* 2005 Dec;26(6):421-58.

(iv) *Breakfast cereals*

43. Breakfast cereals are unsuitable as they are not consumed by 30% of women<sup>10</sup>.

*Regulation of Voluntary Fortification*

44. SACN modelled the effects of mandatory fortification with current levels of voluntary fortification and without any voluntary fortification (paragraph 33). A different approach could be explored allowing some voluntary fortification, for example of some foods (paragraph 45).

45. The legislative controls on voluntary fortification and associated claims are set out in Annex 8. Further controls might be by voluntary or statutory agreement, and could range from stopping all voluntary fortification to capping levels in foods and/or restrictions on the products that could be fortified. These controls would need to be notified to the European Commission before implementation to allow trade implications to be identified.

46. Two manufacturers of low fat spreads (whose products account for about a third of the reduced and low fat spreads consumed currently) fortify their products to high levels (1000 micrograms / 100 grams), however following concerns raised by SACN on high intakes of folic acid, these companies have agreed to reduce this level to 500 micrograms / 100 grams.

*Labelling*

47. The addition of folic acid to wheat flour on a voluntary basis would require labelling. A decision to fortify on a mandatory basis could be implemented by amending the UK Bread and Flour Regulations 1998, although there would be issues around the labelling of both the flour that has been fortified with folic acid and products made with flour that has been fortified with folic acid, that would require further detailed consideration, including the need to develop a *threshold* below which labelling may not be required for products containing only small amounts of flour (see Annex 8). Consideration of *thresholds* for labelling would need to take into account industries who may wish to make a claim.

*Trade*

48. Mandatory fortification is thought unlikely to be a barrier to trade in flour or imports into the UK of derived products from a legal viewpoint (Annex 8). Industry is, however, concerned that importers in other countries might choose not to purchase fortified UK goods, particularly if labelling for folic acid is required. This could be in part addressed for products that contained only small amounts of wheat flour by the application of *thresholds* for folic acid labelling (paragraph 47).

49. Advice from the USA (Food and Drug Administration (FDA)) suggests there have been no obvious trade effects, although there has been no specific analysis of impact.

50. About 4.4 million tonnes of flour is produced in the UK<sup>18</sup> (at a value of just under £1 billion / year), about 3% of which is exported; an amount equal to about 1% of domestic production is imported. There are a large number of different wheat-containing products traded: the monetary value of exports of sweet biscuits and cakes is about 10% UK domestic production (total value of UK production is £1.5 billion and £1.2 billion for sweet biscuits and cakes respectively), whereas imports are roughly equal to 10% and 30% of the value for domestic sweet biscuit and cake production respectively<sup>19</sup>.

### **Consumer Research**

51. The Agency carried out deliberative consumer research with a small but population representative sample of 60 adults to explore the details of their views on this issue. As this was not a large quantitative survey numerical data should not be extrapolated from it. Most participants initially preferred Option 2 (more advice to women on folic acid) but on further deliberation this option lost favour because it was seen as having a low possibility of success by participants. By the end of the research process, Option 4 (mandatory fortification) was supported by more participants than any other option as it was seen to have the greatest possibility of success (support for the other options was fairly evenly split). It should be noted, however, that some participants continued to consider Option 4 unacceptable, mainly because of concerns about limiting choice and/or potential risks to others (Annex 9).

52. The Agency also conducted qualitative research amongst approximately 30 young mothers living in deprived communities. Most supported Option 4. Many of the participants reported very limited health related behavioural change before or during pregnancy, noting that they found this hard to achieve. This research suggests that uptake of folic acid supplements by this group is likely to remain low (Annex 9).

### **Ethical Opinion**

53. The Agency commissioned an expert view on the ethical issues that could be taken into account when considering the policy options for improving folate intake and preventing NTD-affected pregnancies (Annex 9). The authors used the

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<sup>18</sup> Trade data was obtained from HMRC (see <http://www.uktradeinfo.com>), and flour production data was obtained from the Defra Flour Millers Survey (see [http://statistics.defra.gov.uk/esg/index/list.asp?i\\_id=022](http://statistics.defra.gov.uk/esg/index/list.asp?i_id=022))

<sup>19</sup> Sweet Biscuits (October 2005) and Cakes and Cake Bars (June 2006). These Mintel reports provide retail sales data. We can estimate UK production of a given item by subtracting imports and then adding exports to the retail sales figure.

*United Nations Universal Declaration on Bioethics and Human Rights (2005)*<sup>20</sup> as a basis for their assessment. The principle ethical conflict to be addressed is between the ideal of individual's autonomy, which requires that an individual should always retain control over any decisions about their own health, and the ideal of social responsibility and justice, which proposes that societies have a duty of care to work, mainly through government, towards the greatest level of health for their members, particularly those who suffer from social and economic disadvantage.

## **Results of Consultation**

54. There have been 202 responses (Annex 10). Many respondents saw advantages in more than one of the options, for example supporting Option 1 or 2 in combination with 3 or 4. The issue raised most frequently in responses were the likely impact on NTDs, risks, limiting consumer choice and the need for controls on voluntary fortification. Industry responses also raised the issues of the potential impact on business of possible trade effects, labelling requirements and freedom to fortify products voluntarily. They also discussed the practicalities of bread and flour fortification.
55. There were 139 responses from individuals. These favoured Options 1, 2 and 4. Mandatory fortification was the option which received the most support, but many responses argued strongly against this because of the impact on choice. Many individuals argued that if Option 4 were to be pursued, wholemeal flour, and possibly some other specialist breads, should be exempt.
56. Responses were also received from food businesses; trade associations; groups representing those affected by NTDs; other charities; bodies representing health professionals; academics; consumer groups; government organisations; and MP/MEPs (Annex 10, Tables 2 and 7).
57. Groups representing those affected by NTDs and bodies representing health professionals, with one exception, supported Option 4 on the basis that it was most likely to reduce NTDs. Many did so with the *proviso* that voluntary fortification should be controlled. The majority of health professional groups supported efforts to encourage women to follow current advice on folic acid as part of a package of actions to improve folate intakes.
58. Only two responses were received from consumer groups: one opposed mandatory fortification because of uncertainties on risk, the other supported mandatory fortification. Two responses were received from groups representing

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<sup>20</sup>United Nations Economic, Social and Cultural Organization, *Universal Declaration on Bioethics and Human Rights*, 2005, Geneva.

the elderly: one supported mandatory fortification with the proviso discussed above, the other opposed because of concerns about choice/risk.

59. Many industry responses saw the decision on this as being one for Government as the experts on public health.

60. A number of industry responses indicated that further voluntary fortification of bread or breakfast cereals was unlikely. The baking industry raised practical concerns about the fortification of bread; both they and the millers would prefer mandatory fortification of flour, and for there to be a uniform decision across the UK. These industries noted that there would be several difficulties in the implementation of flour fortification on a country by country basis within the UK because of the integration of the business. They also noted that bread making flour cannot easily be separated from other flours in mills.

61. Many industry responses argued for the continuation of voluntary fortification but both the Food and Drink Federation and the British Retail Consortium suggested that their members would discuss voluntary regulation of this activity.

62. Responses from academics and other non-industry groups were split between options 2 and 4. Details of the scientific responses can be found in Annex 10, Appendix 1.

63. Some of the responses included references to scientific research. Most of the issues and studies cited in these responses had already been considered and addressed by SACN in their report. Studies which had been published after the SACN report were examined by SACN's scientific secretariat who concluded that the findings from these studies would not change SACN's overall conclusions and recommendations.

### **Food Advisory Committees (FACs)**

64. Annex 10 summarises FACs responses.

#### *Scotland (S-)*

65. S-FAC supported increased efforts on advice to women to take folic acid (Option 2), feeling that consumers were more sensitive to campaigns than they were in the 1990s. It saw mandatory fortification (Option 4) as disproportionate to the problem of NTDs.

#### *Wales (W-)*

66. W-FAC supported mandatory fortification (Option 4) alongside controls on voluntary fortification and the safeguards set out by SACN. However, it agreed

that if these safeguards could not be delivered then mandatory fortification should still go ahead.

#### *Northern Ireland (NI-)*

67. NI-FAC supported mandatory fortification (option 4) of most standard breads alongside controls on voluntary fortification. It also stated that this should not militate against consumer choice or discriminate against those on low income.

#### **Partial Regulatory Impact Assessment (RIA)**

68. An assessment of issues for industry is outlined in the partial RIA as well as the issue of sustainability. This can be viewed at the following link: (<http://www.food.gov.uk/consultations/ukwideconsults/2006/folate>). The cost/benefit analysis is summarised in Annex 11. The Agency estimate that the net economic benefits of mandatory fortification with no voluntary fortification would be around £13-14 million<sup>21</sup> per annum depending on whether or not wholemeal flour is fortified. Estimates are also given for net benefits if current levels of voluntary fortification continue alongside mandatory fortification.

#### **Discussion**

69. The challenge is to improve the folate intakes of women of reproductive age, with the aim of reducing the incidence of NTD-affected pregnancies; avoid increasing the risk of others having inappropriately high intakes of folic acid; provide consumers with some choice of unfortified products; and take account of practical, legal and trade issues.

#### *Option 1: Maintaining Current Efforts*

70. This option maintains current levels of consumer choice and would not increase the numbers exceeding guidance levels (GL/UL) on folic acid. However, there is no reason to expect a significant change in numbers of NTD-affected pregnancies and their associated costs, or in the number of individuals with low folate intakes.

71. Without additional controls on voluntary fortification or guidance on the use of folic acid containing supplements, current levels of voluntary fortification and supplement use by groups other than women planning a pregnancy are likely to remain maintaining the current levels of risk. If either voluntary fortification or supplements use increases then more people may exceed the GL/UL for folic acid.

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<sup>21</sup> The lower £13 million figure excludes wholemeal flour, although this option offers enhanced consumer choice.

72. If this option is preferred then the evidence base in relation to folic acid and disease should be re-assessed in not less than 5 years' time, which should allow time for sufficient substantive new evidence to emerge.

73. From an ethical point of view, if this option is preferred personal autonomy will be prioritised above social responsibility.

*Option 2: increase efforts to encourage women to follow advice on folic acid supplements*

74. In theory, this Option could reduce the number of NTD-affected pregnancies without restricting choice for consumers or increasing numbers exceeding GL/UL on folic acid. However, experience and the high level of unplanned pregnancies in the UK indicate that even sustained, high quality campaigning would be unlikely to increase the proportion of women with low folate status who take folic acid as recommended in the very early stages of pregnancy (see paragraph 17). The costs of an effective campaign are difficult to estimate but the cost of the HEA campaign in the 1990s was £2.3 million (not corrected for inflation) and phase 3 of the Agency's salt campaign costs about £4 million per year. There would need to be discussion with Health Departments on the nature and funding of any health education campaign.

75. This Option is similar to Option 1 in that it also leaves voluntary fortification uncontrolled and the guidance on supplement use remaining the same.

*Option 3: further encouraging voluntary fortification of foods*

76. To date encouraging voluntary fortification has produced benefits in reducing NTD-affected pregnancies and the numbers of individuals with low folate status. It has also contributed, however, to the number of individuals exceeding the GL/UL for folic acid (see paragraph 34). The impact of choosing this option on benefit, risk and choice would depend on the range and proportion of food types affected and levels of fortification.

77. Responses to the consultation suggest that bread would not be fortified voluntarily to any significant extent, and discussions with industry suggest further fortification of cereal products is unlikely. Fortification of low-fat spreads has been concentrated in premium brands unlikely to be consumed regularly by women with the lowest folate status, who tend to have low incomes. Since these are the foods most suitable for fortification (see paragraph 11) this approach is unlikely to achieve further reductions in NTD- affected pregnancies.

78. If this Option is chosen, it will be necessary to optimise the impact of any further voluntary fortifications by introducing controls to prevent an increase in the number of individuals exceeding the GL/UL for folic acid, as discussed below under Option 4. Currently there is no guidance on either the type of foods or the

level of fortification. Businesses fortifying foods voluntarily may wish to make claims, and may therefore wish to provide at least 15% of the RDA (30 micrograms / 100 grams of the product; allowing a claim that the product is a source of folic acid).

*Option 4: Mandatory Fortification of Wheat Flour or Bread*

79. The scientific evidence shows that this approach is likely to reduce NTD-affected pregnancies and the number of individuals with low folate status. However, it could also increase the number of individuals exceeding the GL/UL for folic acid and it would reduce consumer choice.
80. The risk of an increase in the number of individuals exceeding the GL/UL could be averted by linking mandatory fortification with controls on voluntary fortification. This would have the effect of redistributing intakes, producing a more uniform profile across the population. The modelling exercise undertaken by SACN (paragraph 33), based on a dose of 300 micrograms / 100 grams of white and brown wheat flours (which would increase the average folic acid intake of the UK population by about 80 micrograms / day), has identified one way in which this could be done, which is by not allowing any voluntary fortification. However, there are other possibilities, for example, the fortification limiting the range of foods that could be fortified and/or introducing maximum levels of voluntary fortification. In order to identify suitable foods and levels detailed discussions with stakeholders and further modelling work would be needed to identify the most suitable approach and to determine whether a voluntary approach is achievable. These controls, whether voluntary or statutory, would need to be notified to the European Commission (see paragraph 45) before implementation.
81. Fortification of wheat flour rather than bread has significant practical advantages, (see paragraph 39) and the following discussion therefore focuses on this vehicle.
82. To mitigate the impact on choice, wholemeal flour could be exempted, as is the case for current wheat flour fortificants, and this would have significant practical advantages (see paragraph 39). Imported wheat flour would also be exempt (see paragraph 39). Industry has highlighted that there would be significant practical difficulties in introducing other exemptions, such as excluding flour for biscuits and cakes or stone ground flours other than wholemeal, in accordance with the Bread and Flour Regulations (see paragraph 39). It would be important to label wheat bread to show that folic acid had been added to the flour so that consumers have access to this information. It would also be important to label other wheat flour containing products as containing folic acid, providing the product did not contain only small amounts of flour and therefore insignificant amounts of folic acid. The use of a *threshold* for labelling would require EU agreement (paragraph 47) but would offer practical advantages to industry and could also help provide accurate information to consumers who might be given

the impression, if folic acid is labelled on all wheat products, that they are consuming nutritionally meaningful amounts of the nutrient.

83. This option also raises a number of potential intra-UK and export issues. Firstly, advice from industry is that implementation of mandatory fortification in a single country of the UK would not be feasible because the milling industry is integrated across the UK; however the decision is for devolved administrations. Secondly, consumers in Northern Ireland may be affected by decisions taken in the Republic of Ireland; in particular, bread fortified at the lower level agreed in Ireland might reduce the benefit to Northern Ireland consumers eating Irish bread. Thirdly, the cake and biscuit sector is concerned about the potential impact on exports if customers choose not to purchase products made from fortified flour. It is not possible to predict the impact of mandatory fortification on trade in wheat products, however reports from the USA suggest that it has had little effect on trade.

84. From an ethical point of view this option achieves social responsibility by protecting vulnerable individuals at risk of NTDs but limits personal autonomy.

### **Recommendation**

85. The incidence of NTD affected-pregnancies in the UK is likely to be reduced if mandatory fortification of wheat flour with folic acid is introduced. If this approach is combined with controls on voluntary fortification and guidance on the use of folic acid containing supplements then the overall effect will be to:

- improve the nutritional well-being of the population by substantially increasing the numbers of people meeting nutritional recommendations for folate (of particular benefit to women of reproductive age and the elderly as poor folate intakes are common in these groups);
- prevent an increase in the risk of some consumers having intakes above the GL/UL for folic acid; and
- allow consumers to choose unfortified wholemeal wheat products.

86. On balance, therefore, taking into account the scientific advice, practical and technical issues, the findings of consumer research, the views of consultation respondents and the associated ethical issues, it is recommended that the Board agree to advise UK Health Ministers to introduce mandatory fortification with folic acid with the following provisos:

- that mandatory fortification apply to white and brown wheat flour;
- that the folic acid should be labelled when it is present at nutritionally significant levels; and

- that controls on voluntary fortification and guidance on the appropriate use of supplements' containing folic acid should be introduced.
87. In the first instance, an approach of voluntary constraint by food industry (either by stopping or restricting voluntary fortification with folic acid by capping the level of addition and / or by limiting the range of foods to which it can be added) and advice from the supplements industry should be pursued, but if this is not successful then mandatory controls should be introduced.
88. These controls should, in combination with mandatory fortification be devised to deliver:
- an average increase in folic acid intakes of 60-100 micrograms / day;
  - numbers not achieving the reference nutrient intake for folate not exceeding about 10 %; and
  - numbers exceeding the GL/UL for folic acid not increasing above current levels.
89. The primary decisions for the Board are set out in the box below. This includes a recommendation that progress towards implementation should be reported back to the Board in about 12 month's time, depending on the outcome of the Ministerial decision.
90. In addition, if mandatory fortification is pursued folic acid intakes and status of the UK population and postulated risks, including cancer, should be carefully monitored. The data on the benefits and possible risks should be reviewed five years after the introduction of mandatory fortification.
91. If it is decided not to implement this advice on mandatory fortification because of concerns about cancer risk or because of concerns about limiting freedom to choose unfortified products then the decision should not be reviewed for at least five years which would give time for sufficient new evidence to emerge or for a significant shift to occur in consumer views.
92. Whether or not mandatory fortification is pursued, Health Departments should be recommended to maintain, as a minimum, current efforts to encourage more women to follow current advice on folic acid.
93. Finally, attention of Health Departments should be drawn to SACN's advice to UK Health Department's that a clinical strategy is needed to manage vitamin B12 deficiency irrespective of any decision on folic acid fortification.

## DECISION FRAMEWORK

### **The primary decisions to be made are:**

- whether to support mandatory fortification or not;
- what food or foods should be fortified;
- whether the folic acid should be labelled;
- whether controls on voluntary fortification and advice on use of supplements should be introduced to manage high intakes of folic acid; and
- whether such controls should be voluntary or statutory and the parameters within which they should be determined.

### **If mandatory fortification with controls on voluntary fortification is chosen, it will deliver:**

- an average increase in folic acid intake of 60-100 micrograms / day;
- numbers not achieving the reference nutrient intake for folate not exceeding about 10%; and
- numbers exceeding the GL/UL for folic acid not increasing above current levels; and
- **progress towards implementation should be reported back to the Board in about 12 month's time.**

## NEURAL TUBE DEFECTS: CURRENT COSTS AND NUMBERS

Table 1: TABLE SHOWING THE CURRENT ECONOMIC COST OF NTDs

Category of NTD	Number of cases within this category	Monetary cost / individual in this category	Total monetary cost for all individuals of this category
Still birth / neonatal death	110	£881,940	£97,042,474
Spina bifida with standard life expectancy	79	£486,816	£38,523,378
Terminations	611	£542	£331,072
		<b>Total monetary cost:</b>	<b>£135,896,924</b>

### Important notes regarding the current cost of NTDs:

1. All numbers in this table have been calculated and then rounded to the nearest pound or unit.
2. The values have been computed by decomposing the SACN estimate of the number of NTDs per year (700-900; we take the average value 800, Annex 5) into three categories: (i) still births and neo-natal deaths, (ii) cases of spina bifida with a standard life expectancy, and (iii) terminations. There is a different monetary cost per individual associated with each category of NTD; the total cost per category of NTD is calculated using these costs per individual, and the resulting total costs are then added to give an overall cost of NTDs (i.e. circa £136 million per year).

3. Data published in Health Statistics Quarterly<sup>1</sup> is used to decompose the 800 NTDs into the above three categories (i) to (iii). This paper matches data from the National Congenital Anomaly System (NCAS) on the number of live births and still births, with external data on the number of neo-natal deaths and terminations. This allows us to establish the proportion of NTD pregnancies in each of categories (i) to (iii) mentioned above. Specifically, NCAS data is used to identify the number of still births, and the external data is used to identify the number of terminations and neo-natal deaths. Lastly, the number of cases of NTD with a Standard Life Expectancy (SLE) is estimated by subtracting the aforementioned number of neo-natal deaths from the NCAS data on the number of live births.
4. It is important to note that the costs per individual for categories (i) and (iii) are not just equal to the associated NHS costs; they also reflect willingness-to-pay to avoid pain, grief and suffering. It should also be noted that the calculations do not currently include estimates of the cost to the NHS or to HM Government of modified cars, homes and so on for NTD sufferers. The Agency's Economics Branch intend to add these costs at a later date; when included, they will make the cost per individual for category (ii) even larger than the figure stated in the table.
5. Lastly, it should be noted that the Agency's Economics Branch are also considering feedback relating to the potential to account for an 'intrinsic value of life' element into this work (as the developing Value of Life literature now suggests). This may have the effect of increasing the monetary costs associated with categories (i) and (ii) in the above table.

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<sup>1</sup> ONS, Summer 2001

## NUMBERS OF NTD-AFFECTED BIRTHS AND PREGNANCIES IN THE UK

**Table 2: Reported numbers and rates of NTD-affected births in UK in 2002 & 2003**

COUNTRY	2002		2003	
	NUMBER	RATE/10,000	NUMBER	RATE/10,000
England & Wales	119 (77%)	2.0	121 (78%)	1.9
Scotland	22 (14%)	4.5	24 (15%)	4.9
Northern Ireland	4 (9%)	6.5	11 (7%)	5.1
<b>TOTAL</b>	<b>155</b>		<b>156</b>	

**Table 3: Reported numbers and rates of NTD-affected pregnancies in UK in 2002 & 2003**

COUNTRY	2002		2003	
	NUMBER	RATE/10,000	NUMBER	RATE/10,000
England & Wales*	374 (86%)	6.2	418 (90%)	6.7
Scotland	59 (14%)	12.0	49 (10%)	9.9
Northern Ireland	N/A	N/A	N/A	N/A
<b>TOTAL</b>	<b>433</b>		<b>467</b>	

Source of data

**England & Wales: Source of birth data: National Congenital Anomaly System.**

Source of termination data: Series AB ONS Abortion statistics 1995-2001; DH Statistical Bulletin - Abortion statistics 2002-2004.

Scotland: Source of birth data: Scottish Perinatal and Infant Mortality & Morbidity Report (2003), Information & Statistics Division, National Health Service Scotland

Source of termination data: General Register Office for Scotland and Notifications (to the Chief Medical Officer for Scotland) of abortions performed under the Abortion Act 1967

Northern Ireland: Source of birth data: Child Health Systems (Northern Ireland and Social Services Boards)

\*Separate data available from the Congenital Anomaly Register and Information Service for Wales suggest higher rates of NTD-affected pregnancies in Wales: 19 per 10,000 births in 2002 and 14 per 10,000 births in 2003.

## CONSUMPTION DATA

1. This annex presents a folate, folic acid, food and supplement consumption patterns derived from the analysis of UK National Diet and Nutrition Survey (NDNS) data. It also includes some data from the Low Income Diet and Nutrition (LIDNS) due for publication by the Agency later this year.

### **Consumption of wheat flour and wheat flour containing products according to levels of folate intake and income**

2. Women of child bearing age with low folate intakes are more often in receipt of benefits than high folate consumers. Table 1 illustrates this using NDNS data for 19-34 year olds. Flour and bread consumption is however relatively uniform; there are no apparent trends across different levels of folate intake.
3. Table 2 compares women in the LIDNS survey with those in NDNS. It shows that a greater proportion of the LIDNS sample have intakes below the reference nutrient intake (RNI) in all age groups except the over 60s. White bread consumption was similar in both surveys.

**Table 1: Consumption of wheat flour and wheat flour containing products by quintile of folate intake for women aged 19-34 years**

Women aged 19-34 years	Folate intake quintiles									
	Quintile 1 (lowest)		Quintile 2		Quintile 3		Quintile 4		Quintile 5 (highest)	
Mean age (years)	26		28		28		28		28	
Percentage from benefit households <sup>1</sup>	44		27		14		16		13	
	Flour consumption (grams / day)									
Total flour consumption (grams / day) of which	55		56		67		66		56	
Flour from bread	44		40		48		51		38	
Flour from other products	11		15		18		15		18	
	Consumption of flour containing products									
	mean g/day	% consumers	mean g/day	% consumers	mean g/day	% consumers	mean g/day	% consumers	mean g/day	% consumers
White bread	63	91	53	94	64	100	56	90	37	82
Softgrain bread	0	0	0	0	0	2	2	4	0	0
Other bread	8	31	13	41	14	53	28	68	28	70
Pizza	6	16	11	33	16	40	13	39	15	30
Other cereals <sup>2</sup>	4	22	6	31	5	38	3	34	4	26
Biscuits	6	49	7	63	11	73	9	70	9	60
Buns, cakes, pastries and fruit pies	10	45	17	65	15	56	12	52	16	58
Cereal based puddings	4	14	3	18	5	18	7	13	12	29

Source: NDNS adults 19-64 years (2000/01)

<sup>1</sup> Receipt of income related benefits by the respondent or anyone else in the household

<sup>2</sup> The 'other cereals' food group includes products such as dumplings, Yorkshire pudding, poppadoms, pancakes, cous cous, polenta etc.

**Table 2: Comparison of population mean total folate intake from food and mean daily bread consumption between the National Diet and Nutrition Survey (NDNS) series and the Low Income Diet and Nutrition Survey (LIDNS).**

Age (yrs) and sex group		Data from NDNS series	Data taken from LIDNS <sup>3</sup>
11-18 females <sup>4</sup>	Mean daily folate intake ( $\mu\text{g}$ )	212	201
	% of the population with intakes <RNI <sup>5</sup>	51	56
	Mean white bread consumption (g/d)	59	56
	Mean wholemeal bread consumption (g/d)	6	5
19-34 females <sup>6, 7</sup>	Mean daily folate intake ( $\mu\text{g}$ )	249	207
	% of the population with intakes <RNI	35	59
	Mean white bread consumption (g/d)	54	47
	Wholemeal bread consumption (g/d)	10	9
35-49 females <sup>6, 7</sup>	Mean daily folate intake ( $\mu\text{g}$ )	280	208
	% of the population with intakes <RNI	26	57
	Mean white bread consumption (g/d)	50	48
	Mean wholemeal bread consumption (g/d)	15	10
65+ females <sup>8</sup>	Mean daily folate intake ( $\mu\text{g}$ )	220	220
	% of the population with intakes <RNI	48	46
	Mean white bread consumption (g/d)	46	41
	Mean wholemeal bread consumption (g/d)	22	16

<sup>3</sup> This table uses data taken from the unpublished Low Income Diet and nutrition Survey (LIDNS) which is due to be published by Food Standards Agency in 2007.

<sup>4</sup> Gregory J, Lowe S, Bates CJ, Prentice A, Jackson LV, Smithers G, Wenlock R & Farron M. National Diet and Nutrition Survey: young people aged 4 to 18 years. Volume 1: Report of the diet and nutrition survey. TSO (London: 2000)

<sup>5</sup> Reference Nutrient Intake for folate is 200 $\mu\text{g}/\text{day}$  for adults and children aged 11 years and above. Department of Health. Dietary Reference Values for food Energy and Nutrients in the United Kingdom. (Report on Health and Social Subjects, No. 41). London: HSMO, 1991.

<sup>6</sup> Hederson L, Gregory J, & Swan G. National Diet and Nutrition Survey: adults aged 19 to 64 years. Volume 1: Types and quantities of foods consumed. TSO (London: 2002)

<sup>7</sup> Henderson L, Irving K, Gregory J, Bates CJ, Prentice A, Perks J, Swan G & Farron M. National Diet and nutrition Survey: adults aged 19 to 64 years. Volume 3: Vitamin and mineral intake and urinary analytes. TSO (London: 2000)

<sup>8</sup> Finch S, Doyle W, Lowe C, Bates CJ, Prentice A, Smithers G & Clarke PC. National Diet and Nutrition Survey: people aged 65 years or over. Volume 1: Report of the diet and nutrition survey. TSO (London: 1998)

## **Folate consumption of women of childbearing age - contributions of different dietary sources**

4. Table 3 taken from the SACN report *Folate and Disease* illustrates current folate intakes for women of childbearing age by quintiles. It can be seen that:
- Women in the lowest quintiles have on average, total folate intakes below the RNI of 200 micrograms / day (132 micrograms / day folic acid for the lowest quintile and 195 micrograms / day folic acid for the second lowest quintile).
  - Natural folate provides the majority of folate in the diet for the lowest quintiles (95% for the lowest quintile, 91% for the second lowest quintile).
  - Folic acid from supplements and fortified fat spreads make very little or no contribution to the total folate intake of the lower quintiles. The main source of folic acid for this group is fortified breakfast cereals (5% of total folate for the lowest quintile and 9% of total folate for the second lowest quintile).
  - In the highest quintile the majority of folate in the diet is consumed in the form of folic acid (52%).

**Table 3:** Contribution of fortified breakfast cereals, fat spreads and supplements to total folate intake for women of childbearing age represented in quintiles of the population and as a percentage of total folate intake in brackets.

Female age group (yrs)	Quintile	Total folate (µg/day)	Natural folate (µg/day) (% of total folate)	Folic acid from fortified breakfast cereals (µg/day) (% of total folate)	Folic acid from fortified spreads (µg/day) (% of total folate)	Folic acid from supplements (µg/day) (% of total folate)	Folic acid from fortified breakfast cereals, fat spreads and supplements (µg/day) (% of total folate)
14-18	1 <sup>st</sup>	118	109 (92%)	10 (8%)	0	0	10 (8%)
	2 <sup>nd</sup>	168	153 (91%)	15 (9%)	0	0	15 (9%)
	3 <sup>rd</sup>	203	174 (86%)	29 (14%)	0	0	29 (14%)
	4 <sup>th</sup>	282	215 (76%)	43 (15%)	20 (7%)	5 (2%)	68 (24%)
	5 <sup>th</sup>	488	238 (49%)	123 (25%)	100 (20%)	27 (6%)	250 (51%)
19-34	1 <sup>st</sup>	125	120 (96%)	5 (4%)	0	0	5 (4%)
	2 <sup>nd</sup>	188	169 (89%)	19 (10%)	0	1 (1%)	20 (11%)
	3 <sup>rd</sup>	242	208 (86%)	31 (13%)	0	3 (1%)	34 (14%)
	4 <sup>th</sup>	319	242 (76%)	52 (16%)	21 (7%)	5 (2%)	78 (24%)
	5 <sup>th</sup>	512	250 (49%)	80 (16%)	83 (16%)	98 (19%)	262 (51%)
35-49	1 <sup>st</sup>	143	136 (95%)	6 (4%)	0	1 (1%)	7 (5%)
	2 <sup>nd</sup>	209	191 (91%)	17 (8%)	0	1 (1%)	18 (9%)
	3 <sup>rd</sup>	265	226 (85%)	38 (14%)	0	1 (1%)	39 (15%)
	4 <sup>th</sup>	359	256 (71%)	70 (19%)	22 (6%)	11 (3%)	103 (29%)
	5 <sup>th</sup>	591	279 (47%)	74 (13%)	95 (16%)	144 (24%)	313 (53%)
Weighted Mean of 14-49	1 <sup>st</sup>	132	126 (95%)	6 (5%)	0	0	6 (5%)
	2 <sup>nd</sup>	195	177 (91%)	18 (9%)	0	1 (1%)	19 (10%)
	3 <sup>rd</sup>	247	212 (86%)	34 (14%)	0	2 (1%)	36 (15%)
	4 <sup>th</sup>	332	245 (74%)	59 (18%)	21 (6%)	8 (2%)	88 (27%)
	5 <sup>th</sup>	543	261 (48%)	83 (15%)	90 (17%)	109 (20%)	282 (52%)

### The consumption of folate, wheat flour and products bread

5. Table 2 compares folate intakes as average values and proportions below the RNI (200 micrograms / day) for women from the general population assessed using NDNS data and the low income population using LIDNS data. A greater proportion of women of child bearing age in the low income group have folate intakes below recommended levels. Bread consumption levels were broadly similar in NDNS and LIDNS for different age groups of women according to folate intake (Tables 1 and 2), age and sex (Table 4) and receipt of benefits (Table 5). The consumption of flour containing products is presented according to age and sex (Table 6) and receipt of benefits (Table 7).

**TABLE 4: Mean wheat flour consumption (total, as bread, as other foods) (grams / day) by age and sex**

Source	Age and sex											
	4 – 10 yrs		11 – 18 yrs		19 – 49 yrs		50 – 64 yrs		65+ yrs (free living)		65+yrs (institutions)	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
<b>Total flour of which:</b>	67	58	84	64	86	59	90	58	79	56	82	69
<b>Flour from bread</b>	41	35	56	43	64	43	64	38	50	35	47	36
<b>Flour from other foods</b>	27	23	28	21	22	17	26	20	29	22	35	32

Source: NDNS young people aged 4-18 (1997)  
 NDNS adults aged 19-64 (2000/01)  
 NDNS people aged 65 years and over (1994/95)

**TABLE 5: Mean wheat flour consumption (total, as bread, as other foods) (grams / day) by household receipt of benefits<sup>9</sup>**

Source	YOUNG PEOPLE – aged 4–18				ADULTS – aged 19–64				OLDER PEOPLE (free living) – aged 65+			
	Males		Females		Males		Females		Males		Females	
	Receivin g	Not receivin g	Receivin g	Not receivin g	Receivin g	Not receivin g	Receivin g	Not receivin g	Receivin g	Not receivin g	Receivin g	Not receivin g
<b>Total flour of which:</b>	64	80	59	62	82	88	55	60	77	80	62	60
<b>Flour from bread</b>	41	51	37	40	65	64	40	41	47	50	36	35
<b>Flour from other foods</b>	23	29	22	22	16	24	14	18	30	30	26	25

Source: NDNS young people aged 4-18 (1997)  
 NDNS adults aged 19-64 (2000/01)  
 NDNS people aged 65 years and over (1994/95)

<sup>9</sup> Receipt of income related benefits by the respondent or anyone else in the household

**TABLE 6: Mean consumption of wheat flour-containing foods (grams / day) by sex and age**

Food	Age and sex											
	4 – 10 yrs		11 – 18 yrs		19 – 49 yrs		50 – 64 yrs		65+ yrs (free living)		65+yrs (institutions)	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
<b>White bread</b>	59	50	80	60	83	52	81	46	66	46	65	51
<b>Wholemeal bread<sup>10</sup></b>	7	6	7	6	17	12	21	16	28	22	18	18
<b>Other breads</b>	7	6	10	10	20	18	24	16	16	11	11	8
<b>Pasta and dishes<sup>11</sup></b>	26	25	27	29	34	28	22	18	9	6	5	4
<b>Buns, cakes and pastries and fruit pies</b>	27	21	26	22	20	16	33	25	42	29	42	41
<b>Biscuits</b>	20	20	18	13	13	10	15	12	17	14	19	16
<b>Pizza</b>	9	8	22	13	20	9	6	6	1	1	1	0
<b>Cereal based puddings</b>	11	8	7	7	6	7	10	9	10	8	38	38
<b>Other cereals<sup>12</sup></b>	3	3	4	5	6	5	4	3	4	3	5	4

Source: NDNS young people aged 4-18 (1997)  
 NDNS adults aged 19-64 (2000/01)  
 NDNS people aged 65 years and over (1994/95)

<sup>10</sup> Wholemeal flour not included in modelling

<sup>11</sup> Pasta has not been included in the modelling work carried out by SACN (Report Folate and Disease Prevention) as the majority consumed is imported

<sup>12</sup> The 'other cereals' food group includes products such as dumplings, Yorkshire pudding, poppadoms, pancakes, cous cous, polenta etc.

**TABLE 7: Mean consumption of wheat flour-containing foods (grams / day) by household receipt of benefits<sup>13</sup>**

Food	YOUNG PEOPLE – aged 4–18				ADULTS – aged 19–64				OLDER PEOPLE (free living) – aged 65+			
	Males		Females		Males		Females		Males		Females	
	Receivin g	Not receivin g	Receivin g	Not receivin g	Receivin g	Not receivin g	Receivin g	Not receivin g	Receivin g	Not receivin g	Receivin g	Not receivin g
<b>White bread</b>	61	72	52	56	95	81	53	50	60	66	49	47
<b>Wholemeal bread<sup>14</sup></b>	4	8	5	7	15	19	8	14	19	27	11	23
<b>Other breads</b>	4	10	7	8	10	23	12	18	17	15	10	10
<b>Pasta and dishes<sup>15</sup></b>	23	28	23	29	29	31	20	26	4	9	5	6
<b>Buns, cakes and pastries and fruit pies</b>	22	28	21	22	16	25	13	20	39	42	32	33
<b>Biscuits</b>	16	20	17	16	12	14	9	11	18	17	17	15
<b>Pizza</b>	11	18	8	12	8	17	10	8	0	1	0	1
<b>Cereal based puddings</b>	10	9	7	8	5	8	4	8	22	14	18	17
<b>Other cereals<sup>16</sup></b>	4	4	5	4	4	6	4	5	3	4	5	3

Source: NDNS young people aged 4-18 (1997)  
 NDNS adults aged 19-64 (2000/01)  
 NDNS people aged 65 years and over (1994/95)

<sup>13</sup> Receipt of income related benefits by the respondent or anyone else in the household

<sup>14</sup> Wholemeal flour not included in modelling

<sup>15</sup> Pasta has not been included in the modelling work carried out by SACN (Report Folate and Disease Prevention) as the majority consumed is imported

<sup>16</sup> The 'other cereals' food group includes products such as dumplings, Yorkshire pudding, poppadoms, pancakes, cous cous, pole

## THE UK FOLIC ACID CAMPAIGN

1. From autumn 1995 to spring 1998 the Health Education Authority ran a UK-wide integrated campaign aimed at increasing the average daily intakes of folates and folic acid in women who might become pregnant by at least 400 micrograms from foods containing natural folate, foods fortified with folic acid and folic acid supplements. The objectives of the campaign were to:
  - increase awareness of the importance of taking additional folic acid before conception and 12 weeks into pregnancy in the general female population and in influential professional groups
  - increase the availability of fortified breads and breakfast cereals
  - increase the number and availability of appropriate supplements, especially those that are licensed (medicines)
  - make fortified products and supplements more easily identifiable.
2. The campaign targeted the public (primarily women planning pregnancy and women of childbearing age); health professionals and others such as journalists and teachers; and the commercial sector including food manufacturers and retailers, trade associations and manufacturers of ovulation predictor and pregnancy testing kits.
3. A critical element of the campaign was to create local and national partnerships with the voluntary, public and commercial sectors; health professionals were integral to the work's success. A range of strategies was adopted to convey different messages to various audiences and to influence the behaviour of professionals and the public. Elements of the work were designed to reinforce one another and included:
  - developmental research, literature reviews, monitoring surveys, policy analysis
  - public and professional information i.e. leaflets, posters, advertising, public relations, media work
  - collaboration with health professional bodies
  - developing a folic acid 'flash' labelling scheme for foods fortified with folic acid (especially breads and breakfast cereals); the 'flash' is a circular logo including a central letter "F" and the words "with extra folic acid" or "contains folic acid" depending upon the folic acid content of the product

- producing an education pack for secondary school teachers containing guidance on how folic acid advice could be given as part of core curriculum subjects and personal, social and health education lessons
- joint promotions with retailers and trade organisation e.g. National Association of Master Bakers.

## Results

4. All stages of the planning, execution and evaluation of the campaign were underpinned by an extensive programme of research which showed that:
  - unprompted awareness of folic acid among women of childbearing age had increased from 9% (1995) to 49% (1998)
  - prompted awareness among women of childbearing age had risen from 51% (1995) to 89% (1998)
  - the proportion of recently-pregnant women claiming to take folic acid when trying for a baby had risen from 24% (1997) to 38% (1998)
  - the proportion of recently-pregnant women claiming to take folic acid during the first 12 weeks of pregnancy had risen from 54% (1997) to 68% (1998)
  - the proportion of health professionals who spontaneously identified folic acid as “very important” for women planning a pregnancy rose from 64% (1996) to 71% (1997)
  - 49% of health professionals who had seen campaign information claimed to have changed their practice as a result
  - the range of fortified foods and supplements increased; 18 companies, representing over 250 products, signed up to the folic acid flash labelling scheme
  - the number of unlicensed (food) 400 microgram supplements increased from 9 (May 1996) to 18 (March 1998)
  - the number of licensed 400 microgram folic acid supplements doubled and the prescription rates for folic acid increased.

## Folic Acid: Influencing Low-income groups – Literature Reviews

5. In June 2006 the Agency commissioned three complementary literature reviews to examine whether research evidence indicated any possibilities for improving

the use of folic acid supplements in the UK, particularly among young, low-income women.

6. The purpose of the first review was to gain a picture of the types of initiatives which are successful in encouraging women to take a positive action in order to reduce a possible future risk e.g. behaviour such as attending screening, eating fruits and vegetables, or practising contraception. The second review examined the effectiveness of various approaches to preconception care. The third review examined research aimed at encouraging women, particularly young women or low-income women, to take folic acid supplements in the periconceptual period.

7. Key findings were:

- Very few relevant research studies have been undertaken in the UK; findings from other countries may not be applicable in the UK context. In addition many studies only collected results for a short time after the intervention, so it was difficult to say how sustained any effects were.
- All three reviews reinforced previous finding on the characteristics of effective health promotion interventions. These include using a 'package' of complementary components using different communication channels, locations, and health promotion approaches, and sustaining the intervention over a long period of time.
- Generally the most effective health promotion approaches: targeted high risk groups; worked with families, peers, and organisations/places which provided access to the target groups; and included practical steps to make the 'positive action' easier.
- There is some evidence, mostly from the USA, that preconception care can have a positive impact on health behaviours, including folic acid uptake. Preconception care programmes, in place in a small number of European countries, are designed to promote health and prevent disease in women of reproductive age in order to improve birth outcomes. They may include, for example, screening women seeking family planning for risk conditions and providing women with certain metabolic conditions (e.g. diabetes, phenylalanaemia) with nutrition services. There are only two preconception clinics in the UK (Glasgow and London) and these focus on women with previous adverse pregnancy outcomes. For preconception care programmes to be available to all women would need changes to current practices within the UK health care system and to training and ongoing support for health professionals.
- Folic acid supplement uptake reported by pregnant women and new mothers ranged from 7% to 53%. Factors that are particularly associated with lower awareness and rates of uptake are: unintended pregnancy; lower household

income; lower educational attainment; being a lone parent, unemployed, from a lower socio-economic group, young, or from a minority ethnic group; lacking awareness/knowledge of the potential benefits, not being convinced of efficacy; and having a less healthy lifestyle.

- Four integrated public health campaigns (in South Australia, Canada, the Netherlands, and the UK) had qualified success in increasing uptake of folic acid supplements. However, in Australia, there was no evidence that the effects would be sustained; in Canada, even at the end of the study there was 'considerable room for improvement' in uptake of folic acid supplements; and in the Netherlands, there was particular concern about reaching women in lower socio-economic groups.
- At the end of the campaigns in England, Scotland, Wales and Northern Ireland (in 1998), only 38% of pregnant women, asked retrospectively, said they had taken folic acid supplements when trying for a baby. Among women who were not planning pregnancy ('leaving things to chance') the figure was 9%. This, together with data from the other national and regional campaigns, indicates that even high quality and intensive national campaigns apparently result in under half of women in the target group taking supplements. In addition, campaigns have the potential to exacerbate inequalities in folic acid use between women in lower and higher socio-economic groups.

## FOLIC ACID FORTIFICATION STRATEGIES IN OTHER COUNTRIES

**Table 1: Folic acid fortification strategies in other countries**

Country	Fortification position	Information on fortification level
<b>Australia</b>	<b>Voluntary (1996)</b>  <b>Mandatory fortification under consideration</b>	<b>Voluntary – includes breakfast cereal, some bread &amp; marmite (levels unavailable). Bread will no longer be fortified voluntarily in line with new legislation.</b>  <b>80-180 micrograms/100g bread as consumed</b>
<b>Belgium</b>	<b>Voluntary</b>	<b>For product to be labelled as fortified with folic acid the daily portion has to contain 15 to 200% of 200micrograms</b>
<b>Bolivia, Colombia, Paraguay Ecuador</b>	<b>Mandatory fortification</b>	<b>Wheat flour - 60-300µg/100g</b>
<b>Brazil</b>	<b>Legislation pending</b>	<b>150µg/100g wheat &amp; maize flour</b>
<b>Canada</b>	<b>Mandatory (1998)</b>	<b>See separate table below</b>
<b>Chile</b>	<b>Mandatory (2000)</b>	<b>220µg/100g flour</b>
<b>Czech Republic</b>	<b>Voluntary</b>	<b>Information on foods unavailable – level 200micrograms/100g</b>
<b>France</b>	<b>Voluntary</b>	<b>Breakfast cereals and products aimed at children or women – levels unavailable</b>  <b>Goats milk at 4.5micrograms/100g</b>
<b>Germany</b>	<b>Voluntary</b>	<b>Breakfast cereals and products – levels unavailable</b>
<b>Greece</b>	<b>Voluntary</b>	<b>Unavailable</b>
<b>Hungary</b>	<b>Voluntary</b>	<b>Previously fortified @ 60µg/100g bread</b>
<b>Iceland</b>	<b>Voluntary</b>	<b>Breakfast cereals and products 30-700micrograms/100g, flour and rice 30-100micrograms/100g</b>
<b>Ireland</b>	<b>Mandatory fortification recommended</b>	<b>120 micrograms/100g of white, brown and wholemeal bread as consumed</b>

	<b>(pending legislation)</b>	
<b>Israel</b>	<b>Voluntary (Legislation pending)</b>	<b>Wheat flour (rate unknown) Co-fortification with vitamin B<sub>12</sub> being considered</b>
<b>New Zealand</b>	<b>Voluntary (1996)  Mandatory fortification under consideration</b>	<b>Voluntary – includes breakfast cereal, some bread &amp; marmite (levels unavailable). Bread will no longer be fortified voluntarily in line with new legislation.  80-180 micrograms/100g bread as consumed</b>
<b>Sweden</b>	<b>Mandatory fortification has been under consideration</b>	<b>Swedish Council on Technology Assessment in Health Care agreed not to recommend mandatory fortification in March 2007. Their report is now open for comments. Final decision to be taken before summer 2007.</b>
<b>UK</b>	<b>Voluntary</b>	<b>Breakfast cereals and products 8-643micrograms/100g; flora spread products 1000micrograms/100g.</b>
<b>USA</b>	<b>Mandatory (1998)</b>	<b>See separate table below.</b>

The effects of different levels of mandatory fortification on folic acid intakes and NTD incidence are compared in Annex 6

**Table 2: Issues relating to fortification strategies in USA and Canada**

USA*			
Regulation	Practical issues	Effect on trade	Effect on consumption patterns
<p><u>Cereal flours &amp; related products (per 100g)</u></p> <ul style="list-style-type: none"> <li>Enriched bromated flour, enriched flour, enriched self-raising flour: 154 µg</li> <li>Enriched corn meal: 154-221 µg</li> <li>Enriched farina: 154-192 µg</li> <li>Enriched rice: 154-308 µg</li> </ul> <p><u>Bakery products (per 100g)</u></p> <ul style="list-style-type: none"> <li>Enriched bread, rolls, buns: 95 µg</li> </ul> <p><u>Macaroni &amp; noodle products (per 100g)</u></p> <ul style="list-style-type: none"> <li>Enriched macaroni products, enriched non-fat milk macaroni products, enriched vegetable macaroni products, enriched noodle products, enriched vegetable noodle products: 198-265 µg</li> </ul> <p>Under US mandatory nutrition labelling regulations, folic acid is not required to be declared unless a claim is made about it. If a manufacturer decides to voluntarily declare folic acid, the actual amount in a serving of the product must be declared along with the % Daily Value based on Reference Daily Intakes (RDI). The RDI for folic acid is 400 µg/day.</p>	<p><u>Overage</u></p> <p>Originally estimated that mandatory fortification would provide an additional 80-100µg folic acid / day. However it has been estimated that mandatory fortification increased typical folic acid consumption by 215-240 µg/d, due mainly to overage.</p> <p>When a single fortification level is specified, the regulation allows for 'reasonable overages within the limits of current good manufacturing practice'.</p> <p><u>Enforcement</u></p> <p>Food producer responsible for ensuring that the standardised food is properly fortified in accordance with the relevant standard of identity. When FDA pursue enforcement action against a company, they check to see who is named on the product: this will be either the manufacturer, the packer, or the distributor.</p>	<p>The FDA does not track or monitor the type of data necessary to know whether mandatory fortification had an effect on other countries importing fortified products. Not aware of any adverse effect that mandatory folic acid fortification had on standardised foods that were being imported prior to the addition of folic acid such that they did not remain on the market because of the requirement.</p>	<p>FDA does not track or monitor the type of data necessary to answer this. There has been a move towards consumption of more "whole grain" products which are not fortified. However, the change in consumption habits can't be attributed to fortification. It is more likely that the change is due to government dietary recommendations to consume more whole grain foods. The foods that are required to be enriched with folic acid are not whole grain foods but rather cereal grain products that have been through a refining process and fortified to contain all of the enrichment nutrients, not just folic acid.</p>
CANADA**			
<p><u>Cereal flours (per 100g)</u></p> <ul style="list-style-type: none"> <li>Flour, white flour, enriched flour or enriched white flour: 150 µg</li> </ul> <p><u>Bakery products (per 100g)</u></p> <ul style="list-style-type: none"> <li>Enriched bread, enriched white bread: 100µg</li> </ul> <p><u>Alimentary pastes (per 100g)</u></p> <ul style="list-style-type: none"> <li>Enriched alimentary paste (used to make macaroni, spaghetti, noodles): 200-270 µg /100g</li> </ul> <p>When flour fortified with folic acid is sold as food, whether in consumer package or for further manufacturing uses, it is required to declare the folic acid content. However when flour is an ingredient in another food, it is exempt from declaring its components in the list of ingredients in the final food<sup>1</sup>. The minimum compositional requirements for making nutrient content claims is that the food must contain a minimum 5% of the recommended daily intake for that nutrient in a serving of the food.</p>	<p><u>Enforcement</u></p> <p>The legal requirement to ensure that a food is being sold meets requirements applies to all levels of trade. However, from a practical point of view, it is the manufacturer and importer who are responsible for ensuring that the foods they sell are fortified in accordance with the regulations.</p>	<p>Information not available. However since the US has similar requirements for the addition of folic acid to flour, and since the US is a major trading partner, the fortification of flour would not be expected to have an effect on trade in flour across Canada's borders. Foods that are manufactured for export are not required to meet Canadian fortification requirements, but may comply with the requirements of the exporting country.</p>	<p>Information not available.</p>

\* Information provided by the Food & Drugs Administration (FDA), USA

\*\* Information provided by the Canadian Food Inspection Agency and Health Canada

<sup>1</sup> When vitamins & minerals are declared as components of ingredients in the ingredients list, those nutrients must be declared in the Nutrition facts table. While flour is currently exempted from this requirement, an amendment is underway to remove this exemption.

## **SCIENTIFIC ADVISORY COMMITTEE ON NUTRITION: FOLATE AND DISEASE PREVENTION**

### **Background**

1. In 2004, the Scientific Advisory Committee on Nutrition (SACN) was asked by UK Health Ministers to consider the wider impact of folic acid fortification, particularly in relation to the elderly.
2. The main issues considered were: UK dietary intakes of folate and other B vitamins; trends in rates of NTD-affected pregnancies in the UK and in countries with fortification policies; possible effects of fortification on people aged 65 years and over with vitamin B<sub>12</sub> deficiency; the relationship between folate and cardiovascular disease, cancer, cognitive function, depression, and bone health. The report also explored the potential impact of mandatory fortification of flour with folic.

### **Recommended upper intake level for Folic Acid in the USA, Europe and UK**

3. In the USA and Europe, the tolerable upper intake level (UL<sup>1</sup>) of 1 milligram / day for adults has been set for folic acid. In the UK, the evidence for adverse effects of folic acid was considered insufficient to confidently establish a safe upper level<sup>2</sup> (SUL). Instead, a Guidance Level (GL) of 1 milligram / day was recommended for adults. The GL is less robust than an SUL as it is based on limited data and represents an approximate indication of intakes that would not be expected to cause adverse effects. The UL/GL for folic acid was based on concerns relating to vitamin B12 deficiency.
4. There are no data to suggest that high intakes of folic acid have any adverse effects on children. The critical endpoints relating to vitamin B12 deficiency which were used to set the UL/GL for adults, have not been reported for children. ULs set for children in the USA and Europe were therefore extrapolated from the UL for adults on the basis of body weight. In the UK, GLs were not recommended for children.

### **Dietary intakes and status of Folate, Vitamins B<sub>2</sub>, B<sub>6</sub>, and B<sub>12</sub> in the UK**

5. Data from the National Diet and Nutrition Survey (NDNS) series was used to assess the intakes and status of the UK population. Although average daily folate

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<sup>1</sup> The UL represents the highest level of a daily nutrient that is likely to pose no risk of adverse health effects

<sup>2</sup> The SUL represents the amount of nutrient that can be consumed daily over a lifetime without significant risk to health.

intakes were above the recommended nutrient intake (RNI<sup>3</sup>) in all age groups, there was some evidence of marginal folate status in young women and people aged 65 years and over. Lower intakes of vitamin B<sub>2</sub> and marginal vitamin B<sub>2</sub> status were widespread in all age groups, particularly in women, girls, and boys. Most age and sex groups had adequate vitamin B<sub>6</sub> intakes but a relatively high proportion of females aged 15-24 years, and over 65 years, had intakes below the lower reference nutrient intake (LRNI<sup>4</sup>). Marginal vitamin B<sub>6</sub> status was found in 10% of the UK population. Although there was no evidence of inadequate vitamin B<sub>12</sub> intakes, serum concentrations indicated poor vitamin B<sub>12</sub> status in older adults.

## **Folate and NTD**

6. Although supplementation with folic acid is advised prior to conception until the 12<sup>th</sup> week of pregnancy approximately half of all pregnancies are unplanned, which limits the value of recommendations. European Union countries with policies recommending women to consume folic acid supplements to reduce NTDs have observed no effect on NTD reduction.
7. Available data on the number of NTD-affected pregnancies are insecure due to under-reporting. Taking account of under-reporting in England and Wales, but not in Scotland and Northern Ireland, there were approximately 700-900 NTD-affected pregnancies in the UK in 2003.

## **Folic Acid Fortification Strategies and incidence of NTD in other Countries**

8. Countries that have introduced mandatory fortification (USA, Canada, Chile) have reported significant reductions in NTD-affected pregnancies of 27% to over 50%. As a result of *overage*, the impact of fortification on folate status has been greater than predicted.

## **Possible adverse effects of Mandatory Fortification of Flour with Folic Acid**

### *Risks to Older People with Vitamin B<sub>12</sub> Deficiency*

9. There are concerns that mandatory fortification of flour with folic acid might have adverse effects on neurological function in people aged 65 years and over with vitamin B<sub>12</sub> deficiency. Clinical signs of vitamin B<sub>12</sub> deficiency are anaemia and/or neurological impairment. Folic acid can alleviate the anaemia and therefore delay diagnosis of vitamin B<sub>12</sub> deficiency, which can lead to the irreversible and serious condition of sub acute combined degeneration of the spinal cord.

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<sup>3</sup> The RNI represents the amount of a nutrient that is considered sufficient to meet the requirements of 97.5% of the population.

<sup>4</sup> The LRNI is the amount of a nutrient that is considered sufficient to meet the requirements on 2.5% of the population.

10. The assessment of vitamin B<sub>12</sub> deficiency is complicated by the limitations of current diagnostic techniques. Low serum concentrations of vitamin B<sub>12</sub> are not always predictive of a clinical response to vitamin B<sub>12</sub> therapy. The prevalence of low vitamin B<sub>12</sub> status in the UK has been estimated to be 5% in people aged 65-74 years and 10% in people aged 75 years and over.
11. Evidence suggests that masking of vitamin B<sub>12</sub> deficiency is not associated with doses of folic acid up to 1 milligram / day. There are no reports from countries that have introduced mandatory fortification indicating deleterious effects on older people with low vitamin B<sub>12</sub> status.

### *Epilepsy*

12. It has been suggested that folic acid modifies the pharmacokinetics of phenytoin, an anti-epileptic drug, and may lower serum phenytoin concentrations leading to poorer seizure control. Evidence from Canada has shown that mandatory fortification, estimated to provide an average of 200 micrograms / day did not lower serum phenytoin concentrations in epileptic patients.

### *Multiple Births*

13. There is no substantive evidence to suggest that folic acid fortification is associated with multiple births resulting from natural conception. However, high intakes of folic acid may increase the likelihood of twin births in women undergoing multiple embryo transplant fertility treatment.

### *Embryo Selection*

14. It has been proposed that the use of folic acid in pregnancy could increase survival of embryos with genotypes associated with deleterious effects. There is no substantive evidence from countries where supplementation is advised or mandatory fortification has been introduced to support this.

### *Anti-folate Chemotherapy*

15. There are concerns that folic acid may reduce the efficacy of anti-folate drugs used in chemotherapy regimens and treatment of autoimmune diseases. There are insufficient human data on the effect of folic acid on antifolate medication or the doses at which folic acid might affect their action to conclude that mandatory folic acid fortification would modify their efficacy.

### *Unmetabolised Folic Acid in the Systemic Circulation*

16. The appearance of unmetabolised folic acid in the systemic circulation has raised concerns regarding the long-term effects of high intakes of folic acid. Overall,

there are insufficient data in humans to assess the long-term effects of exposure to unmetabolised folic acid in the systemic circulation.

## **Folate, B vitamins, and Chronic Disease**

### *Folate and Cardiovascular Disease*

17. Observational studies have suggested a protective effect of increasing folate intake, but not circulating folate concentrations, on CVD risk. No randomised controlled trials (RCTs) have demonstrated a beneficial or harmful effect of folic acid supplements on CVD risk. One RCT found an increased CVD risk with supplementation of folic acid in combination with vitamins B<sub>12</sub> and B<sub>6</sub>.

### *Folate and Cancer*

18. Some animal studies suggest that folic acid may inhibit tumour development in normal tissues but promote the progression of established neoplasms. The doses of folic acid used in these studies were considerably higher than the amounts that would be consumed by humans as a result of fortification.

19. Although evidence from prospective studies in humans suggests a trend towards a protective effect of folate intake on colon cancer risk, some studies did not adjust for all confounding factors. No RCTs designed to investigate the relationship between folic acid and cancer incidence have yet reported.

20. Time trends for colorectal cancer (CRC) incidence in the USA and Canada show that mandatory fortification of foods with folic acid occurred at around the same time as non-significant increases in CRC incidence. If this was caused by folic acid fortification, the effect of folic acid on cancer progression would have to have been immediate, which may not be plausible. The increase in rates occurred at different times for men and women and in different age groups. The timing of changes in average blood folate concentrations of the USA population was also not clearly consistent with changes in CRC incidence.

21. The evidence for an association between folic acid and increased or reduced cancer risk in humans is equivocal.

### *Folate and Cognitive Function*

22. Overall, the evidence for either beneficial or deleterious effects of folic acid or vitamin B<sub>12</sub> therapy on cognitive function in older people is presently inconclusive.

## *Folate and Bone Health*

23. There is insufficient evidence to suggest beneficial effects of folic acid on bone health and no evidence to suggest any deleterious effects.

### **The Potential Impact of Mandatory Fortification of Flour with Folic Acid**

24. The potential effect of fortifying flour with different doses of folic acid (100-450 micrograms / 100 grams) on total folate intake (including current levels in fortified foods, supplement use, processing losses, overage) of different population age groups was investigated by modelling intake data from the NDNS series. The aim of the modelling exercise was to explore the effect of mandatory fortification on: risk of NTD-affected pregnancies; the number of people with folic acid intakes above the UL/day<sup>5</sup>; and the number of people aged 65 years and over with low vitamin B12 status, exceeding folic acid intakes of 1 milligram / day.
25. Results from the modelling exercise (Annex 6, Table 1) showed that at current levels of folic acid intake (including intake from voluntarily fortified foods and supplements) mandatory fortification of flour with folic acid would progressively reduce NTD risk. However it would increase the proportion of people with folic acid intakes above the UL/day and the number of people aged 65 years and over with low vitamin B12 status consuming more than 1 milligram / day of folic acid.
26. If no foods were voluntarily fortified, the option that would provide the optimum balance between benefits and possible risks is mandatory fortification at a level of 300 micrograms of folic acid / 100 grams flour (excluding wholemeal flour). At this level it is estimated that, compared to current levels: 77-162 NTD-affected pregnancies per year could be prevented (11-18% risk reduction); the proportion of the population with intakes below the RNI would be reduced from 23% to 5%; the number of people with folic acid intakes above the UL / day would be reduced by 12,000; there would be no change in the number of adults aged 65 years and over, with low vitamin B<sub>12</sub> status, exceeding intakes of 1 milligram / day.
27. Without folic acid intake from voluntary sources, mandatory fortification would confer a more even distribution of folic acid intakes across the population compared to current voluntary fortification and supplement use. This means that women at greatest risk of NTD-affected pregnancies, i.e. those with the lowest folate intakes, would be reached through mandatory fortification.

## **Conclusions**

28. The current recommendation is that women planning a pregnancy should supplement their diet with 400 micrograms / day of folic acid (5 milligrams / day for women with a previous pregnancy affected by NTD) prior to conception until

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<sup>5</sup> As GLs were not set for children in the UK (see paragraph 4) ULs were used for the purpose of the modelling exercise.

the twelfth week of pregnancy. About half of all pregnancies are unplanned which limits the value of recommendations. Policies in the EU, recommending folic acid supplementation to reduce NTD-affected pregnancies have been ineffective.

29. Introduction of mandatory fortification of flour with folic acid at current levels of folic acid intake (including intake from voluntary fortification and supplements) would reduce the risk of NTD-affected pregnancies in the UK. However, it would also increase the proportion of people in the population at risk of exceeding folic acid intakes above the UL / day and the number of people aged 65 years and over with low vitamin B12 status at risk of consuming more than 1 milligram / day of folic acid.
30. There are approximately 127,000 people in the UK who are currently consuming intakes of folic acid above the UL / day from voluntarily fortified foods and supplements. As there are presently no controls on the levels of folic acid which can be added to foods, the number of people with intakes above the UL / day could be higher if levels in these foods are increased in the future.
31. Without the contribution of folic acid from voluntarily fortified foods, mandatory fortification would reduce risks of intakes exceeding the UL / day for folic acid relative to the current practice of voluntary fortification. This is because voluntary fortification of foods with folic acid and inappropriate supplement use are harder to quantify and control and, unlike flour, their consumption is very variable.
32. Replacement of voluntary folic acid fortification of certain foods with mandatory fortification of flour would result in a redistribution of folic acid intakes within the population and would be the most effective way to reach those sections of the population with the lowest folate intakes, i.e., younger women from the most socio-economically deprived areas.
33. Without the contribution of folic acid intakes from voluntarily fortified foods, the optimal level for mandatory fortification of flour with folic acid would be 300 micrograms / 100 grams flour. This level would be effective in reducing NTD risk without increasing the number of people with intakes of folic acid above the UL per day or the number of adults aged 65 years and over, with low vitamin B<sub>12</sub> status and folic acid intakes above 1 milligram / day. Exempting wholemeal flour from fortification would have little effect on NTD risk but would further reduce numbers with intakes of folic acid above the UL / day.
34. There is currently insufficient evidence from RCTs examining chronic disease risk (cardiovascular disease, certain cancers, bone disease and age-related cognitive decline) to either support or advise against mandatory fortification of flour with folic acid on these grounds.

35. There is currently insufficient evidence for an adequate risk assessment of folic acid and cancer risk or the intake levels which might be associated with risk. A substantial increase in current average population intakes of folic acid and the numbers consuming more than the GL/UL per day for folic acid should therefore be avoided.

## **Recommendations**

36. As previously recommended by COMA (DH, 2000), all women who could become pregnant should take 400 micrograms / day folic acid as a medicinal or food supplement prior to conception and until the twelfth week of pregnancy. Women with a history of a previous NTD-affected pregnancy are advised to take 5 milligrams / day of folic acid prior to conception and until the twelfth week of pregnancy. This recommendation is applicable even if mandatory fortification of flour with folic acid is introduced.

37. Individual long-term intakes of folic acid from fortified foods and supplements above the GL/UL per day for folic acid should be avoided. The risk currently posed by voluntary fortification of food with folic acid and supplement use in contributing to intakes above the GL/UL per day for folic acid needs to be addressed.

38. Mandatory fortification of flour with folic acid would improve the folate status of women most at risk of NTD-affected pregnancies. However, if mandatory fortification is combined with the current practice of voluntary fortification of foods with folic acid and inappropriate supplement use, the numbers of people consuming levels of folic acid above the GL/UL per day would be substantially increased.

39. Mandatory fortification should only be introduced in the UK if it is accompanied by:

- Action to reduce folic acid intakes from voluntarily fortified foods to ensure that the numbers of people with intakes above the GL/UL per day do not exceed current levels and there is no substantial increase in mean intakes or in the folate status of the UK population;
- Measures for careful monitoring of emerging evidence on the effects of long-term exposure to folic acid intakes above the GL/UL per day and postulated adverse effects, including neurological damage, CVD, and cancer.

40. The establishment of a new baseline for folic acid intakes and blood folate concentrations will be required prior to fortification to ensure that mandatory fortification does not lead to substantial increases in folic acid intake/status and so trends can be monitored in future surveillance programmes. The adoption of a common standard analytical method to measure folate status at baseline and all

future surveillance studies will also be required as well as the establishment of suitable reference ranges to predict folate adequacy and deficiency.

41. If mandatory fortification is introduced, careful consideration should be given to the issue of overage and the evidence on benefits and postulated adverse effects should be reviewed after a period of five years.
42. Clear guidance is needed on the use of folic acid containing supplements by the general population.
43. More reliable diagnostic indices to identify vitamin B<sub>12</sub> deficiency should be developed. The development of a clinical strategy to manage issues related to vitamin B<sub>12</sub> is necessary irrespective of a decision on future mandatory fortification of flour with folic acid.
44. The prevalence of poor vitamin B<sub>2</sub> status in the UK needs to be addressed.

## THE POTENTIAL IMPACT OF MANDATORY FORTIFICATION OF FLOUR WITH FOLIC ACID

### Modelling exercise

1. The effect of fortifying flour with different doses of folic acid on the total folate intake (taking account of current levels in fortified foods, supplement use, processing losses, overage) of different population age groups was investigated by modelling intake data from the National Diet and Nutrition Survey series.
2. Flour was considered the most appropriate vehicle for fortification because of its near universal and narrow variability of consumption in the population.
3. The purpose of the modelling exercise was to explore the effect of mandatory folic acid fortification of flour on the:
  - average intakes of folic acid;
  - proportion of the population with folate intakes below the recommended nutrient intake (RNI<sup>1</sup>);
  - risk of NTD-affected pregnancies;
  - total numbers in the population who might be exposed to doses of folic acid above the tolerable upper level (UL) per day set for folic acid<sup>2</sup>;
  - number of people aged 65 years and over, with low vitamin B<sub>12</sub> status, who might be exposed to doses of folic acid above 1 milligram / day.
4. In the UK, a Guidance Level<sup>3</sup> (GL) of 1 milligram / day for folic acid was set for adults, however no GLs were set for children. ULs were set for children in Europe and the USA, which were extrapolated from the UL for adults on the basis of body weight. The ULs were therefore used for the purpose of the modelling exercise in order to estimate the total proportion of the UK population (including children) who might be exposed to high intakes of folic acid.

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<sup>1</sup> The RNI is the amount of a nutrient that is considered sufficient to meet the requirements of 97.5% of the population. The RNI for adults & children: 100µg/d for 4-6y; 150µg/d for 7-10y; 200µg/d for 11y and above.

<sup>2</sup> The UL represents the highest level of daily nutrient that is likely to pose no risk to health. UL for adults (≥18y) : 1mg/d; UL for children (Europe): 300µg/d for 4-6y; 400µg/d for 7-10y; 600µg/d for 11-14y; 800µg/d for 15-17y.

<sup>3</sup> The Guidance Level is an approximate indication of intakes that would not be expected to cause adverse effects.

5. The potential effects of mandatory fortification of flour with folic acid were assessed at four different levels / 100 grams of flour: 100, 200, 300 and 450 micrograms. After processing losses this would result in actual levels of 75, 150, 225 and 338 micrograms / 100 grams food respectively.
6. The modelling exercise also considered the effect of mandatory fortification of flour with folic acid *excluding* the contribution of folic acid intakes from:
  - fortified breakfast cereals and fortified fat spreads but *including* the contribution from supplements;
  - fortified breakfast cereals, fortified fat spreads, and supplements.

## Results of Modelling exercise

**Table 1: Effects of mandatory fortification of flour with folic acid (excluding fortification of wholemeal flour)**

Level of folic acid micrograms / 100g flour (level in food after processing)	Average increase in folic acid intake (micrograms / day) <sup>4</sup>	Estimated mean total folate intakes (micrograms / day)	Estimated % of people with intakes below RNI <sup>5</sup>	Estimated number of people exceeding the UL of folic acid / day <sup>6</sup>	Estimated number aged 65y+ with low vitamin B <sub>12</sub> status exceeding 1 milligram / day folic acid	Estimated NTD pregnancies prevented / year (% risk reduction)
<b>Includes folate and folic acid from all sources (including estimates of overage)<sup>7</sup></b>						
0	0	302	23	127,000	900	0
100 (75)	51	353	11	225,000	1,700	42-93 (6-10%)
200 (150)	102	403	6	404,000	2,000	82-180 (12-20%)
300 (225)	152	454	3	773,000	2,500	114-261 (16-29%)
450 (338)	228	530	2	2,200,000	6,300	163-369 (23-41%)
<b>Excluding folic acid from fortified breakfast cereals and fat spreads</b>						
0	-74	232	36	18,000	800	-70 (-10%)
100 (75)	-24	283	17	38,000	800	-14 (-2%)
200 (150)	27	334	9	52,000	900	35-63 (5-7%)
300 (225)	78	385	5	115,000	900	77-162 (11-18%)
450 (338)	154	461	3	559,000	900	126-279 (18-31%)
<b>Excluding folic acid from fortified breakfast cereals, fat spreads and supplements</b>						
0	-85	217	38	0	0	-91 (-13%)
100 (75)	-34	267	18	0	0	-35 (-5%)
200 (150)	17	318	9	0	0	21-36 (3-4%)
300 (225)	68	369	6	55,000	0	63-126 (9-14%)
450 (338)	144	445	3	470,000	0	112-252 (16-28%)

*To note: the figures in brackets in the first column represent the actual levels in food after processing losses.*

<sup>4</sup> Across all population groups.

<sup>5</sup> For each age group (DH, 1991)

<sup>6</sup> For each age group (European Scientific Committee on Foods, 2001).

<sup>7</sup> Mean of values for overage applied and not applied.

*Effects of mandatory fortification including current levels of Folic Acid intake from voluntary fortification and supplements*

7. See first section of table, headed: *Includes folate and folic acid from all sources.*
8. It can be seen from Table 1 (line 1: fortification level, 0) that at current levels of folic acid intake in the UK (from voluntary fortification and supplements):
  - The average folate intake of the population is approximately 302 micrograms / day;
  - Approximately 23% of the population (13,261,000 people) have intakes below the RNI for folate;
  - Approximately 127,000 people are exceeding the UL / day set for folic acid (the largest proportion are children aged 4-10 years [57% or 72,000 children] as the ULs / day are much lower for these age groups [300-400 micrograms / day] than for adults [1 milligram / day]);
  - Approximately 900 adults aged 65 years and over with low vitamin B<sub>12</sub> status are exceeding folic acid intakes of 1 milligram / day.
9. It can be seen that mandatory fortification at increasing levels of folic acid would progressively reduce NTD risk and the percentage of the population with intakes below the RNI for folate. However it would also progressively increase the proportion of the population with intakes above the UL / day for folic acid and the number of adults aged 65 years and older with low vitamin B<sub>12</sub> status exceeding folic acid intakes of 1 milligram / day.

*Effect of mandatory fortification excluding folic acid intakes from fortified breakfast cereals/fortified spreads and including folic acid intake from supplements*

10. See second section of Table 1, headed: *Excluding folic acid from fortified breakfast cereals and fat spreads.*
11. It can be seen that, in the absence of mandatory fortification, removing the contribution of folic acid intakes from fortified breakfast cereals and fortified fat spreads (but including intakes from supplements) would increase the NTD risk and the percentage of the population with intakes below the RNI for folate but would reduce the percentage of the population with intakes above the UL / day for folic acid and the number of adults aged 65 years and over with low vitamin B<sub>12</sub> status and folic acid intakes above 1 milligram / day:
  - The average folate intake of the population would decrease by 74 micrograms / day.

- Approximately 70 more pregnancies would be affected by NTDs (10% increase in risk).
- The percentage of the population with intakes below the RNI for folate would increase from 23% to 36%.
- Approximately 18,000 people would exceed the UL / day for folic acid intake (decrease of 86%).
- Approximately 800 adults aged 65 years and over, with low vitamin B<sub>12</sub> status, would exceed folic acid intakes of 1 milligram / day (decrease of 11%).

12. The lowest level of mandatory fortification with folic acid required to overcome the increased NTD risk caused by removal of folic acid from fortified breakfast cereals and fortified fat spreads would be 200 micrograms / 100 grams flour. Mandatory fortification at 300 micrograms / 100 grams flour would further reduce the risk of NTD-affected pregnancies (by 11-18%) without increasing the number of people with intakes above the UL (115,000 compared to the current level of 127,000) or the number of adults aged 65 years and over with low vitamin B<sub>12</sub> status, exceeding intakes of 1 milligram / day. The proportion of people with intakes below the RNI would be reduced from the current level of 23% to 5%. Mandatory fortification with folic acid above this level would further reduce the risk of NTD-affected pregnancies and the proportion of the population with intakes below the RNI, however the numbers with intakes above the UL / day would be substantially increased.

*Effect of mandatory fortification of flour with folic acid excluding the contribution of folic acid intakes from fortified breakfast cereals, fortified spreads, and supplements*

13. See third section of Table 1, headed: *Excluding folic acid from fortified breakfast cereals, fat spreads and supplements.*

14. Without folic acid intakes from fortified breakfast cereals, fortified fat spreads, and supplements:

- The average folate intake of the population would decrease by approximately 85 micrograms / day.
- Approximately 91 more pregnancies would be affected by NTDs (13% increase in risk).
- The percentage of the population with intakes below the RNI for folate would increase from 23% to 38%.
- Unlikely that anyone would exceed folic acid intakes above the UL / day.

- Unlikely that any adults aged 65 years and over, with low vitamin B<sub>12</sub> status, would exceed folic acid intakes of 1 milligram / day.

15. Mandatory fortification with folic acid at a minimum level of 200 micrograms / 100 grams flour would be required to overcome the increased risk of NTD-affected pregnancies caused by removing the contribution of folic acid intakes from fortified breakfast cereals/fortified spreads and supplements.

*Comparison of the effects of excluding Folic Acid intakes from fortified breakfast cereals and fat spreads only with excluding Folic Acid intakes from fortified breakfast cereals, fat spreads, and supplements*

16. Including or excluding folic acid intakes from supplements would result in little difference in the number of people with intakes below the RNI for folate: 36% including supplements and 38% excluding supplements. This suggests that compared to fortified foods, supplements do not make an important contribution to helping people achieve the RNI for folate intake.

17. The increased risk of NTD-affected pregnancies is lower if folic acid intakes from supplements are included (10% increased risk) than if they are excluded (13% increased risk), indicating that supplements make an additional contribution to reducing NTD risk.

18. Approximately 127,000 people in the UK are currently exceeding the UL / day for folic acid. Out of this total, 14% can be attributed to supplement consumption (18,000 people) and 86% (109,000 people) to consumption of fortified foods. This suggests that folic acid intakes above the UL / day for folic acid are largely due to consumption of foods fortified with folic acid.

### *Summary*

19. Current intakes of folic acid above the UL / day for folic acid intake are largely due to consumption of foods voluntarily fortified with folic acid. Present consumption patterns of supplements and foods voluntarily fortified with folic acid contribute to the highly variable intakes of folic acid, resulting in large sections of the population with intakes below the RNI for folate and considerable numbers of people with intakes of folic acid above the UL / day.

20. Results from the modelling exercise suggest that, without the contribution of folic acid from voluntary sources, mandatory fortification of flour with folic acid would confer a more even distribution of folic acid intakes across the population compared to current voluntary fortification and supplement use. The redistribution of folic acid intakes would mean that women at greatest risk of NTD-affected pregnancies, i.e. those with the lowest folate intakes, would be reached through mandatory fortification.

21. If no foods were voluntarily fortified, the option that appears to provide the optimum balance between benefits and possible risks is mandatory fortification at a level of 300 micrograms of folic acid / 100 grams flour (excluding wholemeal flour); the actual level in food after processing losses would be 225 micrograms / 100 grams food. At this level it is estimated that: average folic acid intake would increase by 78 micrograms / day; the estimated mean total folate intake would be 385 micrograms / day (compared to the current average intake of 302 micrograms / day). 77-162 NTD-affected pregnancies per year could be prevented (11-18% risk reduction) without increasing the number of people with folic acid intakes above the UL / day or the number of adults aged 65 years and over, with low vitamin B<sub>12</sub> status, exceeding intakes of 1 milligram / day; and the proportion of the population with intakes below the RNI would be reduced from 23% to 5%.

### **Comparison of results from the SACN Modelling exercise with the experience in the USA and Canada, following Mandatory Fortification of Flour with Folic Acid**

22. There are a number of difficulties in making comparisons with countries that have mandatory folic acid fortification policies. This is because:

- different countries have fortified different groups of food products with varying levels of folic acid (see Table 2);
- there are differences in the available data for the estimated effects of folic acid on NTD incidence;
- the effect of folic acid on reducing NTD risk is dependent on background blood folate concentrations so at a particular dose of folic acid the proportional reduction in NTD risk will be higher in populations with lower initial blood folate concentrations.

23. There are also difficulties in comparing the fortification levels modelled by SACN which would be equivalent to the increase in folic acid intake observed in other countries with mandatory fortification because SACN considered a number of scenarios (i.e. mandatory fortification: including current intakes of folic acid from voluntary fortification and supplements, excluding voluntary fortification but including supplements; excluding voluntary fortification and supplements) with and without wholemeal flour. The comparisons below are therefore of the estimates from the SACN modelling which include the effects of mandatory fortification of all flour and include folic acid intakes from voluntary fortification and supplements as this most closely resembles the situation in other countries.

24. SACN's recommendation for mandatory fortification of 300 micrograms / 100 grams flour excludes fortification of wholemeal flour and folic acid from voluntary sources, so the estimated increase in folic acid / day and the corresponding NTD

risk reduction is lower than observed in the USA and Canada and predicted for the Republic of Ireland.

## USA

25. Mandatory fortification with folic acid at an average level of 140 micrograms / 100 grams cereal product was intended to increase average intakes of folic acid by approximately 100 micrograms / day. It has been estimated that mandatory fortification has actually increased folic acid intakes by approximately 215-240 micrograms / day. This is mainly because controls apply at final food level and to ensure minima are met there has been over addition at ingredients level. The additional increase in folic acid of 215-240 micrograms / day, has resulted in a 27% decline in NTD-affected pregnancies. Data from the SACN modelling exercise suggest that to achieve an increase in folic acid intake equivalent to that observed in the USA, would require fortification of all flour (including wholemeal flour) at a level somewhere between 300 and 450 micrograms / 100 grams (because fortification at 300 micrograms would be too low and 450 micrograms would be too high). This would result in an additional folic acid intakes of somewhere between 172 micrograms / day and 258 micrograms / day and reductions in NTD-affected pregnancies somewhere between 18 and 42%.

## CANADA

26. Mandatory fortification with folic acid at an average level of 150 micrograms / 100 grams flour was intended to increase average intakes of folic acid by approximately 100 micrograms / day. There are no nationally representative data for the estimated daily increases in folic acid intakes in Canada, however it has been estimated that folic acid intakes increased by approximately 70 micrograms / day for women (aged 19-44 years) in Newfoundland which resulted in a 78% decline in NTD rates. This decline in NTD rates is higher than observed for other provinces in Canada (Ontario, 51%; Nova Scotia, 54%; Quebec, 32%). Data from the SACN modelling exercise suggest that the increase in folic acid intake observed in Newfoundland is roughly equivalent to fortification at a level somewhere between 100 and 200 micrograms / 100 grams flour (including wholemeal flour) which would result in an additional intake of folic acid somewhere between 50 and 100 micrograms / day for women of childbearing age (not shown in Table 1, which is for the whole UK population) and reductions in NTD-affected pregnancies somewhere between 7 and 22%.

27. In Ontario, it has been estimated that mandatory fortification increased average folic acid intake by 150 micrograms / day (for the whole population), which resulted in a 51% decline in NTD rates. (However measurement of blood folate levels were from clinical samples and may differ from folate blood levels in the general population). Data from the SACN modelling exercise suggest that the increase in folic acid intake observed in Ontario is roughly equivalent to fortification at a level somewhere between 200 and 300 micrograms / 100 grams

flour (including wholemeal flour) which would result in an additional intake of folic acid somewhere between 115 and 172 micrograms / day and reductions in NTD-affected pregnancies somewhere between 13 and 32%.

### **Comparison of results from the SACN Modelling exercise with proposed Fortification Level in Republic of Ireland**

28. The National Committee on Folic Acid Food Fortification (NCFAFF) in Ireland estimated that fortification at 120 micrograms / 100 grams bread would provide women of child bearing age with an average additional daily intake of 110 micrograms folic acid and reduce NTD risk by 24%. Results from the SACN modelling suggest that this is equivalent to a fortification level somewhere between 200 and 300 micrograms / 100 grams flour (including wholemeal flour). This which would result in an additional folic acid intake of somewhere between 100 and 150 micrograms / day for women aged 14-49 years (not shown in Table 1, which is for the whole UK population) and reductions in NTD risk somewhere between 13 and 32%.
29. The most likely explanation for the differences in NTD risk reduction predicted by SACN & NCFAFF is that SACN used a more developed model which accounted for losses in the food chain and used 2 different approaches to model NTD risk because of uncertainties in the available data. The two methods provided an estimated range of NTD-affected pregnancies which could be prevented at the different fortification levels. SACN compared the NTD risk reduction estimated from the modelling exercise with the reduction in NTD risk observed in the USA following mandatory fortification and found that the change in NTD rates in the USA falls within the range of values for NTD risk reduction estimated by the modelling. The predicted NTD risk reduction in Ireland of 24%, in response to an increase in folic acid intakes of 110 micrograms / day following mandatory fortification, is similar to the actual reduction in NTD risk observed in the USA (27%) after an increase in folic acid intakes of approximately 215-240 micrograms / day.

**Table 2: Comparison of results from SACN modelling exercise with proposed fortification in Republic of Ireland and with experience in USA & Canada following mandatory fortification**

Country	UK (SACN predicted estimate)	Republic of Ireland (NCFAFF predicted estimate)	United States (measured estimate)	Canada (measured estimate)
Fortification level	<ul style="list-style-type: none"> <li>300µg/100g cereal flour (equivalent to 225µg/100g of food)</li> </ul> <p><i>(excluding wholemeal flour and excluding folic acid from voluntary sources)</i></p>	<ul style="list-style-type: none"> <li>120µg/100g bread</li> </ul> <p><i>(exclusion of some minor bread products)</i></p> <p><i>(voluntary fortification also permitted)</i></p>	<ul style="list-style-type: none"> <li>154µg/100g cereal flours</li> <li>95µg/100g enriched bread, rolls, buns</li> <li>154-308µg/100g enriched rice</li> <li>198-265µg/100g macaroni &amp; noodle products</li> </ul> <p><i>(voluntary fortification also permitted)</i></p>	<ul style="list-style-type: none"> <li>150µg/100g cereal flours</li> <li>100µg/100g enriched bread</li> <li>200-270µg/100g pasta</li> </ul> <p><i>(voluntary fortification also permitted)</i></p>
Estimated increase in folic acid intake (µg/day)	78 <sup>8</sup> <i>(whole population)</i>	110 <i>(women of childbearing age)</i>	215-240 <sup>9</sup> <i>(whole population)</i>	National data unavailable
Reduction in NTD risk <sup>10</sup>	11-18%	24%	27%	Ontario: 51% Nova Scotia: 54% Quebec: 32% Newfoundland: 78%

<sup>8</sup> The estimated daily increase in folic acid intake is lower than other countries because it excludes fortification of wholemeal flour and folic acid from voluntary sources.

<sup>9</sup> It was anticipated that mandatory fortification would increase folic acid intakes by about 100 µg/day.

<sup>10</sup> Comparison of NTD risk is complicated because of differences in ascertainment of NTD data and completeness of data can be affected by methods of collation. The effect of folic acid on reducing NTD risk is also dependent on background blood folate concentrations so at a particular dose of folic acid the proportional reduction in NTD risk will be higher in populations with lower initial blood folate concentrations.

## TECHNICAL AND PRACTICAL ISSUES TO TAKE INTO ACCOUNT: FOLIC ACID FORTIFICATION

### General Points

1. The synthetic form of folate used as a food fortificant and in supplements is folic acid. It is more heat stable than other forms of folate but is degraded by acids (such as in fruit drinks) and to some extent on heating. The amount lost in processing depends on a number of factors including the cooking time, surface area and volume of the product (greater losses occur in products such as biscuits than family loaves of bread); for example, 12 and 20% of folic acid is lost from large and small bread rolls respectively during baking<sup>1</sup>. SACN took processing losses into account in their modelling exercise (Annex 6).
2. Foods that are suitable as vehicles for fortification and increasing the folic acid intakes in women most at risk of NTD-affected pregnancies must be consumed by women of reproductive age regularly, universally and in relatively uniform amounts. They must also not be consumed by others (particularly children) in large volumes as this would increase the risk of exceeding safe guidance levels.
3. Analysis of NDNS data shows no foods are only consumed by women of reproductive age.

### Flour and Bread Fortification

4. Bread is consumed by almost all women (98%) in relatively uniform amounts. Folic acid is also relatively stable in bread (except for soda bread).
5. There are two main potential methods for fortification of bread:
  - Fortification of flour at the milling stage (either all flours or all flour except wholemeal).
  - Fortification of flour at the bread making stage (either some or all breads).
6. The bread and milling industry indicates that the fortification of all flour except for wholemeal at the milling stage is the preferred option. This would build upon the existing requirements for the fortification of all flour except wholemeal in the UK with iron, calcium, thiamine and niacin<sup>2</sup> and so would capitalise on existing

<sup>1</sup> Johansson M, Witthöft C, Bruce Å, Jägerstad M, Study of wheat breakfast rolls fortified with folic acid. *European Journal of Nutrition* 2002; 41: 279-286.

<sup>2</sup> The Bread and Flour Regulations require that flour should contain not less than 0.24 micrograms thiamine (vitamin B1), 1.60 micrograms nicotinic acid and 1.65 micrograms of iron per 100g of flour. These amounts are found naturally in wholemeal flour. White and brown flours must be fortified to restore their nutritional value. In addition calcium carbonate at a level of not less than 235 micrograms

technology and regulation. Choice could be provided to consumers who want an unfortified product through wholemeal bread (which provides 40 micrograms / 100 grams folate compared with unfortified white bread, which provides 25 micrograms / 100 grams). Ethnic breads made by using white and brown flour would be included (white, brown and wholemeal chapatti flours are milled in the UK).

7. Fortification at the bread making stage would be preferred from a consumer choice perspective however the baking industry have raised concerns about achieving accurate dosing within bread. The results of product testing within the Republic of Ireland suggest large variation in folic acid levels of bread fortified in the bakery.
8. The milling industry advises that bread-making flour cannot be separated from other flours in mills easily; that millers are not always aware of the destination or final use of the flour being milled and that bread, pastry and biscuit makers may use the same flours. The Republic of Ireland is, however, currently exploring the separation of bread-making flour from other flours in the mills. They, however, have only two main flour mills and may be able to use one for the production of bread-making flour only, which will be fortified with folic acid. Also they are not adding any other nutrients to flour by mandate. The industry is significantly more complicated in the UK; there are about 60 mills.

## **Other Foods**

### *Breakfast cereals*

9. The consumption of breakfast cereals is relatively uniform but not universal. They are consumed by about 70% of women aged 19-64 years and 55% of 19-24 years women according to NDNS.

### *Soft drinks, fruit juice and milk*

10. Not all women consume these drinks (Table 1). The consumption of these drinks can vary greatly, for example for women aged 19 to 64 years, average milk consumption is about 200g/day but some consume more than 500g/day according to NDNS. Also these drinks can be consumed in large volumes by children, for example some 7 to 10 years olds consume more than a litre of soft drinks per day. Folic acid is also degraded in carbonated drinks and fruit drinks.

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and not more than 390 micrograms per 100g of flour is added to all flours except wholemeal (and certain self raising varieties).

**Table 1: Table to show percentage consumption of soft drinks in young women per week (data from NDNS)**

<b>Type of drink</b>	<b>% women per week (19-24 years)</b>
Fruit Juices	50%
Soft drinks (not low calorie)	78%
(low calorie)	53%
Milk (whole, semi-skimmed and skimmed)	87%

### *Chewing gum*

11. A low proportion of women report chewing gum. NDNS data give the percentage of girls in each age group who reported eating chewing gum during the survey week (Table 2).

**Table 2: Table to show percentage of women who consume chewing gum per week**

<b>Females</b>	<b>% (number) who ate chewing gum in the survey week</b>
11-14 years (238)	22 (46)
15-18 years (208)	14 (26)
19-24 years (77)	8 (6)
25-34 years (212)	3 (9)
35-49 years (378)	6 (22)

12. For those who ate chewing gum, the mean consumption was about 1-2 grams / day in each age group (a standard weight of 2g was used for a piece of gum). Consumption at the 97.5%ile was 8-9 grams / day.

13. Consumer groups would be expected to oppose fortification of gum on the grounds that adding vitamins to confectionery could encourage consumption - they have made this point in negotiations on EU legislation currently under negotiation. Indeed for this reason, the EU claims legislation would intend prohibiting, via nutrient profiles, any claims relating to addition of folic acid to a high sugar food, an approach we have supported.

## THE REGULATION OF VOLUNTARY FORTIFICATION

1. Currently the voluntary addition of vitamins and minerals to food is controlled by:
  - i) s.7 of the Food Safety Act (as amended), which makes it an offence to render a food injurious to health;
  - ii) Article 14 of Regulation (EC) 178/2002, which states that food shall not be placed on the market if it is unsafe; and
  - iii) Regulation 4 of the General Food Regulations which creates offences for breaches of certain Articles in Regulation (EC) 178/2002, including Article 14.
2. From 1st July 2007 European Regulation 1925/2006 on the addition of vitamins and minerals and of certain other substances to foods will apply. This Regulation puts in place a positive list of the vitamins and minerals that can be added to food, including folic acid, and the vitamin formulations and minerals substances that can be used.

### Maximum and Minimum Levels

3. The Regulation EC 1925/2006 makes provision for the setting of maximum and minimum levels for vitamins and minerals being added to food. The details of what these levels will be have not yet been developed. However minimum levels are already foreseen by alignment to the criteria for nutrition labelling, that is 15% / 100 grams of the Recommended Daily Amount (RDA) where one has been set. We would expect work to begin on setting minima where RDAs have not been set, as well as reviewing the relevance of RDAs to fortification. The Commission has started the process of considering how to set maximum levels for fortified foods and food supplements and we await further progress on this.

### Further Restriction

4. The Regulation also includes the possibility, when applying maximum levels, of restricting the fortification of foods where intake levels of vitamins or minerals are close to the upper safe intake level determined as a result of risk assessment.

### National Restrictions on Voluntary Fortification

5. National restrictions on voluntary fortification could limit the range of foods that could be fortified and / or set a maximum level for fortification. As a national measure, this would be notifiable in draft to the Commission and to the World Trade Organisation if appropriate. The justification for the measure would be the protection of public health in the UK. A consequence of notification is that Member States and the Commission would have the option to oppose the measure being brought in. There is a standstill period of six months and, if

objections are made, a decision at EU level, which could be a vote for non-implementation. Failure to comply would incur legal action in the European Courts. It is likely that both voluntary schemes and statutory controls on folic acid fortification would need to be notified.

### **Mandatory Fortification**

6. Regulation 1925/2006 requires Member States to notify the Commission of national provisions on the mandatory addition of vitamins and minerals (see paragraph 5 above).

### **Export Issues**

7. European Regulation 1925/2006 is a harmonising measure which aims to remove barriers to trade of fortified foods throughout the EU. Export of foods made from wheat flour fortified under mandatory measures of the type discussed in this paper would be compliant with this Regulation and should be able to circulate freely. The only permitted recourse to an import ban would be safeguard action on safety grounds. Such action would be subject to scrutiny and a decision at EU level.

### **Nutrition and Health Claims**

8. Claims are currently controlled by both the Trade Descriptions Act 1968 and the Food Safety Act 1990 which make it an offence to falsely describe a food or provide misleading information regarding its nature, substance or quality. The Food Labelling Regulations 1996 (as amended) make it compulsory to provide prescribed nutritional labelling on any product for which a nutrition claim is made and set criteria a product must meet to make certain nutrition claims. At present products must contain one sixth of the RDA to make the claim "contains folic acid". To make the claim "high in folic acid" the product must contain half the RDA.
9. From 1 July 2007, European Regulation (EC) No 1924/2006 on nutrition and health claims made on foods will apply. This will set a positive list of nutrition and health claims that can be made on foods and the criteria a product must meet to use them. The Annex of the Regulation contains the list of permitted nutrition claims and the criteria for using them. After 1 July, to claim that a product is a source of folic acid it must contain at least 15% of the RDA / 100 grams and to make a claim that a product is high in folic acid it must contain at least 30% of the RDA / 100 grams. Nutrition labelling will be compulsory where any claim is made.
10. The Regulation will also require health claims to be authorised to be used on food, including an assessment of the supporting science by the European Food Safety Authority (EFSA). Compilation of the list of permitted health claims is currently underway. EFSA has also begun work to establish nutrient profiles,

which foods must comply with in order to avoid further restriction to claims. If the food is out of profile, no health claims may be made; but if it is out of profile on one nutrient only, a nutrition claim may be made, provided it is accompanied by the statement “High in [failed nutrient]”. The mandate given to EFSA also asks for consideration of foods or food categories that might be exempted from the application of nutrient profiles.

## Labelling

11. If it were decided to fortify on a mandatory basis, it would be important to ensure that the regulatory framework was appropriate and that the new measure did not create unnecessary trade barriers. The new legislative requirement could be implemented by amending the UK Bread and Flour Regulations 1998 (BFR). As a national measure, this would be notifiable in draft to the Commission (see paragraph 5). The BFR do not apply to imported flours.
12. The BFR currently require four nutrients to be added to white and brown wheat flour, but these do not need to be labelled because of a specific national provision in the Food Labelling Regulations 1996 (as amended). This provision is currently being reviewed as part of the EU review of food labelling legislation, and may as a consequence be removed (the timescale for adoption of the new EU food labelling legislation is 2010). The addition of folic acid would, it is suggested in this paper, need to be accompanied by mandatory labelling. In this case folic acid would need to be declared in flour and flour products in all cases. This would mean that some flour products, such as sauces and fish fingers, where the level of folic acid is so low as to be nutritionally insignificant, would have to indicate folic acid on the label. This raises the issue of whether such labelling would be misleading or appropriate. A possible solution would be to explore the possibility of a *threshold* below which labelling the indication of folic acid would not be required. Again, this would be subject to the notification to the Commission (see paragraph 5).

## CONSUMER ISSUES AND VIEW ON RELATED ETHICAL ISSUES

### *Consumer research conducted by the Food Standards Agency*

#### General Population

1. Following the April 2006 Board meeting, the Agency commissioned qualitative research to find out about consumers' attitudes towards, and understanding of, folic acid fortification and the attendant issues<sup>1</sup>. Specific objectives included:
  - To gather consumers' views on the Agency's four options for increasing the folate intake of women of reproductive age and to identify consumer concerns likely to arise in relation to the four options.
  - To encourage and facilitate informed deliberation amongst consumers on the possible fortification of flour with folic acid, and the attendant risks and benefits.
  - To gather consumers' views on, and gauge their understanding of, current fortification practice, and to see whether mandatory fortification is, in principle, an acceptable and appropriate way of tackling a public health issue.
  - To assess consumers' current understanding and awareness of NTD's and the benefits of taking folic acid supplements.
2. A two-stage deliberative process was developed which involved 5 workshops in 5 regions with 'the general public' which were reconvened 2 weeks later. Each session lasted 3 hours and the intervening 2-week period was included to allow for reading of further briefing materials and deliberation. There were 12 participants (6 men / 6 women; 6 ABC1 / 6 C2DE) in each workshop from a range of life stages. None had close personal or professional experience of NTDs, at least half were responsible for food shopping and cooking, all were eaters of bread and some were vegetarians or vegans.
3. In addition, there were 4 paired depth interviews with black and minority ethnic group women. The sample comprised 1 pair of African origin, 1 pair of Caribbean origin, 1 pair Muslim, 1 pair Hindu and was representative of young people, family and older people life stages. Other characteristics were the same as for participants in the workshops.
4. The workshops were structured so that spontaneous views of voluntary and mandatory fortification were gained initially before participants were presented

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<sup>1</sup> <http://www.food.gov.uk/consultations/ukwideconsults/2006/folate>

with a range of information units, which set out some of the facts and issues for them to debate. Participants' views on the options were also tracked throughout the process, providing an insight into how views evolved as participants received further information and had the opportunity to reflect on what they had heard. The fieldwork was carried out in May and June 2006.

5. The research was successful in stimulating a highly informed discussion by participants with little or no previous knowledge of this complex and technical issue. The key findings were:
  - The majority of participants saw NTDs as a serious and significant problem, and supported (at least in principle) action by 'the Government' to address the issue.
  - By the end of the deliberative process, no single option was supported by the majority of participants. However, more participants supported mandatory fortification than any other option, with the remaining support split fairly evenly among the other options.
  - There was a shift towards Option 4 as the research progressed. This was usually because participants came to believe that this was the most likely option to achieve the desired outcome (an improvement in NTD rates) rather than because their anxiety about the risks involved was satisfied.
  - Some participants retained a strong opposition to Option 4. In most cases this was because they considered the potential risks to those other than young women - involved to be unacceptable or because they felt strongly that consumer choice should be maintained.
  - Option 1 - maintaining the status quo - was supported by a number of participants, either because it brought no additional risks or because it was a low cost option. However, a large number came to reject this option as the research progressed, because they did not believe it would be effective in reducing the rate of NTD affected pregnancies.
  - Option 2 – an education campaign – received strong initial support. Support declined as the research progressed, and as participants became less convinced of its likely effectiveness. This option was also considered by many to be an important supporting element to option 3 or 4.
  - Option 3 – encouraging voluntary fortification - was favoured by some as a less risky and less radical option than mandatory fortification. Those who did not support this option were either opposed to fortification *per se*, or preferred the more structured approach of option 4.

- Participants did not feel that the lack of consensus should prevent the Agency from moving forward on this issue. Participants recognised that, in a complex area such as this, consensus was not always possible.
- It was clear that consumers would wish and expect to be informed of any significant change of strategy in this area, especially if mandatory fortification was chosen.
- There was a clear expectation that any increase in fortification (whether on a voluntary or mandatory basis) would be monitored and regulated by an official body to prevent high folate intake by those consumers to whom potential risks may apply.
- In the event of further fortification, whether on a voluntary or mandatory basis, there is a strong demand for the fortificants to be clearly labelled.

## **Young Mothers**

### ***Health and Lifestyle in Pregnancy***

6. The Agency commissioned deliberative research to gather the views of low-income (C2DE) women living in a representative range of socially deprived communities across the UK on the Agency's four options for increasing the folate intake of women of reproductive age<sup>21</sup>.
7. The objective was to explore the lifestyle changes (e.g. using supplements, reducing smoking, changing diet) made before and during pregnancy and the barriers and facilitators to such changes.
8. The project included 24 depth interviews with mothers with children aged between 0 – 3 years old, (including 8 depths with ethnic minority mothers) and 7 friendship group discussions. Respondents, aged from 18-40, included women who reported having made many changes, some changes, few or no changes in pregnancy and those who had had planned and unplanned pregnancies, with a bias towards women with unplanned pregnancies. The research was conducted in September and October 2006.
9. Key findings were:
  - The majority of respondents expressed a preference for mandatory fortification. This emerged as the easiest and most appealing option for this group of women, requiring no behavioural change on their part.
  - Approximately one third of this sample had not taken folic acid supplements before or during pregnancy. For most respondents there was little awareness of the link between folic acid and NTDs.

- Many of this sample had unplanned pregnancies and were not presenting themselves to medical professionals or receiving any formal pregnancy advice until late in the first trimester or later.
- For many respondents, behavioural change (such as using supplements, reducing smoking, eating more fruit and vegetables) proved difficult and was minimal.
- Probably the most critical barrier to behaviour change was the limited awareness and understanding of recommendations made in pregnancy and particularly of the risks and consequences of not following these recommendations.

## **Ethical Considerations**

### **Summary**

10. This report develops an ethical framework to support the Board of the Food Standards Agency (the Agency) in considering options for improving the folate intake of women of reproductive age including mandatory fortification of wheat flour with folic acid<sup>2</sup>. It draws on scientific information from other reports previously commissioned by the Agency and relevant research in peer-reviewed journals. The ethical approach is based on the 2005 United Nations' *Universal Declaration on Bioethics and Human Rights*.
11. The central question is: would it be ethically defensible for the Agency to recommend the mandatory fortification of wheat flour products in order to reduce the number of neural tube defect (NTD) births in the UK?
12. While an increased intake of the vitamin folate prior to conception and during the first 12 weeks of pregnancy has been shown to reduce the risk of NTD development, approximately 50% of UK pregnancies are reported to be unplanned. This implies that at least 50% of women who become pregnant have not been able to make an informed decision about modifying their diet to increase folate intake. Other studies have found efforts to increase the folate intake of women of child-bearing age, through public health education, to be relatively ineffective, particularly among younger women and those from socio-economically disadvantaged backgrounds.
13. Evidence suggests that mandatory fortification of flour will reduce the number of NTD births, or terminations by reason of NTD, but may potentially result in an increased risk to those who suffer from an undiagnosed vitamin B12 deficiency. Other, currently inconclusive, evidence has suggested a possible link between

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<sup>2</sup> Folic acid is a synthetic form of folate.

folic acid intake in excess of the guidance safe levels of intake and certain cancers (SACN, 2006).

14. The principal ethical conflict to be addressed by the Agency is between the ideal of *personal autonomy*, which requires that an individual should always retain control over any decisions relating to her own health and medical treatment, and the ideal of *social responsibility and justice*, which proposes that societies have a duty of care to work, mainly through governments, towards the greatest level of health and happiness for their members, particularly those who suffer from social and economic disadvantage.

15. of the four courses of action presented is that:

- (a) Option 1 (*no change*), while preserving individual autonomy, breaches the social responsibility and equality principles. There is also a strong difficulty with the failure to prevent an identified harm.
- (b) Option 2 (*increased public education*) has been shown to be largely ineffective. For this reason, it would not significantly remedy the breaches of social responsibility and equality presented by option 1. Moreover, it may create additional stigma for those populations already affected by NTDs.
- (c) Option 3 (*voluntary industry fortification*) may also be ineffective, based on the previous failure of option 2 and current existing levels of voluntary fortification. In addition, it may pose additional health risks due to uncontrolled voluntary fortification. An action that is not likely to prevent harm, but may actually cause it, is difficult to defend ethically.
- (d) Option 4 (*mandatory fortification*) poses difficult questions regarding the restriction of autonomy and the balancing of potential harm to one group over the prevention of harm to another. However, the scientific evidence available to the Agency presents a strong argument that, in this instance, individual autonomy may reasonably be limited to benefit specific vulnerable groups, provided that parallel attention is given to minimizing the potential for harm to others. Because there are opportunities to 'opt-out' (for example by choosing wholegrain bread), the reduction of autonomy is less than in comparable scenarios.

SUMMARY TABLES OF CONSULTATION RESPONSES<sup>1</sup>

Table 1: Key to group names

Acronym	Organisation
ABF	Association of British Food
AC	Age Concern
ACFM	Association of Cereal Food Manufacturers
ASBAH	Association for Spina Bifida and Hydrocephalus
BCCCA	Biscuit Cake Chocolate and Confectionary Alliance
BDA	British Dietetic Association
BDF	Birth Defects Foundation (Newlife)
BINOCAR	British Isles Network of Congenital Anomaly Register
BMA	British Medical Association
BNF	British Nutrition Foundation
BRC	British Retail Consortium
CDC	Centre for Disease Control and Prevention
CRN	Council for Responsible Nutrition
EAC	East Ayrshire Council
FDF	Food and Drink Federation
FOB	Federation of Bakers
FWHM	Friends of Welwyn Hatfield Museums
GFV	Gloucestershire Food Vision
HAS	Help the Aged Scotland
HFMA	Health Food Manufacturers Association
HPANI	Health Promotion Agency for Northern Ireland
HW	Heage Windmill
IFR	Institute of Food Research
IFSBH	International Federation for Spina Bifida and Hydrocephalus
IOB	Institute of Biology
MRC-HNR	Medical Research Council Human Nutrition Research
NABIM	National Association of British and Irish Millers
NAMB	National Association of Master Bakers

<sup>1</sup> Note – Board Members should contact Lynda Harrop (0207 276 8928) to access full copies of the consultation responses.

NCT	National Childbirth Trust
NCW	National Council of Women
NIFAC	Northern Ireland Food Advisory Committee
PAGB	Proprietary Association of Great Britain
RAND BC	RAND Business Consultancy
RCGP	Royal College of General Practitioners
RCM	The Royal College of Midwives
RCN	Royal College of Nursing
RCOG	Royal College of Obstetricians and Gynaecologists
RCP	Royal College of Physicians
RCPCH	Royal College of Paediatrics and Child Health
SA	Soil Association
SFAC	Scottish Food Advisory Committee
SRHSBs	Society for Research into Hydrocephalus and Spina Bifida's
SSBA	Scottish Spina Bifida Association
TCG	Traditional Cornmillers Guild
VEGA	Vegetarian Economy and Green Agriculture (VEGA)
WFAC	Welsh Food Advisory Committee

**Table 2: NGO responses**

<b>NGOS INCLUDING CHARITIES AND OTHER ORGANISATIONS RECEIVING MIXED FUNDING</b>			
<b>Respondent</b>	<b>Preferred options</b>	<b>Options rejected</b>	<b>Key points</b>
AC	Option 4	No option rejected	Support a level of fortification of 300ug/100g flour. Support conditional upon removal of voluntary fortification, monitoring of health effects and policy review within 5 years. Would like safeguards for health of older people in the form of a programme of awareness of Vitamin B12 deficiency, control of overage and warnings on taking folic acid supplements.
ASBAH	Option 4	Option 3	Option 4 will increase folate intake in the target group will work. This option will ensure NTD pregnancies will be reduced avoiding trauma and disability. No evidence of harm from those countries that have already fortified. There would be a net benefit to the general population if voluntary fortification is also controlled. Folate deficient older people would also benefit from increased consumption. There are economic benefits of choosing option 4.  Option 3 would be rejected on the grounds that industry is unlikely to fortify voluntarily on a universal or widespread scale. Fortified foods tend to be at a premium and so would not be consumed by the target group.
BDF	Option 4	No option rejected	Despite action by Newlife and Government to encourage increased uptake of folic acid, most women are not taking supplements prior to conception. Many pregnancies are unplanned and in addition many women are confused about the dose of folic acid they should be taking and when they should take it. Populations who already have folic acid added to their food have not suffered any unwanted side effects and may even be experiencing other health benefits such as a reduction in cardiovascular disease.
BINOCAR	Option 4	No option rejected	Advising women to take supplements is of no use when women have an unplanned pregnancy. Adding folic acid to flour could prevent many NTD pregnancies in the UK.

FWHM	No preferred option	No option rejected	<p>Ensure that traditionally produced organic produced stone ground flour is exempt from fortification for the following reasons:</p> <ul style="list-style-type: none"> <li>- Young women are unlikely to be helped by additions to wholemeal flour</li> <li>- Older people who are at risk of B12 deficiency are significant consumers of this bread</li> <li>- Existing production processes do not easily allow for fortification</li> <li>- Existing exemption in bread and flour regs</li> <li>- Might result in cessation of production of this type of flour depriving consumers of healthy eating food source</li> </ul>
HAS	Option 2	No option rejected	Option 2 will avoid the risks to the elderly whilst acknowledging that young women of childbearing age would benefit from greater awareness of the benefits of folate.
HPANI	Option 4	Options 1 & 2	<p>Support this option as public education campaigns have been shown to be ineffective at sustaining supplement intake long term and although education campaigns should continue they are not acceptable as the only policy. 50% of pregnancies are unplanned.</p> <p>Reducing the numbers of NTD pregnancies will have a significant impact on those caring for NTD sufferers. Recognise risk of masking of vitamin B12, those with diabetes and those who are overweight and specific advice should be given to these people. In addition, there are limitations in the techniques for determining B12 deficiency and further work needs to be done to develop these.</p> <p>Fortifying a staple food will also have a worthwhile contribution to the intakes of the general population.</p>
IFSBH	Option 4	No option rejected	<p>Mandatory fortification is necessary to effectively prevent neural tube defects as even with a healthy balanced diet intake is below the necessary level to prevent NTDs. Countries that have implemented fortification have seen a reduction in the level of NTDs but there is evidence to show that campaigns are ineffective.</p> <p>Voluntary fortification would discriminate against those who cannot afford to buy these products, therefore the target group would not benefit.</p> <p>Fortification is a way of maximising consumption for the entire population.</p>

NCT	Options 2 & 4	Options 1 & 3	<p>Option 1 is rejected because it is unlikely to achieve the Government's objective of reducing NTD affected pregnancies.</p> <p>Option 3 is not suitable as an option because those women most at risk of unplanned pregnancies are least likely to choose fortified food or take folic acid supplements. Also current voluntary fortification is resulting in higher than recommended intakes of folic acid in certain groups.</p> <p>Option 4 would not impinge on consumer choice if it is added in line with current bread fortification legislation. Consumer should however be improved by amending current labelling requirements. Steps should be taken to target coeliac sufferers and sufficient information should be given to the public to ensure understanding for the mandatory route. Care must be taken about possible overage and the potential consequences of fortification should be monitored closely, including any increases in B12 deficiency.</p> <p>Option 2 should be used in conjunction with option 4 but not on its own as it has been shown to be ineffective. Greater supplement intake might be achieved by the following:</p> <ul style="list-style-type: none"> <li>- target high risk groups</li> <li>- work with families, peers and organisations providing access to these groups</li> <li>- include practical steps to make action easier</li> <li>- ensure that advice is embedded in a structure and delivered in a committed and relevant way</li> <li>- be sustained over a long period of time</li> <li>- using a health claim might make it easier for women to identify relevant foods and supplements.</li> <li>- develop wider messages and programmes targeted at young women from lower socio economic backgrounds</li> <li>- incorporating consistent messages in school nutrition programmes and incorporating nutritional advice and support into post-natal care.</li> </ul>
NCW	Option 4	No option rejected	Support mandatory fortification of all flours, wheat and corn with the exception of whole-wheat. This will preserve consumer choice whilst promoting the nation's health.
SRHSB's	Option 4	Option 3	<p>Option 1 &amp; 2 should continue in the event of mandatory fortification.</p> <p>Option 3 would not be a viable alternative as it would require consumer knowledge and would be uncontrolled and difficult to monitor.</p> <p>Option 4 is recommended because:</p> <ul style="list-style-type: none"> <li>- only a quarter of women follow the health advice about folic acid and 50 % of pregnancies are unplanned.</li> <li>- there is no evidence of risks from other countries that have fortified over many years.</li> <li>- older people may benefit from additional folate.</li> <li>- risk of vitamin B12 deficiency is minimal at the doses recommended by SACN.</li> <li>- two expert committees (COMA and SACN) have come out in favour of mandatory fortification.</li> </ul>

SSBA	Option 4	Options 1, 2 & 3	<p>Option 1 has little impact in reducing NTD pregnancies in the UK.</p> <p>Option 2 is not effective as it relies too heavily on consumer knowledge and awareness.</p> <p>Option 3 is not recommended as companies will only fortify premium products and so won't reach low socio economic groups. Voluntary measures cannot offer sufficient safeguards in terms of dosage and monitoring and evaluation.</p> <p>Support option 4 alongside control voluntary fortification and advice about supplement use. This would limit the risk of intakes over the recommended upper level with regard to B12 and colon cancer. Scotland has an even greater requirement for fortification as there is an increased prevalence there compared with the rest of the UK. The USA has seen no adverse effects of fortification.</p>
VEGA	Options 2, 3 & 4	No option rejected	<p>Options 2,3 &amp; 4 should be integrated except that those flours not already fortified should be exempt. Flours other than wheat should be considered for those who cannot or do not consume wheat.</p> <p>Appropriate labelling and information should be provided to avoid confusing messages.</p> <p>Flours from GM crops should be fortified but allowances made for exemptions and additions as public attitudes and abstentions develop.</p>
Which	No option supported	No option rejected	<p>Option 2 needs to be developed further in the meantime of any other decision. Crucially it needs to be better explained of the importance of taking folic acid supplements before pregnancies.</p> <p>Option 3 must take into account the need to control voluntary fortification. Also all foods fortified must be clearly labelled.</p> <p>If option 4 is to go ahead, the following should happen first:</p> <ul style="list-style-type: none"> <li>- better understand the relationship between folic acid levels and cancer risk</li> <li>- practicalities of limiting folate intakes below 1mg per day</li> <li>- a process for monitoring vitamin B12 deficiency in older people needs to be established.</li> <li>- ensure consumer choice can be maintained.</li> </ul>

**Table 3: Industry responses**

<b>INDUSTRY</b>			
<b>Respondent</b>	<b>Preferred options</b>	<b>Options rejected</b>	<b>Key points</b>
ABF	Options 2 & 3	Options 1 & 4	<p>Option 1 does not address the current issue.</p> <p>Option 2 is important as women will still need to take a supplement so educating women about supplements and folate rich foods will remain essential.</p> <p>Education campaigns should be part of school curriculum's and through doctor's surgeries.</p> <p>Option 3 would allow changes in patterns of consumption to be taken into account and could be regulated through a best practice code which would identify foods most appropriate for fortification. It would also allow consumer choice. The Government would need to support fortification because of the associated negative effects of increased intakes.</p> <p>If option 4 were carried out the target group would still be required to take supplements and this option would not allow consumer choice. There would be additional costs to industry if separate streams needed to be installed.</p>
ACFM	Options 2 & 3	Option 1	<p>Option 1 would be ineffective as a means of increasing folate intake.</p> <p>Option 2 should be implemented by doing more through schools and GPs and educating women about eating folate rich foods.</p> <p>Supermarkets should also be encouraged to display messages on folate rich foods. However evidence shows that supplements are not necessarily the way to achieve an increased folate intake in the target group.</p> <p>Option 3 is likely to be most effective at reaching the target group as breakfast cereals contribute significantly to the diets of young women. Voluntary fortification allows for flexibility if patterns of consumption were to change.</p> <p>A best practice code should be drawn up to include foods recommended for fortification and by how much. This option allows for consumer choice. The scope of option 3 would be restricted by legislation on addition of nutrients and derogations would be needed to overcome this.</p> <p>Option 4 would only be supported if breakfast cereals could continue to be fortified voluntarily, within a code of practice. ACFM believe mandatory fortification is contradictory to public health recommendations to increase consumption of whole grains. There would be an additional cost to industry and mandatory fortification would be against the spirit of harmonisation in the EU. Monetary aspects of this option have not been fully explored e.g. the monitoring of the health impact, costs of increases in twinning with other countries, the negative impact on export markets and implications for the organic produce industry.</p> <p>If mandatory is introduced it should be at a level to allow voluntary to continue. ACFM believe the safety assessment regarding upper intakes is unrealistic and overly conservative.</p>

BCCCA	Options 2 & 3	Option 4	<p>Mandatory fortification would put UK biscuit and cake manufacturers at a disadvantage against their European competitors who use unfortified flour. If it were to proceed the following things should be taken into account:</p> <ul style="list-style-type: none"> <li>- labelling - if products where flour only forms a small part of the product are required to be labelled it will be misleading to the consumer.</li> <li>- exports - as fortification is not allowed in a number of European countries it could cause rejection of such products.</li> <li>- labelling costs - the requirement to fortify could result in many products being required to change their labels and could incur costs in the region of %5 million for this sector alone.</li> </ul> <p>Therefore there appears to be a disproportion in burden and costs and confusion if flour were to be fortified. BCCCA are concerned about information of adverse effects of additional folic acid such as multiple births, colorectal cancer and cognitive decline.</p>
Boots	Options 2 & 4	No option rejected	<p>Support increased education and building on current activity with renewed effort. Consider that mandatory fortification is likely to benefit young women and unplanned pregnancies. Would support proposals to monitor B12 status in the elderly to ensure that there are no adverse effects. Also important to consider the cost implications of mandatory fortification.</p>
BRC	No option supported	No option rejected	<p>BRC are not qualified to make a decision on mandatory fortification but would like the following considerations to be taken into account:</p> <ul style="list-style-type: none"> <li>- BRC members agree that the most appropriate legislative tool to encompass any new requirement would be the bread and flour regulations.</li> <li>- Flour is more suitable technologically. If bread were chosen a premix would be required and it is likely miscalculations could occur. There are also 50 flourmills against 4000 bakeries so flour fortification would mean that monitoring and enforcement were easier.</li> <li>- Retailers would be willing to discuss reformulation of products currently fortified with folic acid.</li> <li>- Declaration of folate and other vitamins on the ingredients list of all products containing flour could be misleading for the consumer depending how much flour is in the product.</li> <li>- Mandatory fortification will have a big impact of imports and exports. It will be difficult to get suppliers in countries such as France (who are against fortification) to reformulate the batches they produce for export to the UK. Ireland is a particular concern as it would be detrimental for BRC members to end up with different fortification schemes in the two countries.</li> <li>- There is concern about the messages that will be allowed in light of the legislation on nutrition and health claims and believes that an education campaign is crucial</li> <li>- A scheme for monitoring vitamin B12 deficiency should be introduced.</li> <li>- Detailed guidelines should be published alongside any decision taken by Ministers.</li> </ul>

CRN	Options 2 & 3	No option rejected	<p>A combination of options 2 &amp; 3 should be used as this allows both supplementation and structured voluntary fortification with a higher level of targeted education. The advantage of food supplements is they deliver folic acid in small and accurate unit-dose forms. By fortifying a wide range of staples any avoidance of a food group would be less likely to compromise folic acid intake.</p> <p>The fact that there are significant differences in bioavailability between foods and supplements must be taken into account. Foliates in foods are much less bio available than folic acid in supplements and so to achieve a 400ug intake between 600ug and 800ug of folates might be required.</p> <p>Option 4 will cause barriers to trade in the EU. It is also important that consumer choice and availability of supplements is not affected by the eventual policy.</p>
FDF	Options 2 & 3	Option 1	<p>Option 1 does not address the current issues.</p> <p>Although current steps to educate women do not appear to be working, still believe it is worth pursuing. Industry should be encouraged to display messages on folate rich foods and in supermarkets. However, experience shows that supplements are not necessarily the way to achieve an associated increase in folate intake in vulnerable women, as this requires pro-activity and has an associated cost.</p> <p>Option 3 is likely to be effective in targeting the at risk group and industry would like to be able to continue voluntarily fortifying in a responsible manner. There is some concern about the impact of the forthcoming regulation on addition of nutrients and also that the legal responsibility for adding folic acid would fall on industry. This concern could be relieved by the appropriate setting of conditions.</p> <p>If option 4 were introduced industry would wish to continue fortifying voluntarily but within a code of practice. The FSA should have discussions at EU level if the decision is taken for mandatory fortification. Various surveillance programmes should be put in place to mediate the risks of B12 deficiency. The biscuit and cake industry would be put at a significant disadvantage against their European competitors who use unfortified flour. Some manufacturers might have to install separate flour streams with and without folate in order to be able to export products and this would incur significant costs. Labelling of products containing folic acid would also be a significant barrier to trade with other countries. Flour millers expect the cost of adding folic acid to be in the region of £1M</p>
FOB	Option 2	Option 1	<p>Option 1 requires more pro-activity than is currently undertaken and is therefore not acceptable.</p> <p>Option 2 should be carried out whichever option is decided as there is a need to encourage the taking of folic acid supplements and awareness of consumption of folate rich foods.</p> <p>Under present arrangements FOB have not fortified their products to any significant extent.</p> <p>Should be decision for mandatory fortification be taken, it is strongly recommended that it should be done at the flour milling stage as it would be the only practical application of such an option.</p>

Foodaware	Option 4	Option 3	<p>Although dietary intakes are sufficient to meet dietary requirements they are not sufficient to protect against NTDs. Folate supplementation might also be useful for brain function in older people. Mandatory fortification is necessary as those most at risk are the most difficult to reach group.</p> <p>An advantage of option 4 is that only one staple food needs to be fortified thus it will only need to be implemented in one sector of the food industry. Voluntary fortification would need to be restricted so that intakes are not excessive and the issue of those who do not and cannot eat bread needs to be addressed. General support for an education campaign.</p> <p>However there are some concerns about the ethics of extensive fortification for the interests of one group and there is some concern about the adverse consequences on the B12 status of older people. Ongoing monitoring of the folate status of the population as a whole should be implemented.</p> <p>The question of how to offer choice needs to be addressed.</p> <p>Option 3 should be rejected as evidence shows that other initiatives around the world have not been effective and it would also not be easy to control.</p>
HFMA	Options 2 & 4	No option rejected	<p>Favour consumer choice rather than mandatory fortification but in this case there is an overriding public health rationale due to the high incidence of NTDs amongst economically deprived groups and also the evidence from the US that mandatory fortification reduces NTDs but does not increase masking of B12 deficiency.</p> <p>A policy for mandatory fortification should be supported by increased promotion of the importance of taking supplements before women become pregnant. Also a strategy for monitoring and detecting B12 deficiency should be put in place. Voluntary fortification should be prohibited and coeliacs should be given appropriate advice.</p>
HW	No preferred option	No option rejected	<p>Ensure that traditionally produced organic produced stone ground flour is exempt from fortification for the following reasons:</p> <ul style="list-style-type: none"> <li>- Young women are unlikely to be helped by additions to wholemeal flour</li> <li>- Older people who are at risk of B12 deficiency are significant consumers of this bread.</li> <li>- Existing production processes do not easily allow for fortification</li> <li>- Existing exemption in bread and flour regs</li> <li>- Might result in cessation of production of this type of flour depriving consumers of healthy eating food source.</li> </ul>

Kellogg's	Options 3 & 4	No option rejected	Evidence from other countries show that mandatory fortification can co-exist with voluntary fortification, which is a valuable additional help in achieving the desired goal. No adverse effects have been detected in the USA during the 9 years in which their policy of joint mandatory and voluntary fortification have been in place. Fortified breakfast cereals benefit low folate consumers significantly more than other sources currently available. Breakfast cereals are a very minor contributor of excessive folic acid, relative to other sources for those aged 65 yrs and over.
NABIM	No preferred option	No option rejected	<p>Option 1 would have no impact on the flour milling sector or the target population. Some form of education campaign would be required regardless of the option chosen. Voluntary fortification would avoid problems associated with labelling and international trade and would allow consumer choice. However, it would be difficult to achieve widespread fortification, which the Government desires.</p> <p>Mandatory fortification would achieve widespread intakes but would raise concerns about consumer choice. It is considered appropriate that mandatory fortification should be in line with the bread and flour regulations. Other things to take into account are labelling and claims, trade (to ensure fortified products could be exported) and imports (care needs to be taken that manufacturers do not switch to imported unfortified flour, thus going against the policy goal).</p>
NAMB	No preferred option	Option 1 & 3	<p>Option 1 is not viable if the Government wish to tackle the problem.</p> <p>Option 2 appears to have had limited success and has made little or no difference to the incidence of NTDs. There is no evidence to suggest that a more pro active or high profile campaign will encourage young women to take supplements and eat more folate rich foods. It takes a very long time to change public perceptions, attitudes and behaviours, therefore how long would a campaign have to run for.</p> <p>Opposed to option 3 as it should not be for the food industry to decide which foods to fortify. There is also no indication of what foods young women eat and how over consumption can be prevented. In the 90s a HEA campaign to encourage baking industry to fortify was unsuccessful and there was a considerable amount of wastage.</p> <p>Option 4 is the only viable option although the following needs to be taken into account:</p> <ul style="list-style-type: none"> <li>- bread is not the preferred option as it would be the most costly, difficult to control and monitor and constitutes the biggest administrative burden. Fortifying bread poses problems because of the small amounts involved and it would need to be added by means of a premix. There is the issue of how much testing and monitoring would be required to ensure right levels were being added. There would be disproportionate costs to craft bakers due to the small volumes of bread produces. If the bread route is chosen an option could be to fortify only 800g sliced wrapped bread, involving mainly plant bakeries, although they would likely object to being singled out in this way.</li> <li>- If flour were fortified it would remove a lot of the uncertainties about the amount of folic acid being added.</li> </ul>

			<p>The number of flourmills involved is considerably less and therefore testing and monitoring costs will be lower. Systems are already in place in flourmills.</p> <ul style="list-style-type: none"> <li>- bread-making flour is not a feasible option as there is no such thing. Flour milled for bread can also be used in many other products. To fortify all flour would require a change to the bread and flour regulations.</li> <li>- labelling needs consideration. The scope of the bread and flour regulations could be extended to include folic acid and this would have no cost implications for industry. However it is likely the Government will want to publicise the fact that folic acid has been added. Declaring folic acid in all products would have huge cost implications due to the minute amounts of flour in many products. Declaring all the fortificants in flour will have similar cost implications to only declaring just folic acid. If fortificants are to be declared, consideration needs to be given to the threshold for declaration. Also non pre-packed products and pre-packed products for direct sale need to be considered.</li> <li>- publicising the presence of folic acid and whether it constitutes a claim needs to be considered and guidance would have to be prepared for industry.</li> </ul>
Nutragen	Option 1 & 4	No option rejected	Evidence shows that only 50% of pregnancies are planned and therefore support option 4 combined with option 1. Also recommend that a slightly broader fortification target may be required.
PAGB	Options 1 & 2	No option rejected	Support increased promotion of current advice. There is evidence to suggest that the HEA education campaigns in the 90s were successful in increasing awareness of the importance of folic acid supplementation. The Government is currently running an NHS Healthy Start Vitamins Scheme, which is aimed at targeting those in minority groups, and this scheme provides supplements to women throughout their pregnancies.
RAND BC	No preferred option	No option rejected	Provides evidence that health & economic gains of fortification far outweigh the losses for the US population & that an increase in the fortification level in the US deserves further consideration in order to maximise net gains.

SA	Option 2	Option 4	<p>Oppose option 4 as it removes consumer choice, is a disproportionate measure and would bolster the health image of nutritionally poor processed foods. If option 4 is selected organic products should be exempt, as well as wholemeal flour. In addition, the FSA should address food production processes such as the Chorley Wood bread-making process, which results in reduced levels of natural folate.</p> <p>The current advice of option 1 should be improved. In addition birth control pills cause a lowering of folic acid reserves in the body and women should be informed of this disadvantage. In addition the Cochrane Review of 21 studies on folic acid concluded that there is not enough evidence to evaluate whether folic acid supplementation has any effect on the clinical outcomes for mother and baby.</p> <p>Option is not supported as not convinced that fortification is effective. Fortification also forces people to consume synthetic amounts of the synthetic substance their whole lives and can lead to excessive intakes in some. There are particular concerns with masking of B12 deficiency in the elderly. SACN admit that there are concerns about the safety of high intakes of synthetic folic acid but that natural folate is safe.</p> <p>There are also concerns about folic acid being produced from genetically modified sources.</p> <p>Soil Association, supported by Doves, Shipton and FWP Matthews (organic flour millers) are all opposed to the option of mandatory fortification.</p> <p>The long-term effects of synthetic folic acid intake remain unknown.</p> <p>It was noted that in the US there was a decline in folate levels in women following mandatory fortification. Some women have a mutation that reduces the body's ability to metabolise and retain folic acid and this may account for the 200 cases of NTDs per year.</p> <p>Possible methods to improved folate levels in food include:</p> <ul style="list-style-type: none"> <li>- choosing suitable agricultural cereal varieties as folate levels are highly affected by the choice of variety.</li> <li>- production of white flour removes almost half the naturally present folate.</li> <li>- Chorley-Wood process, which has an accelerated fermentation process, decreases the health benefits of bread.</li> <li>- blanching/freezing operations can destroy up to 50% of folic acid levels.</li> <li>- folic acid is destroyed by food irradiation.</li> <li>- the issue of green potatoes needs to be addressed.</li> </ul>
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TCG		Option 4	<p>Concerns with option 4 because of the following:</p> <ul style="list-style-type: none"> <li>- most members do not have the equipment to add folic acid to flour.</li> <li>- it will threaten the integrity of their products.</li> <li>- disproportionate response to the problem</li> <li>- burden and costs of regulation</li> <li>- threat to a traditional artisan craft.</li> </ul> <p>Would like the possibility that there is a range of labelled non folic acid bread and flour products, not just wholemeal. There should also be an opt out for small, traditional and organic flour millers, or those who produce less than 650 tonnes of flour per year.</p>
Waitrose	Options 1, 2, 3 & 4	No option rejected	<p>Option 1 should remain in place.</p> <p>Option 2 needs to continue and be developed although it is not the whole solution. Alongside education, retailers should be encouraged to highlight products, which supply folic acid in the diet.</p> <p>Option 3 is already occurring in many products such as breakfast cereals although appreciate that it is not having the desired effect with regard to decreasing neural tube defects. However agree with SACN that mandatory fortification is put in place then voluntary fortification should be discouraged. Those foods already fortified should be allowed to remain.</p> <p>In favour of option 4 as consider flour to be a suitable vehicle for fortification. Recommend that folic acid is added in line with the current bread and flour regulations. If fortification is implemented consideration needs to be given to those who avoid wheat and also vitamin B12 deficiency should be closely monitored.</p>

**Table 4: Academic responses**

<b>ACADEMIC AND LEARNED SOCIETIES</b>			
<b>Respondent</b>	<b>Preferred options</b>	<b>Options rejected</b>	<b>Key points</b>
BBSRC	No preferred option		<p>Support desire to reduce NTDs in the target population &amp; appreciate effectiveness of a whole population strategy to achieve this purpose. However recommend caution in this approach given the low target group &amp; the potential for systemic exposure to unmetabolised folic acid which may provoke deleterious effects. Evidence provided on the following areas:</p> <ul style="list-style-type: none"> <li>- Folic acid and cancer</li> <li>- Folic acid &amp; its inter-relationship with effects of vitamin B12 deficiency</li> <li>- Unmetabolised folic acid</li> </ul>
BNF	No preferred option	No option rejected	<p>Option 1: Do not support as poor uptake of folic acid supplements among women prior to conception &amp; because of unplanned pregnancies.</p> <p>Option 2: Not adequate in isolation but would be a necessary adjunct to either option 3 or 4.</p> <p>Option 3: To avoid intakes exceeding UL would be important to achieve control over which foods are fortified &amp; levels of folic acid in supplements. Combined with option 2, this option has potential for success, however: Motivation of millers, manufacturers and retailers to voluntarily fortify food may be limited. Some sectors of food industry expressed concern about potential requirement to stop fortification as many products are manufactured for a global market that does not have restrictions on folic acid fortification. Important to follow SACN's recommendations of monitoring folate status &amp; potential benefits and adverse effects. Would need to target foods eaten by women in socio-economically deprived areas. Pricing may be an issue if these foods are more expensive than non-fortified options.</p> <p>Option 4: Research concerning folate &amp; cancer still emerging so maybe premature to proceed with mandatory fortification. With regard to B12, seems to be complex interplay, e.g. folate may protect against cognitive decline in people who are folate replete but accelerate decline in those with low B12 status.</p> <p>Another issue is consumer concern about the impact of mandatory fortification on choice &amp; also issues for food industry.</p>
MRC-HNR	Option 4	Options 1 & 2	<p>Support the recommendation for fortification with controls on fortification. This will narrow the distribution of intakes in the population, reducing numbers with low intakes, whilst controlling numbers with intakes above 1mg/day.</p> <p>Options 1 &amp; 2 do not tackle the problem and option 3 risks increasing the prevalence of high intakes.</p>
NS	Option 2 & 4	Options 1 & 3	<p>Option 1 is not supported considering the significant proportion of women who do not plan their pregnancies or follow advice on supplementation.</p> <p>Option 2 should be implemented regardless of which option is chosen.</p>

			Option 3 is rejected because it is unlikely to reach the target groups. Option 4 is acceptable only with the controls recommended by SACN.
Royal Free Hampstead	Option 4	No option rejected	Recommend mandatory fortification as there is no evidence for an increase in vitamin B12 deficiency at the levels recommended.
Professor John Scott	Option 4		Requirement for mandatory fortification should apply to flour for bread use. There would be a 'lag period' until fortification was implemented and this would allow proof of any unacceptable risk to emerge from the USA/Canada. Voluntary folic acid should be restricted but not banned. Very highly fortified foods, such as spreads, that have very variable intakes should not be allowed to be fortified with high levels. Taking supplements is an elective practice. Unfair that people who decide to take folic acid supplements ought to be able to interfere with general public health policy.
University of Oxford	Option 2	Option 4	Targeted publicity techniques could be used more effectively than previous campaign (1996-99). Targeted campaign would only treat the targeted group and not the rest of the population. Reject option 4 for following reasons: Insufficient knowledge of possible harmful effects. Some evidence of potential harm was published after SACN report. Control of voluntary fortification and advice about supplement use are restrictions on consumer choice and would be very difficult to achieve. Will cause confusion if public told they MUST take folic acid supplements for pregnancy but MUST NOT take at any other time. If mandatory fortification is implemented then monitoring (as recommended by SACN) is essential but concerned that it will be rejected by government as too expensive. Also problem of liability. If folic acid increases the incidence of cancer then fortification would have to be stopped, which would cause alarm in the population. FSA would lose credibility and be held responsible for a wrong decision because they did not ensure that fortification was safe before introducing it. Important to consider whether potential harm to the many exposed to folic acid is outweighed by the benefits to the few. Conclude that if fortification is introduced the FSA has a duty to inform the public that, based on recent research, an increasing number of scientists have some doubt about whether folic acid is good for everyone, and this concern should be made public, particularly to those groups that could be at risk.

**Table 5: Health professional responses**

<b>HEALTH PROFESSIONALS INCLUDING ROYAL COLLEGES</b>			
<b>Respondent</b>	<b>Preferred options</b>	<b>Options rejected</b>	<b>Key points</b>
BDA	Options 2 & 4	No option rejected	Option 2 should be used alongside option 4 to continue to encourage supplement intake. This should be built into information and activities targeted at young people and back up by adequate training of professionals. Specific advice should be given to those groups that do not consume flour e.g. coeliacs Option 4 is the only effective way to redistribute the folic acid intakes and improve intakes. BDA supports fortification in line with the bread and flour regulations to allow consumer choice. Monitoring of possible high intakes in other groups of the population should occur.
BMA	Option 4	Option 1	Clear that current approach is not working. Recommend mandatory fortification of all flour, not just wheat flour as this will target ethnic minorities and those who cannot tolerate gluten. In order to mitigate against excessive folic acid intake and the associated risk of delayed diagnosis of B12 deficiency it is recommended that voluntary fortification is controlled and that a level of 300ug/100g if used for fortification.
IOB	Option 2	Option 4	Consider option 2 to be the most appropriate. Option 4 is not desirable given the lack of certainty regarding consumer choice of safe levels or of bread consumption between different sectors of the population.
MWF	Option 4	No option rejected	Support the introduction of fortification as experience has shown that advice of this nature is rarely heeded, particularly in deprived areas.
RCGP	Option 4	No option rejected	If mandatory fortification goes ahead there are various areas, which should be monitored. Also note that SACN have flagged up the possibility of B2 deficiency and this should be examined in greater detail before any recommendations can be made.
RCM	Options 1 & 2	No option rejected	Support option 1 but only in conjunction with option 2 as alone it would not be effective. Option 4 is unlikely to be fully effective and supplements would still need to be taken. Compulsory fortification runs counter to the notion that individuals must take personal responsibility for their own health. Costs to industry are also likely to be borne by consumers. Option 3 is unworkable because of the costs to industry and that they may be unwilling to voluntarily engage in the widespread fortification of foods. It might also result in some having a level of folate that is too high.

RCN	Option 4	No option rejected	Fortification of flour will result in the reduction in the incidence of neural tube defects. Introduction of such measures in other countries has yielded enormous benefits.
RCOG	Option 4	No option rejected	Health education strategies have failed to ensure that the majority of women take supplements preconceptionally and therefore would support fortification but with further research into the adverse population effects.
RCP	No preferred option	No option rejected	Fortification is appropriate considering flour is already adulterated although some might object to forced fortification. Concern that ethnic minorities who do not eat bread or coeliacs.
RCPCH	Options 2 & 4	No option rejected	Supports option 2 in so much that it is consistent with FSA's and DH's advice on healthy eating. Supports option 4 with measures to reduce voluntary fortification.

**Table 6: Government responses**

<b>GOVERNMENT INCLUDING OTHER COUNTRIES</b>			
<b>Respondent</b>	<b>Preferred options</b>	<b>Options rejected</b>	<b>Key points</b>
CDC	No preferred option	No option rejected	Not appropriate to use findings by Morris et al (2007) when formulating folic acid fortification policies in countries other than the USA.
EAC	Option 1 & 2	No option rejected	As folate is aimed at a specific area of the population, a combination of options 1 & 2 should take place. Mass medication of the population is questionable.
GFV	Option 4	No option rejected	There are substantial benefits of option 4 in terms of reduced numbers of NTDs. However, improved education campaigns should run alongside fortification. Essential to communicate to all of the risks and benefits and to communicate to industry, in particular artisan bread and pastry companies, the additional costs that might be incurred.
MP for Peterborough	Option 4	No option rejected	This method of increasing folate intakes in the target group will work and will ensure a reduction in the numbers of NTD pregnancies. Combined with controls on voluntary fortification, there will be a net benefit to the whole population, including older people. Evidence shows that rebalancing folate intakes in this way will result in no additional elderly people exceeding upper limits of folate. There has been no evidence from the US to suggest an increase in those diagnosed with B12 deficiency.
MSP (Dundee East)	Option 4	No option rejected	SNP supported the addition of folic acid in Scotland. Many pregnancies are unplanned and folic acid supplements are not taken. There is also evidence of a reduction in NTDs in other countries that have introduced this policy.
MSP (Green for Highlands and Islands)	Option 2	Options 3 & 4	Folate levels in food can be improved if the length of time between harvesting and consumption is reduced. Introducing fortification might dilute messages and awareness about the importance of good quality local food. Options 3 & 4 are more costly, increase B12 masking and bowel cancer and are unlikely to achieve the folate levels needed to reduce risk of NTDs.
MSP (SNP)	Option 4	No option rejected	SNP supported the addition of folic acid in Scotland. Many pregnancies are unplanned and folic acid supplements are not taken. There is also evidence of a reduction in NTDs in other countries that have introduced this policy.

NIFAC	No preferred option	Option 1	<p>There is an overwhelming view that action should be taken. Alternative options should be explored and pilot programmes developed such as the proactive prescription of supplements to non pregnant women.</p> <p>The majority supported mandatory fortification of most standard breads whilst a minority recommended the FSA increased efforts to encourage women to take folic acid supplements and change their diet to increase the consumption of folate rich foods. If mandatory fortification were to go ahead, the Agency should modify and monitor voluntary fortification.</p>
SFAC	No preferred option	Options 1 & 4	<p>Option 1 was deemed unsuitable.</p> <p>Option 2 should be enhanced with a specific campaign for hard to reach groups. However it should not be seen as a stop gap while waiting for further information to become available.</p> <p>Option 3 would be used for commercial gain and not health reasons and there are therefore dangers of over consumption.</p> <p>Option 4 was deemed unsuitable.</p>
WFAC	Option 4	No option rejected	<p>Option 4 was supported provided safeguards recommended by SACN were put in place. A continuing effort to increase awareness of the need for folate was also supported.</p>

**Table 7: Individual responses**

<b>INDIVIDUALS</b>			
	<b>Preferred options</b>	<b>Options rejected</b>	<b>Key points</b>
39 Individuals	Exemption for stone ground	No option rejected	Ensure that traditionally produced organic produced stone ground flour is exempt from fortification for the following reasons: - Young women are unlikely to be helped by additions to wholemeal flour - Older people who are at risk of B12 deficiency are significant consumers of this bread - Existing production processes do not easily allow for fortification - Existing exemption in bread and flour regs - Might result in cessation of production of this type of flour depriving consumers of healthy eating food source
Individual	Option 4	No option rejected	Options 1, 2 & 3 unsuccessful in achieving objective. The masking of vitamin B12 deficiency has been overstated
Individual	Option 2	No option rejected	Prefers option 2 although option 1 is also ok. Reports about people being allergic and having side effects to folic acid in food.
Individual	Option 2	Option 4	Do not agree with medicating population for the sake of a few women. An education campaign would be a good use of taxpayer's money.
Individual	No preferred option	Option 4	Important to be able to buy unadulterated bread. Voluntary approaches don't work and you cannot get sufficient folic acid even from a healthy diet. Folic acid could be added to bread where there is already other 'improvers' but some millers should be allowed to sell unadulterated bread.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 1 or 2	Option 4	No choice would be inflicted by mandatory fortification
Individual	Option 1 or 2	Option 3 & 4	Object to mass medication especially if non-target groups might be negatively affected. Prefer option 2 and suggest advice is issued through school curriculum. Also suggest folic acid supplements given away for free. Option 1 is also not unethical. Do not agree with option 3. If option 4 is chosen then only mass-produced white bread should be fortified.

Individual	Option 4	No option rejected	Favours option 4 as would target young women. Would also benefit other age groups
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	No preferred option	Option 4	Against mandatory fortification as concerned about detrimental effects later in life. Needs to avoid additives due to allergic reactions. 100% wholemeal flour should be avoided.
Individual	No preferred option	Option 4	No food should be adulterated with chemicals. Shouldn't medicate the majority for the benefit of the minority.
Individual	No preferred option	No option rejected	Concern about impact on osteoporosis and whether general negative effects on the elderly have been considered.
Individual	Option 2	Option 4	Mandatory fortification is a blunderous approach given the numbers of people it involves and would therefore remove choice. Prefer a structured education of pregnant women and free supply of folic acid supplements - option 2
Individual	No preferred option	Option 4	Food is already messed around with enough and folic acid should not be added.
Individual	Option 4	No option rejected	Support option 4 for the following reasons: - difficulty of achieving sufficient folic acid intake through diet alone - potential for reducing suffering and morbidity through reducing NTDs - value added to adult's health through increased consumption of folic acid
Individual	Option 2	Option 1, 3 & 4	Option 2 preferred. Option 1 is clearly not working and options 3 & 4 are too heavy handed nanny state.
Individual	Option 2	No option rejected	Choice for the majority should not be restricted. A price differential in favour of those foods with folate should be encouraged as well as targeted discounts/incentives offered to those women embarking on a pregnancy.
Individual	Option 4	No option rejected	Option 3 - concern about the quantity of food that would be fortified and whether government would subsidise and market it. Option 4 - Concern about risks to the population, consumer choice, medicating healthy people, concern about long term exposure to folic acid
Individual	No preferred option	No option rejected	Should consult arthritis bodies as folic acid can impact on those patients taking methotrexate

Individual	Option 4	No option rejected	Evidence from other countries shows significant reduction in incidence of NTDs following fortification. At appropriate level fortification with folic acid is safe for the majority. Products fortified voluntarily would be at a premium and would not reach the target group i.e. lower income women Most pregnancies are unplanned. Foods fortified with folic acid are bio available.
Individual	Option 4		Has a child with spina bifida as did not know she was pregnant until the first visit by the midwife.
Individual	No preferred option	Option 4	Nothing should be added to food until there is clear evidence of benefits and harmful effects.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Options 2 & 3	Option 1 & 4	More should be done to educate women about folic acid and manufacturers should be encouraged to increase number of products that have folic acid. These products should be clearly labelled. Option 1 is a non-starter as this is an important issue that needs to be addressed. Against mandatory fortification as there is no real benefit to the majority of the population and there is uncertainty about the long-term effects of increased folate intake.
Individual	Option 2	Option 3 & 4	Option 1 should include emphasis to ensure young women are aware that they should take folic acid 3 months before ending contraceptive pill use. Option 2 is preferred as diets are changing and people should be informed about the appropriate dietary choices such as eating folate rich foods and not eating foods such as green potatoes. Option 3 would require additional labelling and there is a risk of over dosage depending on level of fortification. Option 4 is not advisable as in the US there has been a decline in folate levels in women over last 8 years and the UK should not proceed until there is scientifically robust evidence for why things have gone wrong in the US.
Individual	No preferred option	No option rejected	White bread and frozen orange juice were best option in Australia for achieving demographic nutritional improvements.
Individual	No preferred option	Option 4	Biased to weigh the health of one group of people against the other. Is this for political gain?
Individual	Option 2	Options 3 & 4	As the majority of the population are not of childbearing age options 3 & 4 would take away freedom of choice from other members of the population. It would be more sensible to encourage women to take folic acid in advance of pregnancy.

Individual	Option 1	Options 2, 3, & 4	Option 1 targets the correct group and places responsibility on agencies that provide advice. It preserves freedom of choice. Option 2 is unacceptable because of the inclusion of 'a food fortificant'. Option 3 is only acceptable if fortified foods are provided at a uniform cost and are sufficiently available to those who need it. Option 4 is unacceptable due to the restrictions on consumer choice if all flour is fortified.
Individual	Option 2	Option 4	Consumers should have a choice of bread and flour and mandatory fortification might discourage some from eating a balanced diet. Deciding on an appropriate level of fortification might also be a problem. As many people have a mistrust of government initiatives raising awareness of low folic acid intakes might be more effective than forcing people to eat fortified bread.
Individual	Option 2	No option rejected	Should not fortify when the numbers of pregnancies with NTDs are still relatively small. Still learning about potential benefits and risks of folic acid for many other aspects of nervous system function, health and disease. Option 2 would target issue of NTDs in young women Option 3 leaves open possibility of choice for the public Option 4 would still require additional folic acid supplements to be taken and there is misunderstanding & under-estimation of potential long-term risks. Mandatory fortification is both diffuse and hugely disproportionate.
Individual	Option 4	No option rejected	Concerned about slow progress in UK on this issue considering all the evidence available to show the positive effect of fortification implementation in other countries on NTDs. The notion of harm of B12 deficiency is dated to the days prior to treatment of doses of folic acid without blood tests. The planned periconceptual folate option has proved impossible for the majority of at risk pregnancies.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	No preferred option	Option 4	There are no apparent health advantages for people in their 60s and a precautionary principle should be adopted. If this proposal is adopted then there should be a range of flours, bread and related foods that are not fortified.
Individual	No preferred option	Option 4	There are options other than fortification, which consider to be an extreme state response. For example there could be a tax on pure flour, or those products not fortified could be labelled as such.

Individual	Option 4	No option rejected	Evidence in the US and Canada shows a reduction in NTDs that is not observed in the same time frame in the UK. No evidence to support the hypotheses that folic acid may be harmful. It would be a very good idea if there was a requirement to also add vitamin B12 to flour. Seems strange that there is no option to add vitamin B12.
Individual	Option 4	No option rejected	Doubt that businesses will introduce fortification on a voluntary basis and if they do they will charge extra which means that the poorer households who need these products are unlikely to benefit.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 1	Options 3 & 4	Totally against mandatory fortification or addition of any substances to food as it masks B12 deficiency. Anything added to food must show a benefit to the whole population. If manufacturers want to add folic acid to food it should be clearly labelled.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4	No option rejected	Potential benefits outweigh any possible risks (in relation to anaemia in the elderly and bowel cancer).
Individual	Option 1	No option rejected	Support this option
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4	No option rejected	Flour is already fortified and mills already equip to add an extra nutrient and therefore mills could become birth defects and folate deficiency anaemia prevention factories.
Individual		Option 4	Food should not be interfered with, as there are already too many unnecessary additives. Adding folic acid will take away freedom of choice. For this reason, option 3 would be ineffective. Option
Individual	No preferred option	Option 4	The proposal to add folic acid to bread could be detrimental to a lot of people.
Individual	No preferred option	No option rejected	Depending on option chosen, various recommendations given regarding targeting those with epilepsy and young women.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid

Individual	Option 2	Options 1 & 4	Opposed to mass medication where the benefit is for such a small minority. However option 1 is not acceptable, as it does not address the issue appropriately. Option 3 is a possibility if uniform implementation and practical problems could be overcome. The drawbacks of option 2 would need to be evaluated after a fair trial and adjustments to the campaign.
Individual	Option 3	Option 4	Disapprove of the proposal to add folic acid as it takes away freedom of choice. One way to ensure choice is to encourage industry to fortify more foods voluntarily and that the products should be labelled.
Individual	Option 2	Option 1, 3 & 4	Option 4 runs counter to consumer choice and will be ineffective as there is no mechanism to force young women to consume bread. For the same reason, option 3 would be ineffective. Option 1 is evidently not working. Option 2 is the preferred option as it can be appropriately targeted and the results monitored by well-established survey methods.
Individual	Option 4	No option rejected	Option 4 is best way to stand up for rights of unborn child. Carry out screening for B12 deficiency in patients over 60 years Ensure food industry takes steps to reduce the risk of over-dosage of folic acid (margarines etc)
Individual	No preferred option	No option rejected	Consider it important for traditionally produced organic stone-ground flour to be excluded from any legislation requiring the addition of folic acid.
Individual	No preferred option	No option rejected	Concern that some older people might be disadvantaged since B12 could be masked and for this reason would like the exemption of traditionally produced organic stone ground flour.
Individual	Option 1 or 2	Options 3 & 4	Prefer option 1 but if it is considered necessary to make change then option 2 should be considered to reinforce existing advice. Option 3 should be rejected, as it will make it difficult for the consumer to know which products to choose, either basic ingredients or manufactured items. Adding it to all flour would remove consumer choice.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4		Support compulsory fortification of white flour with folic acid
Individual	Options 1 & 2	Options 3 & 4	Object to the mass medication of the population for the benefit of a few individuals.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4	No option rejected	As well as preventing NTDs, fortifying flour will virtually eliminate folate deficiency in the population. Minimal costs of this option.

Individual	Options 1 & 2	Option 4	Options 1 & 2 are only ones necessary. The number of elderly who could be adversely affected far outweighs the numbers of babies affected.
Individual	Option 2	Option 4	Concerned that entire population would be medicated, not just target group and it may set a dangerous precedent. Solution should be to address the problem of young women not taking supplements directly.
Individual	Option 4	No option rejected	Fortification would prevent unnecessary anxiety for pregnant mothers to whom the pregnancy came as a surprise.
Individual	Options 1 & 2	Option 4	To attempt to address the problem by dosing the whole population is inappropriate, particularly as young women will still be required to take folic acid supplements. Also the wider risks to the population in relation to cancer and vitamin deficiencies are not properly known.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 1	Option 2, 3 & 4	Option 1 is realistic and adequate for the vast majority of the population. Option 2 has cost implications, which may not attract commensurate benefits. Option 3 is a hit and miss approach and there would be cost implications to industry. Option 4 is unacceptable as it ignores the harm to some sectors of the population and it is morally unacceptable to medicate one sector of the population at the expense of another.
Individual	Option 1 or 2	Options 3 & 4	People should be allowed to make a choice about whether to eat products fortified with folic acid. It is unacceptable to medicate the whole population when the target group is such a small percentage. There are negative effects of folic acid in that it can mask vitamin B12 deficiency and folic acid can cause complications with anticonvulsant drugs for epileptics.
Individual	Option 1 or 2	Option 3 & 4	Content with current advice to continue or supplementary advice to be given although consider that advice should be emphasised to increase consumption of naturally folate rich foods rather than supplements. Consider that some groups might be harmed by a policy of voluntary fortification. There is no justification for mandatory addition of a drug to any foodstuff.

Individual	Option 2	Option 1, 3 & 4	Option 2 is a targeted and appropriate response to the issue. Options 1, 3, 4 would be ineffective in terms of failing to prevent the majority of NTDs. Reject option 3 & 4 as they are associated with number of scientific & ethical uncertainties & potential public health risks including: Increased risk of cancer, particularly colorectal cancer· Decreased cognitive function· Increased risk of compromised immunity· Lack of evidence of protection against coronary heart disease
Individual	Options 1 & 2	Options 3 & 4	Options 3 & 4 are too big an intrusion and manipulation with regard to the scale of the problem
Individual	Options 1 & 2	Option 4	Options 1 & 2 provide the most targeted and cost effective way forward. Option 4 is overkill for 900 babies affected per year.
Individual	No preferred option	Option 4	This option is abhorrent but if it did go ahead it only white sliced bread should be fortified. This option would also miss those from cultural backgrounds who do not consume bread.
Individual	No preferred option	Option 3 & 4	The whole population should not be force fed just because some women do not take supplements
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 2	Options 3 & 4	There should be an increased effort to encourage young women to take supplements. Options 3 & 4 take away consumer choice.
Individual	No preferred option	Option 4	Suffer from IBS and increasing intake of folic acid aggravated symptoms. Concern that products other than bread would be affected thus limiting choice further.
Individual	Option 2	Options 1, 3 & 4	Option 1 is currently failing and options 3 & 4 remove personal choice for little benefit
Individual	No preferred option	Option 4	Object to food being contaminated and concern that there are insufficient studies to show the long term effects of folic acid consumption
Individual	Option 4	No option rejected	The issue of B12 masking is spurious and the UK should implement fortification as soon as possible to reduce NTDs
Individual	Option 2	Option 4	Support option 2 with 1 & 3 next. Do not agree with mass medication under any circumstances.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 1	Option 2, 3 & 4	Continue with current policy, as government should not encourage one diet over another. Option 4 is completely immoral. Option 3 is immoral, as industry should not be encouraged to add anything to their foodstuffs.
Individual	Option 2	Options 3 & 4	Use of vitamin supplements where necessary should be encouraged. Both options 3 & 4 result in the speculative and unnecessary medication of involuntary recipients and set alarming precedents.

Individual	Options 1 & 2	Options 3 & 4	Options 1 & 2 should be supported. Option 3 should be left to the free market to respond to as it wishes. Option 4 should not be supported as it can trigger epileptic seizures and can cause problems with B12 deficiency. It is also impossible to calculate or estimate the intake of folic acid if it is in every flour product.
Individual	Option 4	No option rejected	Support compulsory fortification of white flour with folic acid
Individual	Option 4	No option rejected	Recommend mandatory fortification of flour at a fortification level of 300micrograms/100g flour. A number of suggestions for public education campaign: Integrating into regular sex education curriculum· Provide info in leaflet with contraceptive pills· Provide info leaflets in GP practices about folic acid and vitamin B12· Provide folic acid supplement (200micrograms) with contraceptive pill· Public needs to be informed about benefits of extra folic acid· Urgent need to educate over 40s and medical community about wide prevalence of vitamin B12 deficiency in the elderly. The estimation of risk of folic acid using presence or absence of megaloblastic anaemia in a B12 individual, as a criteria is obsolete. Need to monitor effects on population intakes & prevalence of symptoms associated with potential risks. The safe upper limit, which is based on masking of B12 deficiency, is obsolete. Recommend co-fortification with vitamin B12 (10 micrograms / 100 grams flour).
Individual	No preferred option	Option 4	The whole population should not be forced to ingest something against their will.
Individual	Option 4	No option rejected	Favour this option as other options have not worked and the young women that are hard to reach are most likely to have a low intake of folic acid.
Individual	Option 1	Option 4	Freedom of choice is most important issue
Individual	No preferred option	Options 1, 2 & 3	There is already a precedent in the UK for adding fortificants to food. Evidence from US and Canada shows that there has been a reduction in NTDs following introduction of mandatory fortification. Initial results from the US do not show any significant problems resulting from fortification. UK should continue to learn from and work closely with countries that have already carried out fortification.
Individual	No preferred option	Option 4	Concern about the effects on the rest of the population who are not pregnant. Danger that a precedent is being set.
Individual	Options 1 & 2	Options 3 & 4	No ingredients should be included whether voluntarily or by obligation for any other reason than the necessity of the product. There is no objection to options 1 & 2
Individual	Option 1	Option 4	Education is available to everyone should they choose to take it in. We cannot legislate for those who choose not to take advice. The current practice of advising women should remain in place.

Individual	Option 2	No option rejected	Option 2 is the best option although none of the options are likely to reduce NTDs
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**Table 8: Overview of views by groups and individuals**

	<b>Total number options</b>	<b>Option 1</b>	<b>Option 2</b>	<b>Option 3</b>	<b>Option 4</b>	<b>No option supported</b>
<b>Individuals</b>	<b>150</b>	<b>19 (13%)</b>	<b>31 (21%)</b>	<b>2 (1%)</b>	<b>37 (25%)</b>	<b>61 (41%)</b>
<b>NGOs</b>	<b>16</b>	<b>0 (0%)</b>	<b>3 (19%)</b>	<b>1 (6%)</b>	<b>10 (63%)</b>	<b>2 (13%)</b>
<b>Industry</b>	<b>33</b>	<b>3 (9%)</b>	<b>11 (33%)</b>	<b>7 (21%)</b>	<b>6 (18%)</b>	<b>6 (18%)</b>
<b>Health Professionals</b>	<b>13</b>	<b>1 (8%)</b>	<b>4 (31%)</b>	<b>0 (0%)</b>	<b>7 (54%)</b>	<b>1 (8%)</b>
<b>Government</b>	<b>11</b>	<b>1 (9%)</b>	<b>2 (18%)</b>	<b>0 (0%)</b>	<b>5 (45%)</b>	<b>3 (27%)</b>
<b>Academics</b>	<b>8</b>	<b>0 (0%)</b>	<b>2 (25%)</b>	<b>0 (0%)</b>	<b>4 (50%)</b>	<b>2 (25%)</b>
<b>Total</b>	<b>231*</b>	<b>24</b>	<b>53</b>	<b>8</b>	<b>69</b>	<b>75</b>

\*This number is greater than the total number of responses (200) as multiple options were supported

**Table 9: Table to show views on each option**

Option/ question	Comment	Respondent
<b>General comments</b>		
	Depending on option chosen, various recommendations given regarding targeting those with epilepsy and young women.	Individual
<b>Option 1 – do nothing</b>		
<b>For option 1</b>		
	Support this option	11 individuals
	This option should continue in the event of option 4	1 individual SRHSBs Waitrose
	Preserves freedom of choice	Individual
	Support this option combined with option 2 as alone it would not be effective	RCM
	This option if sufficient to address the problem, although could be combined with option 2 if necessary	1 individual SRSHBs Waitrose
	If this option is chosen there should be an emphasis on connecting the commencement of folic acid 3 months before cessation of the contraceptive pill.	1 individual SRSBHs Waitrose
	Option 1 is realistic and adequate for the vast majority of the population.	1 individual SRHSBs Waitrose
	Provides the most targeted and cost effective way forward	Individual

	This option should take place as folate is aimed at a specific area of the population	EAC
	The current advice of option 1 should be improved. In addition birth control pills cause a lowering of folic acid reserves in the body and women should be informed of this disadvantage.	SA
<b>Against option 1</b>		
	Current state of affairs is clearly not working	4 Individuals BMA
	Does not adequately address the problem	2 Individuals ABF MRC HNR NAMB FDF NCT NIFAC
	Ineffective as a means of increasing folate intake and therefore reducing NTD pregnancies in the UK.	ACFM SSBA
	Requires more proactivity than is currently undertaken and is therefore not acceptable.	FOB
	This option is unsuitable	SFAC
	No impact on flour milling sector or target population	NABIM
	Option 1 is not supported considering the significant proportion of women who do not plan their pregnancies or follow advice on supplementation.	NS
	Do not support as poor uptake of folic acid supplements among women prior to conception & because of unplanned pregnancies.	BNF
<b>Option 2 - Campaigns</b>		

For option 2		
	<p>Support this option for following reasons:</p> <ul style="list-style-type: none"> <li>- allows consumer choice</li> <li>- folate is aimed at a specific area of the population</li> <li>- avoids the risks to the elderly whilst acknowledging that young women of child bearing age would benefit from greater awareness of the benefits of folate.</li> <li>- consistent with FSA's and DH's advice on healthy eating.</li> <li>- education is key to achieving the objective</li> <li>- might be effective than fortification due to mistrust of government initiatives</li> <li>- directly addresses the problem of young women not taking supplements</li> <li>- most targeted and cost effective way forward</li> <li>- A combination of options 2 &amp; 3 should be used and this allows both supplementation and structured voluntary fortification with a higher level of targeted education. Food supplements deliver folic acid in small and accurate unit-dose forms.</li> <li>- should continue in the event of mandatory fortification</li> <li>- should continue regardless of option chosen</li> <li>- evidence to suggest that the HEA education campaigns in the 90s were successful in increasing awareness of the importance of folic acid supplementation. The Government is currently running an NHS Healthy Start Vitamins Scheme which is aimed at targeting those in minority groups and this scheme provides supplements to women throughout their pregnancies.</li> <li>- Important as women still need to take supplements</li> <li>- appropriate response to the issue</li> <li>- justified use of taxpayers money in place of mandatory fortification</li> <li>- This option addresses the issue of freedom of choice and will prevent any allergic or other adverse reactions</li> <li>- appropriately targeted and the results monitored by well established survey methods.</li> <li>- this option should be combined with option 3</li> </ul>	<p>22 Individuals  Foodaware  IOB  WFAC  EAC  HAS  RCPCH  CRN  SRHSBs  NABIM  NS  PAGB  ABF  Boots  BCCCA</p>
	<p>Suggest a more structured education campaign of pregnant women alongside a free supply of folic acid supplements</p>	<p>2 Individuals</p>
	<p>This option is preferable as dietary habits have changed over the year's thus increasing folate intake. However things such as consumption of green potatoes needs to be addressed.</p>	<p>Individual</p>

	The drawbacks to this option should be evaluated after a fair trial and adjustments to the campaign.	Individual
	If this option is chosen advice should emphasize consumption of naturally folate rich foods rather than supplements.	Individual
	Use of vitamin supplements where necessary should be encouraged.	Individual
	This option should be implemented by doing more through schools and GPs and educating women about eating folate rich foods. Supermarkets should also be encouraged to display messages on folate rich foods.	ACFM
	Should be used alongside option 4 to encourage supplement intake. Should be built into information and activities targeted at young people and backed up by adequate training of professionals. Specific information should be given to those groups who do not consumer flour e.g. coeliacs	BDA
	Although current campaigns are not working further campaigns should be pursued such as encouraging industry to display messages on folate rich foods and in supermarkets.	FDF
	Alternative options should be explored such as the proactive prescription of supplements to non pregnant women.	NIFAC
	This option should be enhanced with a specific campaign for hard to reach groups. However it should not be seen as a stop gap whilst waiting for further information to become available.	SFAC
	Folate levels in food can be improved if the length of time between harvesting and consumption is reduced. Introducing fortification might dilute messages and awareness about the importance of good quality local food.	MSP

	Options 2, 3 & 4 should be integrated except that those flours not already fortified should be exempt. Flours other than wheat should be considered for those who cannot or do not consume wheat. Appropriate labelling and information should be provided to avoid confusing messages. Flours from GM crops should be fortified but allowances made for exemptions and additions as public attitudes and abstentions develop.	VEGA
	Option 2 needs to continue and be developed although it is not the whole solution. Alongside education, retailers should be encouraged to highlight products which supply folic acid in the diet.	Waitrose
	Option 2 needs to be developed further in the meantime of any other decision. Crucially it needs to be better explained of the importance of taking folic acid supplements before pregnancies.	Which?
	A price differential in favour of those foods with folate should be encouraged as well as targeted discounts/incentives offered to those women embarking on a pregnancy.	Individual
	Support but only in conjunction with options 3 or 4.	BNF
	Targeted publicity techniques could be used more effectively than previous campaign (1996-99). Targeted campaign would only treat the targeted group and not the rest of the population.	Uni of Oxford
	Improved education campaigns are crucial alongside fortification	GFV
<b>Against option 2</b>		
	Option 2 has cost implications which may not attract commensurate benefits.	Individual
	Evidence shows that supplements are not necessarily the way to achieve an increased folate intake in the target group.	ACFM
	Experience shows that supplements are not necessarily the way to achieve an increase in folate intake in vulnerable women, as this requires proactivity and has an associated cost.	FDF

	Option 2 appears to have had limited success and has made little or no difference to the incidence of NTDs. There is no evidence to suggest that a more pro active or high profile campaign will encourage young women to take supplements and eat more folate rich foods. It takes a very long time to change public perceptions, attitudes and behaviours, therefore how long would a campaign have to run for.	NAMB
	Option 2 is not effective as it relies too heavily on consumer knowledge and awareness.	SSBA
	public education campaigns have been shown to be ineffective at sustaining supplement intake long term and although education campaigns should continue they are not acceptable as the only policy.	HPANI
	Evidence shows that campaigns are ineffective	IIFSBH
<b>Other</b>		
	Option 2 should be used in conjunction with option 4 but not on its own as it has been shown to be ineffective. Greater supplement intake might be achieved by the following: <ul style="list-style-type: none"> <li>- target high risk groups</li> <li>- work with families, peers and organisations providing access to these groups</li> <li>- include practical steps to make action easier</li> <li>- ensure that advice is embedded in a structure and delivered in a committed and relevant way</li> <li>- be sustained over a long period of time</li> <li>- using a health claim might make it easier for women to identify relevant foods and supplements.</li> <li>- develop wider messages and programmes targeted at young women from lower socio economic backgrounds</li> <li>- incorporating consistent messages in school nutrition programmes and incorporating nutritional advice and support into post-natal care.</li> </ul>	NCT
	A number of suggestions for public education campaign: <ul style="list-style-type: none"> <li>· Integrating into regular sex education curriculum</li> <li>· Provide info in leaflet with contraceptive pills</li> <li>· Provide info leaflets in GP practices about folic acid and vitamin B12</li> <li>· Provide folic acid supplement (200 micrograms) with contraceptive pill</li> <li>· Public needs to be informed about benefits of extra folic acid</li> <li>· Urgent need to educate over 40s and medical community about wide prevalence of vitamin B12 deficiency in the elderly.</li> </ul>	Individual

<b>Option 3 - Voluntary</b>		
<b>For option 3</b>		
	Manufacturers should be encouraged to increase the number of products with added folic acid. These products should be clearly labelled.	Individual
	Acceptable only if outlets are obliged to provide products at uniform cost and at sufficient availability to those who need them.	Individual
	A possibility if practical problems of industry co-operation and uniform implementation could be overcome.	Individual
	One way to ensure choice is to encourage industry to fortify more foods voluntarily and that the products should be labelled.	Individual
	Government should not be recommending one diet over another	Individual
	Would allow for changes in patterns of consumption and could be regulated through a best practice code. It would allow consumer choice. This option would need Government support due to the negative effects of increased intakes.	ABF
	Likely to be most effective as breakfast cereals contribute significantly to the diets of young women. Also allows for flexibility if patterns of consumption change. A best practice code should be drawn up to include foods recommended for fortification and by how much. The scope of this option would be restricted by legislation on addition of nutrients and derogations would be needed to overcome this.	ACFM
	Support this option combined with option 2	BCCCA
	By fortifying a wide range of staples any avoidance of a food group would be less likely to compromise folic acid intake. The fact that there are significant differences in bioavailability between foods and supplements must be taken into account. Folates in foods are much less bio available than folic acid in supplements and so to achieve a 400ug intake between 600ug and 800ug of folates might be required to be consumed.	CRN

	This option is likely to be effective in targeting the at risk group and industry would like to be able to continue to fortify in a responsible manner. There is some concern about the impact of the forthcoming regulation on addition of nutrients and also that the legal responsibility would fall on industry. This concern could be relieved by the appropriate setting of conditions.	FDF
	Options 2,3 & 4 should be integrated except that those flours not already fortified should be exempt. Flours other than wheat should be considered for those who cannot or do not consume wheat. Appropriate labelling and information should be provided to avoid confusing messages. Flours from GM crops should be fortified but allowances made for exemptions and additions as public attitudes and abstentions develop.	VEGA
	Allows consumer choice	Individual
	Voluntary folic acid should be restricted but not banned.	Individual
	Support this option although some restrictions and considerations may be necessary	BNF
	Evidence from other countries show that mandatory fortification can co-exist with voluntary fortification which is a valuable additional help in achieving the desired goal. No adverse effects have been detected in the USA during the 9 years in which their policy of joint mandatory and voluntary fortification have been in place. Fortified breakfast cereals benefit low folate consumers significantly more than other sources currently available. Breakfast cereals are a very minor contributor of excessive folic acid, relative to other sources for those aged 65 yrs and over.	Kellogg's
	The safety assessment regarding upper intakes is unrealistic and overly conservative.	ACMF
<b>Against option 3</b>		
	Too hit and miss as there is no mechanism to force young women to consume appropriate quantities of bread	2 Individuals

	Premium products would not reach young women	Individual ASBAH SSBA NS NCT
	Cost implications to industry	Individual RCM
	Takes away consumer choice	2 individuals
	Disproportionate response	2 individuals
	Nothing should be added to foodstuffs	2 individuals
	Industry unlikely to fortify on a wide scale	ASBAH RCM
	Dangers of over consumption in some groups and sets alarming precedents	SFAC 3 Individuals NCT Royal College of Midwives
	Used for commercial gain only	SFAC
	Has not been effective in other countries around the world	Foodaware
	Difficult to control and monitor	Foodaware SRHSBs
	Existing fortification is not having desired effect in terms of increasing intakes of folic acid	Waitrose
	Voluntary measures cannot offer sufficient safeguards in terms of dosage and monitoring and evaluation.	SSBA

	This option should be left to the free market to respond to as it wishes.	Individual
	This option will increase the risks of B12 masking and bowel cancer	MSP
	Unlikely to achieve the levels required to reduce numbers of NTDs	Individual MSP
	Should not be left to industry to decide which foods to fortify	NAMB
	HEA campaign to encourage fortification of baked goods, was unsuccessful	NAMB
	No indication of how over consumption can be prevented	NAMB
	Increased labelling would be required	Individual
	Difficult for the consumer to know which products to choose	Individual
	Very highly fortified foods, such as spreads, that have very variable intakes should not be allowed to be fortified with high levels.	Individual
	Associated with number of scientific & ethical uncertainties & potential public health risks	Individual
<b>Other</b>		
	Voluntary fortification would avoid problems associated with labelling and international trade and would allow consumer choice. However, it would be difficult to achieve widespread fortification which the Government desires.	NABIM
	Option 3 must take into account the need to control voluntary fortification. Also all foods fortified must be clearly labelled.	Which?
	Foods already fortified should be allowed to remain in place	Waitrose
	A policy for mandatory fortification should be supported by increased promotion of the importance of taking supplements before women become pregnant.	HFMA

<b>Option 4 - Mandatory</b>		
<b>For option 4</b>		
	Other options will be ineffective in reducing NTDs	2 Individuals
	Issue of masking of vitamin B12 has been overstated	4 Individuals Royal Free Hamsted SRHSBs
	Support compulsory fortification	20 Individuals HPANI 2 MSPs NAMB NCW Nutragen RCOG RCP Royal Free Hamsted
	May benefit other sectors of the population at an appropriate level	3 individuals BDF Foodaware HPANI IFSPH MP for Peterborough SRHSBs
	This action would be independent of choice variables in the target group.	Individual
	This option would increase intakes in the target group and reduce morbidity and suffering caused by NTDs	Individual ASBAH Boots Foodaware HPANI MP for Peterborough GFV

	It is difficult to achieve sufficient folic acid intake from diet alone	Individual Foodaware IFSBH
	Evidence from other countries shows significant NTD reduction following fortification with no adverse effects	3 Individuals BDF HFMA IFSBH MP for Peterborough 2 MSPs RCN SRHSBs
	50% of pregnancies are unplanned	3 Individuals BDF Boots BINOCAR HPANI 2 MSPs Nutragen SRHSBs
	Fortified foods are more bio available	Individual
	If fortified products are introduced voluntarily they are likely to be at a premium and will therefore not reach poorer households.	Individual IFSBH
	Benefits outweigh any possible risks	Individual
	Flour is already fortified so mills are equipped to add additional nutrients.	Individual
	Other options have not worked	Individual
	Young women that are hard to reach are most likely to have low intake of folic acid	Individual

	Support fortification conditional upon removal of voluntary fortification	Age Concern BMA NIFAC WFAC Foodaware HFMA MP for Peterborough MRC HNR NS RCPCH SSBA
	Alongside fortification efforts should be taken to monitor any health effects	Individual AC BDA HMFA NCT Waitrose
	There should be a policy review in 5 years.	AC
	The health of older people should be safeguarded by an awareness programme and warnings on supplements.	AC
	Would provide economic benefits	ASBAH
	No evidence of any harm	ASBAH
	Will effectively redistribute folic acid intakes	BDA MP for Peterborough MRC HNR
	Will allow consumer choice if fortification in line with the bread and flour regulations	BDA
	All flour should be fortified, not just wheat flour as this will target ethnic minorities and those who cannot tolerate gluten	BMA

	Only one staple food needs to be fortified and therefore only one sector of the food industry will be affected	Foodaware
	Specific Advice should be given to those at high risk	HPANI NCT
	Advice on supplementation is rarely heeded, particularly in deprived areas	MWC
	Would not impinge on consumer choice if added in line with current bread fortification legislation.	NCT
	Education strategies have failed to ensure women take supplements periconceptionally.	RCOB
	Two expert Committees (COMA and SACN) have come out in favour of mandatory fortification	SRHSBs
	Flour is a suitable vehicle for fortification	Waitrose
	Support fortification of flour except those that are not already fortified should be exempt.	VEGA
	Stands up for rights of unborn child	Individual
	Support fortification in bread for flour use. There would be a 'lag period' until fortification was implemented and this would allow proof of any unacceptable risk to emerge from the USA/Canada.	Individual
	Recommend mandatory fortification of flour at a fortification level of 300micrograms/100g flour.	Individual
	Evidence from US and Canada shows that there has been a reduction in NTDs following introduction of mandatory fortification. Initial results from the US does not show any significant problems resulting from fortification. UK should continue to learn from and work closely with countries that have already carried out fortification.	Individual
	There is evidence to show that health & economic gains of fortification far outweigh the losses for the US population & that an increase in the fortification level in the US deserves further consideration in order to maximise net gains.	RAND BC
<b>Against option 4</b>		

	Disproportionate response to the problem/oppose mass medication for the minority	16 individuals EAC Foodaware SA TCG
	Restricts consumer/freedom of choice	17 Individuals ABF Foodaware SA IOB RCM BNF
	Deals only with symptoms of a much larger problem	Individual
	Concern about effects on other sectors of the population, particularly those with allergies exacerbated by additives	Individual
	Oppose addition of additional substances to bread/food in general	5 individuals
	Oppose addition of substances to food unless there is clear evidence of benefits and harmful effects	Individual
	No real benefits to majority of population	Individual
	Decline in folic acid intakes in women in the US since introduction of mandatory fortification	individual SA
	Should not weigh health of one group against another	Individual
	Addition of folic acid might discourage some from eating a balanced diet	Individual
	A precautionary principle should be adopted	Individual
	There are no health advantages for people in their 60s	Individual
	Fortification can mask B12 deficiency	3 Individuals
	Any fortificant must demonstrate a benefit to the whole population	Individual

	May be negative effects of other sectors of the population	2 Individuals IOB
	This option will be ineffective as there is no mechanism to force young women to consumer bread.	Individual
	The number of elderly affected outweigh the number of babies affected	Individual
	Sets a dangerous precedent	3 Individuals
	Young women will still be required to take supplements	2 Individuals ABF RCM
	Risks about cancer and vitamin deficiencies are not properly known	Individual BCCCA
	Folic acid can cause complications with anti-convulsant drugs for epileptics and can trigger seizures and can aggravate the symptoms of IBS	3 Individuals
	Oppose mandatory fortification	2 individuals SFAC SA(supported by Doves, Shipton and FWP Matthews)
	Would miss those from cultural backgrounds who do not consume bread	Individual RCP
	No studies to show long term studies of folic acid consumption	Individual Soil Association
	Impossible to calculate or estimate the intake of folic acid if it is in every flour product	Individual

	Cost to various sectors of the industry (labelling, installing new streams)	ABF ACFM BCCCA FDF TCG BNF
	Contrary to public health messages on consumption of whole grains.	ACFM
	Against spirit of harmonisation in the EU/barrier to EU trade	ACFM CRN
	Disadvantage UK biscuit and cake manufacturers against European competitors	BCCCA FDF
	Concern about effects on multiple births	BCCCA
	Unlikely to achieve the levels required to reduce numbers of NTDs	MSP
	Bolster health image of nutritionally poor processed foods	SA
	Cochrane Review concludes that there is insufficient evidence to demonstrate whether folic acid supplementation has either a positive or negative effect on the unborn baby	SA
	Fortification forces consumption of artificial substances. SACN admit that there are concerns about the safety of high intakes of synthetic folic acid but that natural folate is safe.	SA
	There are also concerns about folic acid being produced from genetically modified sources.	SA
	Some women have a mutation that reduces the body's ability to metabolise and retain folic acid and this may account for the 200 cases of NTDs per year.	SA
	Costs are likely to be borne by consumers	RCM

	Threaten integrity and artisan craft of traditional products	TCG
	Concern that negative impacts on the elderly population, in particular those suffering from osteoporosis, will not be considered	Individual
	Still learning about potential benefits and risks of folic acid for many other aspects of nervous system function, health and disease.	Individual
	Associated with number of scientific & ethical uncertainties & potential public health risks	Individual
	Support mandatory fortification alongside monitoring of certain areas.	RCGPs
	Insufficient knowledge of possible harmful effects. Some evidence of potential harm was published after SACN report. Control of voluntary fortification and advice about supplement use are restrictions on consumer choice and would be very difficult to achieve. Will cause confusion if public told they MUST take folic acid supplements for pregnancy but MUST NOT take at any other time. If mandatory fortification is implemented then monitoring (as recommended by SACN) is essential but concerned that it will be rejected by government as too expensive.	Uni of Oxford
	Also problem of liability. If folic acid increases the incidence of cancer then fortification would have to be stopped, which would cause alarm in the population. FSA would lose credibility and be held responsible for a wrong decision because they did not ensure that fortification was safe before introducing it. Important to consider whether potential harm to the many exposed to folic acid is outweighed by the benefits to the few.	Uni of Oxford
<b>Other</b>		
	If mandatory fortification is enforced only white bread should be fortified	Individual
	If mandatory fortification is enforced non-fortified flour/other non-fortified products should be available	2 individuals

	Organic produced stone ground flour/small traditional millers should be exempt from fortification	41 individuals HW FWHM TCG SA
	Continue fortifying voluntarily but within a voluntary code of practice	ACFM FDF
	The FSA should have discussions at EU level if the decision is taken for mandatory fortification.	FDF
	Various surveillance programmes should be put in place to mediate the risks of B12 deficiency/risks to the general population	FDF RCOG Foodaware
	White bread and frozen orange juice were best option in Australia for achieving demographic nutritional improvements.	Individual
	If mandatory fortification is enforced it should be done at flour milling stage/in line with Bread and Flour Regulations	FOB NABIM NAMB Waitrose
	If fortification is introduced the FSA has a duty to inform the public that, based on recent research, an increasing number of scientists have some doubt about whether folic acid is good for everyone, and this concern should be made public, particularly to those groups that could be at risk.	Uni of Oxford
	Industry should be informed of any additional costs which may be incurred.	GFV

	<p>Although not qualified to comment on mandatory fortification, the following should be taken into account:</p> <ul style="list-style-type: none"> <li>- BRC members agree that the most appropriate legislative tool to encompass any new requirement would be the bread and flour regulations.</li> <li>- Flour is more suitable technologically. If bread were chosen a premix would be required and it is likely miscalculations could occur. There are also 50 flour mills against 4000 bakeries so flour fortification would mean that monitoring and enforcement were easier.</li> <li>- Retailers would be willing to discuss reformulation of products currently fortified with folic acid.</li> <li>- Declaration of folate and other vitamins on the ingredients list of all products containing flour could be misleading for the consumer depending how much flour is in the product.</li> <li>- Mandatory fortification will have a big impact of imports and exports. It will be difficult to get suppliers in countries such as France (who are against fortification) to reformulate the batches they produce for export to the UK. Ireland is a particular concern as it would be detrimental for BRC members to end up with different fortification schemes in the two countries.</li> <li>- There is concern about the messages that will be allowed in light of the legislation on nutrition and health claims and believe that an education campaign is crucial</li> <li>- A scheme for monitoring vitamin B12 deficiency should be introduced.</li> <li>- Detailed guidelines should be published alongside any decision taken by Ministers.</li> </ul>	BRC
	<p>If option 4 is to go ahead, the following should happen first:</p> <ul style="list-style-type: none"> <li>- better understand the relationship between folic acid levels and cancer risk</li> <li>- practicalities of limiting folate intakes below 1mg per day</li> <li>- a process for monitoring vitamin B12 deficiency in older people needs to be established.</li> <li>- ensure consumer choice can be maintained.</li> </ul>	Which?
	Cost implications of mandatory fortification need to be considered	Boots
	The needs of those who cannot eat bread needs to be addressed.	Foodaware HFMA Waitrose VEGA
	Suggest a slightly broader fortification target might be required	Nutragen
	Flours from GM crops should be fortified but allowances made for exemptions and additions as public attitudes and abstentions develop.	VEGA

	If manufacturers want to add folic acid to food it should be clearly labelled to avoid confusing messages	Individual VEGA
	Only white sliced bread should be fortified if this option were to go ahead	Individual
	There are options other than fortification which consider to be an extreme state response. For example there could be a tax on pure flour, or those products not fortified could be labelled as such.	Individual
	The FSA should address food production processes such as the Chorley Wood bread-making process which results in reduced levels of natural folate. Need to consider other methods to improve folate levels in food including: - choosing suitable agricultural cereal varieties as folate levels are highly effected by the choice of variety. - production of white flour removes almost half the naturally present folate. - Chorley-Wood process which has an accelerated fermentation process decreases the health benefits of bread. - blanching/freezing operations can destroy up to 50% of folic acid levels. - folic acid is destroyed by food irradiation. - the issue of green potatoes needs to be addressed.	SA
	It would be a very good idea if there was a requirement to also add vitamin B12 to flour.	Individual
	Recommend co-fortification with vitamin B12 (10 micrograms per 100g flour).	Individual
	Emerging evidence should be taken into account	BNF
	Not appropriate to use findings by Morris et al (2007) when formulating folic acid fortification policies in countries other than the USA.	CDC
	Also note that SACN have flagged up the possibility of B2 deficiency and this should be examined in greater detail before any recommendations can be made.	RCGP

**Table 10: Overview of views on each option**

<b>Option 1</b>	<b>Numbers</b>	<b>Percentages</b>
For	28	56%
Against	20	40%
Other	2	4%
Totals	50	
<b>Option 2</b>		
For	37	80%
Against	7	15%
Other	2	5%
Totals	46	
<b>Option 3</b>		
For	11	21%
Against	37	71%
Other	4	8%
totals	52	
<b>Option 4</b>		
For	125	39%
Against	115	36%
Other	80	25%
totals	320	

## SCIENTIFIC RESPONSES RECEIVED TO CONSULTATION ON FOLIC ACID

Respondent	Option	Comments	FSA Response
Individual	Not stated	<p>Concerned that paper by Morris et al (2007)<sup>1</sup> and editorial by Smith (2007)<sup>2</sup> has serious flaws and the findings have little relevance to the issue of folic acid fortification.</p> <p>The study by Morris et al suggests that older people with the combination of high serum folate levels (&gt;59 nmol/L) and low vitamin B12 status were more likely to have cognitive impairment.</p> <p>Several potential flaws in study</p> <ul style="list-style-type: none"> <li>• Small size of group with high folate &amp; low B12 status (n=42) &amp; lack of sufficient other info about these participants to determine whether cognitive impairment could have been due to some underlying disease.</li> <li>• As an observational study (where folic acid intake not randomised) there are inherent methodological issues from unmeasured confounding because individuals in the highest level group are likely to be supplement users and those in the lowest group are unlikely to be supplement users. Supplement users have important health related differences compared to non-supplement users.</li> <li>• Failure to consider relative contribution of different sources of folic acid which include supplements and all fortified foods, including breakfast cereals.</li> <li>• 20% of participants had serum folate levels greater than 50 nmol/L. Unlikely that such high levels are easily achievable from consuming folic acid fortified foods anywhere consumption of breakfast cereals low.</li> </ul> <p>Feel these points should be addressed before findings from this study are generalised to the entire USA senior population with low vitamin B12 status.</p> <p>Important to consider dosage and consider that such high levels are associated with supplement use and not from fortification</p> <p>Not appropriate to use findings by Morris et al (2007) when formulating folic acid fortification policies in countries other than the USA.</p>	This paper and editorial were published after the SACN report.

<sup>1</sup> Morris MS, Jacques PF, Rosenberg IH, Selhub J. Folate and vitamin B12 status in relation to anemia, macrocytosis, and cognitive impairment in older Americans in the age of folic acid fortification. *Am J Clin Nutr* 2007;85:193-200.

<sup>2</sup> Smith AD. Folic acid fortification: the good, the bad, and the puzzle of vitamin B12. *Am J Clin Nutr* 2007;85:3-5

Respondent	Option	Comments	FSA Response
Royal College of General Practitioners	4	<p>Suggest following areas should be monitored:</p> <ul style="list-style-type: none"> <li>• NTD conceptions, including terminations, before and after fortification</li> <li>• Intrauterine growth retardation before &amp; after fortification</li> <li>• Bowel cancer diagnoses before &amp; after fortification</li> <li>• Undertake cohort study of B12 &amp; folate status in subjects aged 55y, perhaps over 25y period. Study should monitor serum B12, serum methylmalonic acid, serum homocysteine, serum and red blood cell folate as well as cognitive decline and CVD events. College would welcome opportunity to be involved of such a cohort study and envisage that one of the 8 new GP research networks that government planning to establish could take on this study</li> </ul> <p>Fortification may have generally beneficial effect on cognitive decline but tackling problem of B12 deficiency at the same time would have larger impact.</p> <p>Also note that SACN have flagged up the possibility of B2 deficiency and this should be examined in greater detail before any recommendations can be made</p>	<p>The SACN report notes that improved systems are required for ascertainment of NTD-affected births and terminations. The report recommends that mandatory fortification should be accompanied by careful monitoring of emerging evidence of postulated adverse effects, including cancer and that the evidence on benefits and risks should be reviewed after a period of 5 years.</p> <p>The SACN recommends the development of a clinical strategy to manage issue related to vitamin B12 deficiency irrespective of a decision on mandatory fortification</p>
Individual	4	<p>Some additional points to above response from RCGP.</p> <p>From consumer research it can be seen that most important points raised by general public are that government will be expected to :</p> <ul style="list-style-type: none"> <li>• Stand up for rights of unborn child – option 4 best way to do this</li> <li>• Carry out screening for B12 deficiency in patients over 60 years</li> <li>• Ensure food industry takes steps to reduce the risk of over-dosage of folic acid (margarines etc)</li> </ul> <p>General public less aware that:</p> <ul style="list-style-type: none"> <li>• Serum B12 may not be a reliable test for a screening programme</li> <li>• Genetic testing may soon be cheap enough to be available to GPs for testing those at highest risk of NTD</li> </ul> <p>Suggests:</p> <ul style="list-style-type: none"> <li>• A cohort study of B12 &amp; folate status in subjects aged 55y and followed for 25 years (see above response from RCGP) would be more useful than a screening programme although both could run in parallel.</li> <li>• Encourage GPs already appointed as regional Genetics GPs with special interest to develop testing service for women with history of previous NTD conceptions.</li> </ul>	

Respondent	Option	Comments	FSA Response
Individual	2	<p>Unwise to fortify bread or flour for whole nation on behalf of the relatively small numbers of pregnancies with NTDs when:</p> <ul style="list-style-type: none"> <li>• Still learning about potential benefits and risks of folic acid for many other aspects of nervous system function, health and disease.</li> <li>• Other options which could target issue of NTDs in young women (option 2) or leave open possibility of choice for the public (option 3)</li> <li>• It would still be necessary to encourage additional folic acid supplements after fortification to achieve protection from NTDs.</li> </ul> <p>There is also misunderstanding &amp; under-estimation of potential long-term risks. Attention drawn to following points:</p> <ul style="list-style-type: none"> <li>• Although 'masking' can occur in presence of B12 deficiency, long term use of folic acid can lead to deterioration of neurological &amp; haematological consequences of vitamin B12 deficiency</li> <li>• Risks in presence of vitamin B12 deficiency increase with dose but especially duration of folic acid supplementation.</li> <li>• Long term risks for patients with epilepsy</li> <li>• Little understanding of the role of folate and methylation in epigenetics (switching genes on and off), therefore unwise to expose everyone to excessive amounts over prolonged periods.</li> </ul> <p>For all above reasons recommend option 2. This would have to be done whether or not there is mandatory fortification. Mandatory fortification is both diffuse and hugely disproportionate.</p>	<p>SACN considered the potential risks in great detail.</p> <p>SACN concluded that the overall evidence regarding the effect of high folate intake together with vitamin B12 deficiency is inconclusive.</p> <p>As above.</p> <p>The SACN report concluded that fortification would not have adverse effects on patients with epilepsy.</p> <p>SACN's recommendation for mandatory fortification is with the proviso that voluntary fortification is reduced and guidance is given on supplement intake so that long-term individual intakes are not increased.</p>
Individual	Not stated	<p>Following recommendations offered for consideration:</p> <ul style="list-style-type: none"> <li>• Commission study to look at number of people with epilepsy who would be adversely affected by mandatory fortification, which is likely to affect the effectiveness of anti-epileptic drugs.</li> <li>• Reframing sex education classes to include advice on how to avoid birth defects, in addition to how to avoid pregnancy. Recommend learning material which provide info</li> </ul>	<p>SACN found no evidence of adverse effects of folic acid on anti-epileptic medication at levels used for fortification.</p>

Respondent	Option	Comments	FSA Response
		<p>on how risks of birth defects vary with vegetable intake.</p> <ul style="list-style-type: none"> <li>• Mandatory fortification of 'junk food' breads only (e.g. buns &amp; baps in fast food chains, highly refined white bread etc) as this would help to target women with unhealthy diets.</li> <li>• Offer some financial assistance to Epilepsy Action as primary information provider for people with epilepsy.</li> <li>• Doctors do not provide folic acid to young women put on anti-epileptic medication. Ask GMC or BMA if it would be good practice for all doctors to issue folic acid to women of childbearing age when they are put on anti-epileptic drugs for the first time, or for a warning to be put on drugs that are likely to cause NTDs..</li> </ul>	
RAND Corporation	Not stated	<p>Enclosed manuscript<sup>3</sup> of paper (currently being reviewed) which provides evidence supporting increased concentrations of fortification in the USA as well as in countries like the UK that have yet to fortify.</p> <p>Annual burden of disease, quality adjusted life years (QALYs) and costs were projected for 4 scenarios: 0, 140, 350, 700 mcg of folic acid per 100g enriched flour. Analysis considered four health outcomes: NTDs, myocardial infarction (MI), colon cancer, masking symptoms of B12 deficiency.</p> <p>Results showed that with increasing levels of fortification, greatest benefits predicted in MI prevention. Also reduction in cases of colon cancer and NTDs but increase in cases of B12 masking. Compared with no fortification, fortification strategies provided QALY gains and costs savings for all subgroups.</p> <p>Study concluded that health &amp; economic gains of fortification far outweigh the losses for the US population &amp; that an increase in the fortification level in the US deserves further consideration in order to maximise net gains.</p>	<p>This modelling is based on the assumption that increased folate intake is beneficial in terms of reducing MI and colon cancer. Relative reductions for MI<sup>4</sup> and colon cancer<sup>5</sup> are based on results from one study for each outcome.</p> <p>The SACN report concluded that overall there is insufficient evidence to show a link between folic acid and CVD or cancer.</p>
British Nutrition Foundation		<p>Concerned that research in the area of folates &amp; cancer still emerging. Also, recent data suggests that while folate may protect against cognitive decline in older people replete in vitamin B12, it accelerates decline in those with low B12 status. Suggest therefore that pros and cons of proceeding with mandatory fortification need to be carefully weighed in</p>	

<sup>3</sup> TGK Bentley, MC Weinstein, WC Willett, KM Kunst. Cost-Effectiveness Analysis of Folic Acid Fortification Policy in the United States

<sup>4</sup> Rimm EB, Willett WC, Hu FB et al. Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart disease among women. JAMA 1998;279:359-64.

<sup>5</sup> Giovannucci E, Stampfer MJ, Colditz GA et al. Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study. Ann Intern Med 1998;129:517-24.

Respondent	Option	Comments	FSA Response
		<p>light of emerging evidence as there is currently no evidence from RCTs designed to consider cancer to inform these decisions. Also, the tolerable upper intake level is based on vitamin B12 and does not take account of more recently highlighted concerns about colon cancer. May be prudent to delay any decision until such information becomes available.</p> <p>However if option 4 goes ahead on basis of the clear relationship between folates &amp; NTDs, it should be combined with option 2.</p> <p>Another issue is consumer concern about the impact of mandatory fortification on choice &amp; also issues for food industry. Therefore if option 4 perceived as too premature/problematic than support combination of option 2 &amp; 3.</p> <p><u>Option 1:</u> Do not support as poor uptake of folic acid supplements among women prior to conception &amp; because of unplanned pregnancies.</p> <p><u>Option 2:</u> Not adequate in isolation but would be a necessary adjunct to either option 3 or 4.</p> <p><u>Option 3:</u> To avoid intakes exceeding UL would be important to achieve control over which foods are fortified &amp; levels of folic acid in supplements. Combined with option 2, this option has potential for success, however:</p> <ul style="list-style-type: none"> <li>• Motivation of millers, manufacturers and retailers to voluntarily fortify food may be limited.</li> <li>• If this option selected, still important to follow SACN's recommendations of monitoring folate status &amp; potential benefits and adverse effects.</li> <li>• Would need to target foods eaten by women in socio-economically deprived areas. Pricing may be an issue if these foods are more expensive than non-fortified options.</li> </ul> <p><u>Option 4:</u> Research concerning folate &amp; cancer still emerging so maybe premature to proceed with mandatory fortification.</p> <p>With regard to B12, seems to be complex interplay, e.g. folate may protect against cognitive decline in people who are folate replete but accelerate decline in those with low B12 status.</p> <p>Some sectors of food industry expressed concern about potential requirement to stop fortification as many products are manufactured for a global market that does not have</p>	<p>SACN's recommendation not to increase intakes and to monitor etc was to address the point that evidence in this area is uncertain.</p> <p>SACN considered the evidence regarding vitamin B12 and cognitive health in great detail and concluded</p>

Respondent	Option	Comments	FSA Response
		restrictions on folic acid fortification.	that overall there was insufficient evidence to suggest beneficial or harmful effects of folate in relation to cognitive health.
Individual	2	<p>This option represents that which is most consistent with the nature of the issue, i.e. targeted response to address a presumed congenital malformation in at-risk women.</p> <p>Targeted response appropriate. This option has not been adequately resourced and provides a safer and more effective alternative to monitor and evaluate.</p> <p>Reject options 1, 3, 4 because they would be ineffective in terms of failing to prevent the majority of NTDs.</p> <p>Reject option 3 &amp; 4 as they are associated with number of scientific &amp; ethical uncertainties &amp; potential public health risks including:</p> <ul style="list-style-type: none"> <li>• Increased risk of cancer, particularly colorectal cancer</li> <li>• Decreased cognitive function</li> <li>• Increased risk of compromised immunity</li> <li>• Lack of evidence of protection against coronary heart disease</li> </ul> <p>Also yet to see if folic acid supplementation in utero may result in phenotypic changes in</p>	<p>It has been shown from countries with mandatory fortification policies that mandatory fortification has been effective in reducing NTD affected pregnancies by 27-50%</p> <p>SACN's recommendation not to increase intakes and to monitor etc was to address the uncertainties with regard to cancer risk.</p> <p>SACN noted that the overall evidence regarding benefits and risks of folic acid on cognitive function was inconclusive.</p> <p>1 cross-sectional study<sup>6</sup> has found evidence suggesting altered immune function. This study was considered in the SACN report.</p>

<sup>6</sup> Troen AM, Mitchell B, Sorensen B, et al. Unmetabolized folic acid in plasma is associated with reduced natural killer cell cytotoxicity among postmenopausal women. J Nutr 2006;136:189-94.

Respondent	Option	Comments	FSA Response
		<p>offspring as recently seen in the agouti gene murine experiments</p>	<p>This point was noted by SACN and mandatory fortification was not recommended on these grounds.</p> <p>These findings are from animal studies. Currently no evidence of this in humans.</p>
Kellogg's	Combination of 3 & 4	<p>Evidence from other countries show that mandatory fortification can co-exist with voluntary fortification which is a valuable additional help in achieving the desired goal.</p> <p>Prudent path would be to follow policies proven to be safe &amp; effective, most notably USA. The amount of folic acid added to products ranges from 95-309 mcg/100g of product, which is based on a target level of 140mcg/100g cereal-grain product. No adverse effects have been detected in the USA during the 9 years in which their policy of joint mandatory and voluntary fortification have been in place.</p> <p>Fortified breakfast cereals benefit low folate consumers significantly more than other sources currently available. Breakfast cereals are consumed by people of all socioeconomic status, in relatively consistent daily amounts. Only breakfast cereals make a meaningful contribution to folic acid intakes of women in the lowest quintile intake groups. Therefore not meaningful to group together all fortified sources when considering their ability to deliver controlled amounts of folic acid. This needs to be taken into account when considering the level of fortification in bread &amp; flour based products.</p> <p>Compared with other sources, breakfast cereals make a relatively small additional contribution of folic acid to women with already higher intakes. Other sources of folic acid make a bigger contribution to those with higher intakes.</p>	<p>The modelling carried out by SACN indicated that mandatory fortification alongside current voluntary fortification would increase the number of people with folic acid intakes above safe levels and the number of older people with low vitamin B12 status and intakes above 1mg/day.</p> <p>The SACN report noted that no adverse effects had been reported following mandatory fortification in the USA; however no formal monitoring systems were put in place following the introduction of mandatory fortification.</p> <p>The SACN modelling showed that for women of childbearing age in the lowest and second lowest quintile of folate intake, natural folate was the main contributor to total folate intakes (95% &amp; 91% respectively). Folic acid from breakfast cereals contributes to 5% of total folate intake for the lowest quintile (compared to 0% from fortified spreads &amp; supplements) and</p>

Respondent	Option	Comments	FSA Response
		<p>Breakfast cereals are a very minor contributor of excessive folic acid, relative to other sources for those aged 65 yrs and over.</p> <p>Breakfast cereals are highly effective means of delivering additional folic acid within relatively narrow range of intake. Number of portions typically eaten is 1 or 2 per day. Most Kellogg cereals provide modest but meaningful amounts of folic acid, typically 25% RDA per serving. By exception some Kellogg products with an adult female bias provide 50% RDA per serving.</p> <p>Including folic acid intakes from supplements in risk management not appropriate as leads to management policy which protects supplement takers by restricting their intake of fortified foods, which disadvantages those that are in need of extras folic acid.</p>	<p>9% to the second lowest quintile (compared to 0% from fortified spreads and 1% from supplements).</p> <p>Although breakfast cereals make a smaller contribution to folic acid intake of the highest quintile (15% compared to 17% for fat spreads &amp; 20% from supplements), they make a greater contribution to the 2<sup>nd</sup> highest quintile of intake (18% compared to 6% for fat spreads and 2% from supplements).</p> <p>Both fortified breakfast cereals and fortified fat spreads make a greater contribution to the free-living adults aged 65y and over (14% and 13% respectively) compared to supplements (6%).</p>
Individual	Modified option 4	<p>Support modified option 4 – recommend mandatory fortification of flour at a fortification level of 300mcg/100g flour. Ideal if all flour, including wholemeal, were fortified and small quantities of unfortified flour of all types could be made available to provide consumer choice. Do not support fortification of only bread making flour as monitoring compliance by milers is simpler &amp; less expensive.</p> <p>A number of suggestions for public education campaign:</p> <ul style="list-style-type: none"> <li>• Integrating into regular sex education curriculum</li> <li>• Provide info in leaflet with contraceptive pills</li> <li>• Provide info leaflets in GP practices about folic acid and vitamin B12</li> <li>• Provide folic acid supplement (200 mcg) with contraceptive pill</li> <li>• Public needs to be informed about benefits of extra folic acid</li> <li>• Urgent need to educate over 40s about wide prevalence of vitamin B12 deficiency in the elderly.</li> </ul> <p>Need to educate medical community for increased vigilance in early detection of B12</p>	

Respondent	Option	Comments	FSA Response
		<p>deficiency in the elderly and about more reliable tests for estimation of B12. The understanding that megaloblastic anaemia of vitamin B12 deficiency is masked due to increase in folic acid intake is scientifically incorrect &amp; hence the estimation of risk of folic acid using presence or absence of megaloblastic anaemia in a B12 individual, as a criteria is obsolete.</p> <p>Need to monitor effects on population intakes &amp; prevalence of symptoms associated with potential risks. The safe upper limit which is based on masking of B12 deficiency is obsolete. The new upper limit should be based on risk of cancer development.</p> <p>Recommend co-fortification with vitamin B12 (10 mcg per 100g flour) for a number of reasons including:</p> <ul style="list-style-type: none"> <li>• Vast majority of elderly suffer from mild B12 deficiency which could be easily reversed with low level co-fortification. Clinicians would be required to remain vigilant in detecting B12 malabsorption due to pernicious anaemia &amp; other causes, which requires larger doses of B12 for its management.</li> </ul>	<p>Anaemia does not always occur in vitamin B12 deficiency but is a common symptom. SACN's recommendations include the development of more reliable diagnostic tests to identify vitamin B12 deficiency.</p> <p>The SACN report noted that there is currently insufficient evidence for an adequate risk assessment of folic acid and cancer risk or the intake levels which might be associated with risk.</p> <p>The SACN report noted that as active absorption of vitamin B12 is usually impaired in older people, approximately 1% is absorbed by passive diffusion. This means that a dietary intake 400 times greater than the recommended amount (1.5mcg) may be needed to correct vitamin B12 deficiency. This may not be a feasible option as the as effect of population exposure to such high doses of vitamin B12 is unknown.</p>
Professor John Scott	4	<p>Requirement for mandatory fortification should apply to flour for bread use.</p> <p>The target figure for consumption of extra folic acid in USA following mandatory fortification was an extra 100 mcg/day. Crucial issue would be to ensure that UK extra intake of folic acid/day mirrored the USA/Canada ongoing intakes as close as possible. While initially there was a lot of 'overage' there, this practice has now become much less</p>	

Respondent	Option	Comments	FSA Response
		<p>widespread.</p> <p>A higher level of fortification than used in USA/Canada would not be accepted. If 300 mcg/100g of flour accepted, this will breach the UL in a lot of the population, even if voluntary fortification is banned. If 300 mcg is chosen then this would result in the recommendation not being accepted.</p> <p>If mandatory fortification is agreed in the UK, it would not be expected to be in place until 2010, which would mean it would follow 12-14 years experience of mandatory fortification in the USA/Canada. Although the 'lag period' for a risk such as accelerating cancer growth cannot be predicted, might expect to see it for colon cancer over a decade. Having this 12-14 year buffer provides a valuable dimension and appropriate action can be taken to halt fortification if proof of unacceptable risk should emerge from the USA/Canada. This would only apply if the same level of fortification is used here as in the USA.</p> <p>The target level for optimum prevention of NTDs (400 mcg/day) could not be achieved by mandatory fortification. Elimination of choice to use a food rather than a tablet to meet any shortfall would be unacceptable as a public health measure. Voluntary folic acid should be restricted but not banned. Need an appropriate range of foods that will make small contribution to recommended intakes. Very highly fortified foods, such as spreads, that have very variable intakes should not be allowed to be fortified with high levels.</p> <p>Taking supplements is an elective practice. Unfair that people who decide to take folic acid supplements ought to be able to interfere with general public health policy.</p>	<p>The SACN modelling estimated that a fortification level of 300 mcg/100g flour (excluding wholemeal flour and folic acid from fortified foods and supplements) would lead to an extra 78 mcg/day of folic acid. At this level, compared to current levels, there would not be an increase in the number of people exceeding the UL or the number of adults aged 65 years and over with low vitamin B12 status exceeding 1mg/d of folic acid.</p>
Individual	4	<p>As well as preventing NTDs, fortifying flour will virtually eliminate folate deficiency in the population. The costs of this option are minimal, including regulatory costs. Population studies in the USA have shown that the number of people with severe folate deficiency was reduced by 92%, which is a benefit since severely deficient persons can also have anaemia.</p> <p>In order to prevent excessive overage, recommend that a required target level of folic acid per 100g flour is set rather than minimum and maximum amounts.</p>	<p>The SACN report noted that mandatory fortification would also benefit the folate status of other population groups in the UK.</p>

<sup>7</sup> United States Department of Agriculture

Respondent	Option	Comments	FSA Response
		<p>Info obtained from 2 companies providing premix to millers, based on analysis of 7000 flour samples tested between 2002-5, found overage to be approx 4%. USDA<sup>7</sup> sampling found overage to be 10%. This result shows that millers seek to minimize the amount of added premix in order to keep costs down. Millers in the USA have met requirement for folic acid in fortified foods by adding the minimum amount needed to achieve the food standard.</p>	
Individual	4	<p>Whilst there remains debate about the extent of the benefit of the increase in terms of increased serum folates &amp; reduced serum homocysteine, the evidence that fortification will prevent more CVD than birth defects is quite strong having been observed post fortification in the United States and Canada and not observed in the same time frame in the UK. Current evidence can reasonably be interpreted to mean that the lack of folic acid fortification has harmed in the last 10 years, tens of thousands of citizens in the UK who die too early from folic acid preventable CVD.</p> <p>Suggest white &amp; brown flour be fortified. Recommend fortification at 2.5 ppm.</p> <p>There are no safety issues with fortification. No evidence to support the hypotheses that folic acid may be harmful.</p> <ul style="list-style-type: none"> <li>• Hundreds of studies in the USA before fortification suggestive of folic acid preventing colon cancer &amp; case control studies which provide strong evidence against folic acid causing cancer. These studies have not identified risk.</li> <li>• If there is an issue of cognitive harm for people with low B12 concentrations and high folate levels, then this relates to supplements. Fortification should not be delayed because of a possible problem with supplements.</li> <li>• Paper by Morris et al (2007) shows that concern about folic acid fortification masking anaemia is completely unwarranted as anaemia is 2.7 times as frequent among those with B12 deficiency as it is in those with normal B12.</li> </ul>	<p>SACN carefully considered the evidence on the association between folic acid and CVD and concluded that there was currently insufficient evidence of benefit to recommend mandatory fortification of flour with folic acid on this basis.</p> <p>SACN noted that some of the evidence re safety of high intakes is equivocal.</p> <p>SACN examined the evidence on the association between folic acid in cancer in considerable detail. SACN concluded that the evidence for a link between folic acid and increased or reduced cancer risk is not clear and that there is currently insufficient evidence for an adequate risk assessment or the intake levels of folic acid which might be associated with risk. Therefore SACN recommended that there should not be a substantial increase in average</p>

Respondent	Option	Comments	FSA Response
		<p>It would be a very good idea if there was a requirement to also add vitamin B12 to flour. Seems strange that there is no option to add vitamin B12. If people consumed synthetic vitamin B12 from fortified flour than most would increase their serum B12.</p>	<p>population intakes.</p> <p>SACN concluded that although there are indications of possible benefit of folic acid on cognitive function, the overall evidence on beneficial or deleterious effects is presently inconclusive.</p> <p>Not clear why this observation suggests that masking is unwarranted.</p> <p>SACN noted that as active absorption of vitamin B12 is usually impaired in older people, about 1% is absorbed by passive diffusion. This means that a dietary intake 400 times greater than the recommended amount (1.5 mcg) may be needed to correct vitamin B12 deficiency. This may not be a feasible option as the effect of exposure to such high doses of vitamin B12 is unknown.</p>
Individual	2	<p>Targeted publicity techniques could be used more effectively than previous campaign (1996-99), e.g. paying particular attention to TV. Publicity campaign could emphasise a good diet overall not just folic acid supplementation. Targeted campaign would only treat the targeted group and not the rest of the population where there is little evidence that it will do good but increasing evidence that it may harm.</p> <p>Reject option 4 for following reasons:</p> <ul style="list-style-type: none"> <li>• Insufficient knowledge of possible harmful effects. Some evidence of potential harm was published after SACN report. Particularly relevant in relation to cancer.</li> <li>• Control of voluntary fortification and advice about supplement use are restrictions on consumer choice and would be very difficult to achieve.</li> <li>• Will cause confusion if public told they MUST take folic acid supplements for</li> </ul>	<p>Countries that have implemented policies which rely on advice to take folic acid supplements have not been effective at reducing NTD rates. Also, about half of all pregnancies in this country are unplanned which limits the effectiveness of advice.</p>

Respondent	Option	Comments	FSA Response
		<p>pregnancy but MUST NOT take at any other time.</p> <p>If mandatory fortification is implemented then monitoring (as recommended by SACN) is essential but concerned that it will be rejected by government as too expensive. More relevant monitoring strategy is to check folate &amp; vitamin B12 status in relation to health &amp; disease in population. Programme supporting such research should be established immediately &amp; independently of the option chosen. 5 particularly relevant areas for research:</p> <ul style="list-style-type: none"> <li>• Children – In USA group with highest blood folate levels after fortification are children up to 11 years.</li> <li>• Elderly – prone to low B12 status &amp; combination of low B12 &amp; high folate may be of concern</li> <li>• Vegetarians – data from India suggest children of vegetarian mothers with low B12 &amp; high folate levels when pregnant are at higher risk of developing obesity &amp; insulin resistance. Highly likely scenario for vegetarians in the UK if fortification introduced.</li> <li>• Cancer – in view of possible dual role of folate, essential that there is accurate monitoring of cancer incidence if mandatory fortification is introduced.</li> <li>• Antifolates – important to monitor usage &amp; efficiency of antifolates as fortification may lead to increased prescriptions either because folate-dependent diseases are exacerbated or existing doses are inadequate.</li> </ul> <p>Also problem of liability. If folic acid increases the incidence of cancer then fortification would have to be stopped, which would cause alarm in the population. FSA would lose credibility and be held responsible for a wrong decision because they did not ensure that fortification was safe before introducing it.</p> <p>Important to consider whether potential harm to the many exposed to folic acid is outweighed by the benefits to the few. Growing evidence that raises concern in relation to: unmetabolised folic acid in blood, natural killer cells, interaction with vitamin B12 deficiency, insulin resistance, cancer promotion, interaction with environmental &amp; genetic factors, anti-folate drugs, gene regulation &amp; epigenetics.</p>	<p>No data to suggest high intakes of folic acid have any adverse effects on children.</p> <p>Research in this area is presently inconclusive/</p> <p>As the study to support this suggestion has not yet been published in a peer-reviewed journal, caution should be exercised in its interpretation.</p> <p>SACN's recommendation stipulates that mandatory fortification should only be introduced if there are measures for careful monitoring of postulated adverse effects, including cancer.</p>

Respondent	Option	Comments	FSA Response
		<p>Conclude that if fortification is introduced the FSA has a duty to inform the public that, based on recent research, an increasing number of scientists have some doubt about whether folic acid is good for everyone, and this concern should be made public, particularly to those groups that could be at risk.</p>	<p>SACN's risk assessment considers evidence relating to postulated harmful effects in great detail and recognises the uncertainties in the evidence. This is why SACN recommended that mandatory fortification should only be introduced if voluntary fortification is reduced and guidance is provided on supplement use. This will lead to a redistribution of folic acid intakes - increasing intakes of low consumers and decreasing intakes of high consumers.</p>
The Soil Association	2	<p>Support option 2 to improve diet &amp; promote much greater consumption of whole foods &amp; less refined processed foods; this would also address many serious public health problems that are affecting far more people than NTD births that are also partially caused by unsuitable diets: obesity, cancer, constipation, behavioural problems, heart disease etc.</p> <p><u>Option 1</u> Understand there has already been an enormous reduction in NTD birth in the UK by 96% since 1974. Since there are only around 200 NTD births each year, current food &amp; health advice policies can be considered largely successful. Whilst sensible to continue with advice, difficult to see that this would further reduce the remaining 200 cases. Current advice to young women should be improved. Birth control pills are major cause of lowered folic acid body reserves so women should be informed of this and given clear choice of contraception.</p> <p><u>Option 2</u> Not convinced supplementation is effective. Cochrane Review of 21 studies on folic acid concluded "<i>not enough evidence to evaluate whether folic acid supplementation has any</i></p>	<p>SACN have estimated that there are approximately 700-900 NTD affected pregnancies per year in the UK.</p> <p>Unaware that birth control pills are a major cause of lowered folic acid. Reference not provided to support this</p>

Respondent	Option	Comments	FSA Response
		<p><i>effect, beneficial or harmful, on clinical outcomes for mother and baby”.</i></p> <p><u>Option 3</u> Do not support any approach which is essentially mass medication. Also unconvinced that fortification is effective (see above). Feel it is unethical that fortification forces many people to consume significant amounts of the synthetic version of folate for their whole lives.</p> <p>Uncontrolled approach, which causes some people to consume excessive amounts of folic acid. Already a significant number in the UK are consuming more than the upper limit (1mg/day) due to consumption of fortified cereals. Increasing voluntary fortification would increase this number even further.</p> <p>Particular concern over risk of masking vitamin B12 deficiency in elderly people.</p> <p>Concerned about long term effects of fortification. SACN also admits that there are concerns over the safety of high intakes of synthetic folic acid.</p> <p>FSA should take account of new scientific evidence that many vitamin supplements (A, beta-carotene &amp; E) cause an increase in mortality &amp; do not produce the health benefits found for the natural phytonutrients in diet.</p> <p>Concerned about future possibility of folic acid being produced from genetically modified sources.</p> <p>Should be a public education campaign to raise awareness of the poor general nutritional quality of industrial food and encourage people to eat a more whole food, less processed diet.</p> <p><u>Option 4</u> Completely oppose to this option. Measure would only be targeted at a very small number of people: the 200 babies born with NTD each year &amp; their mothers. Clearly not</p>	<p>Reference not provided for this Cochrane Review. Unclear which clinical outcomes they refer to. The SACN report noted that there is conclusive evidence from randomised controlled trials that folic acid supplementation can prevent NTDs.</p> <p>Mandatory fortification has been shown to be effective in reducing the incidence of NTD-affected pregnancies in countries with mandatory fortification policies (by 27-50%).</p> <p>This is why SACN are suggesting mandatory fortification (with restrictions on voluntary fortification) as this is a more controlled approach and will reduce the numbers with intakes above 1mg/day..</p> <p>The SACN report notes that this is not a concern at levels up to 1mg/day.</p> <p>The SACN report recommends that there should not be a substantial increase in the folate intakes/status of the population. This is why SACN have proposed that mandatory fortification should only be introduced if it is accompanied by action to reduce folic acid intakes from voluntarily fortified foods.</p> <p>SACN carefully assessed the risks specifically associated with folic acid.</p>

Respondent	Option	Comments	FSA Response
		<p>necessary for the rest of the population. NDNS shows that average folate intakes are above RNI for all age groups, with marginal intake only for young women &amp; elderly. Would not be ethical to force millions who do not need this treatment to take folic acid.</p> <p>Note that USA took the route of mandatory fortification in 1998, but in Jan 2007 US Centers for Disease Control (CDC) reported that there had been an 8-16% decline in folate levels of women of child bearing age in 1999-2004.</p> <p>Some women have mutation that reduces the body's ability to metabolise and retain folic acid. This may account for a proportion of the remaining 200 NTD cases in which case fortification would have little effect.</p> <p>Concerned that this would bolster image of processed food &amp; could be used by food industry to promote fortified white flour as healthy. Should not give the message that a diet dominated by processed foods can be healthy.</p> <p>Option would reduce consumer choice. It would not be right to impose mandatory fortification on the organic food sector. If mandatory fortification is adopted, request that organic flour is excluded on grounds that this would not fit organic principles. Would also request that wholemeal bread is excluded.</p> <p>Welcome proposal to give guidance on food supplements.</p> <p><u>Proposal for programme to improve folate levels in food.</u> Provide number of suggestions to increase folate levels in foods, including consideration of suitable agricultural cereal varieties and discouraging blanching-freezing operations and food irradiation.</p> <p>Need to address the selling of green potatoes as there is well established connection between green potatoes and NTD incidence.</p>	<p>SACN have estimated that there are approximately 700-900 NTD affected pregnancies per year in the UK. The SACN modelling estimated that approximately 23% of the UK population currently have folate intakes below the RNI.</p> <p>Reason for this decline unclear. CDC suggest it could be due to changes over time in proportion of women taking folic acid supplements, decreased consumption of foods rich in natural folates or foods fortified with folic acid, or variations in amounts of folic acid added to enriched grain products since fortification was mandated. However, CDC report that evidence to support these explanations is mixed.</p> <p>The SACN report notes that approx 30% of NTD-affected pregnancies may not be responsive to folic acid intake. Other factors such as previous history of NTD-affected pregnancy, inherited variations in genes controlling folate metabolism,</p>

Respondent	Option	Comments	FSA Response
			<p>maternal weight and diabetes also influence NTD risk.</p> <p>Unaware of this evidence. Reference not given to support this.</p>
IFR	Not stated	<p>Support desire to reduce NTDs in the target population &amp; appreciate effectiveness of a whole population strategy to achieve this purpose. However recommend caution in this approach given the low target group &amp; the potential for systemic exposure to unmetabolised folic acid which may provoke deleterious effects. Following reasons for concern:</p> <p><u>Folic acid and cancer</u>  A new paper<sup>7</sup> that post-dates SACN considerations, reports that high folate intake results in an increased risk of colon tumours among men with the adenomatous polyposis coli APC gene. Another new paper<sup>8</sup> suggests that a high intake of folate 'generally attributable</p>	<p>Both these studies are observational studies which have inherent limitations. Folate intake was self-</p>

<sup>7</sup> De Vogel S, van Engeland M, Luchtenborg M et al. Dietary folate and APC mutations in sporadic colorectal cancer. J Nutr. 2006; 136:3015-3021.

<sup>8</sup> Stolzenberg-Solomon RZ, Chang SC, Leitzman MF et al. Folate intake, alcohol use, and postmenopausal breast cancer risk in the prostate, lung, colorectal, and ovarian cancer screening trial. Am J Clin Nutr. 2006. 83:895-904.

Respondent	Option	Comments	FSA Response
		<p>to supplemental folic acid' increases the incidence of breast cancer in postmenopausal women.</p> <p>SACN report notes (para 256) that 'there is no evidence to suggest that folic acid fortification would reduce the efficacy of anti-folate chemotherapy' however SACN noted that a post-hoc analysis of 2 RCTs reported that folic acid (even at 1mg/d) significantly reduced the response of rheumatoid arthritis to treatment with anti-folate methotrexate (para 251).</p> <p><u>Folic acid &amp; its inter-relationship with effects of vitamin B12 deficiency</u> The SACN report's conclusion (para 478) that the prevalence of low vitamin B12 status in</p>	<p>assessed by questionnaires. In the first study (Netherlands), high (natural) folate intake from food was not associated with overall colorectal cancer risk. However, in men, it reduced the risk of APC<sup>-</sup> colon tumours but increased the risk for APC<sup>+</sup> tumours. Folate intakes ranged from 163 mcg/day in the lowest quintile to 280 mcg/d in the highest quintile. (Participants had relatively low intakes of folate as fortification is not permitted in the Netherlands). These associations were not found in women. In the second study, folate from fortified foods alone and natural folates were not associated with postmenopausal breast cancer. Women with supplemental folic acid intakes ≥400 mcg/day had a greater risk of postmenopausal cancer than women not taking folic acid supplements. The SACN report noted that the evidence for a link between folic acid and increased or reduced cancer risk in humans is equivocal.</p> <p>In para 251, the SACN report also</p>

<sup>9</sup> Morris MS, Jacques PF, Rosenberg IH, Selhub J. Folate and vitamin B12 status in relation to anemia, macrocytosis, and cognitive impairment in older Americans in the age of folic acid fortification. *Am J Clin Nutr* 2007;85:193-200.

<sup>10</sup> Pfeiffer CM, Caudill SP, Gunter EW et al. Biochemical indicators of B vitamin status in the US population after folic acid fortification: results from the National Health and Nutrition Examination Survey 1999-2000.

<sup>11</sup> Eussen SJ, de Groot LC, Clarke R et al. Oral cyanocobalamin supplementation in older people with vitamin B12 deficiency: a dose-finding trial. *Arch Intern Med*. 2005. 165:1167-1172.

<sup>12</sup> Sweeney MR, McPartlin J, Scott JM. Folic acid fortification and public health: Report on threshold doses above which unmetabolised folic acid appear in the serum. *BMC Public Health*. 2007. &:41.

Respondent	Option	Comments	FSA Response
		<p>older people over 65 years is 5-10% (mainly due to age-related food cobalamin malabsorption rather than the pernicious anaemia) is an underestimate &amp; at odds with the recent American estimate of 10-30%.</p> <p>SACN concentrated on published research which only represented the response to vitamin B12 supplementation of an extreme minority of patients who had absolute vitamin B12 deficiency related to food-cobalamin malabsorption (para 213). Their conclusion (para 482) that only a high fortification level of vitamin B12 (400 mcg/d) could benefit those suffering from food-cobalamin malabsorption is challenged. This is at odds with the American Institute of Medicine recommendation that those over 50y should meet their requirements by obtaining 2.4 mcg/d of vitamin B12 from dietary supplements (or 'free B12').</p> <p>In some cases B12 insufficiency (rather than folate insufficiency) may play a role in NTDs, low level supplementation/fortification with 'free B12' may assist in the overall reduction of NTDs.</p> <p>Though the SACN report noted (para 369) a study of elderly US subjects that found high folate intake was associated with a faster rate of cognitive decline, SACN concluded that 'the evidence for either beneficial or deleterious effects of folic acid or vitamin B12 therapy on cognitive function in older people is presently inconclusive'. A new paper<sup>9</sup> that postdates the report, appears to confirm that in older Americans with low vitamin B12 status, high serum folate is associated with accelerated decline.</p> <p><u>Other effects</u> The SACN report (paras 260 &amp; 261) notes that unmetabolised folic acid has been found in the systemic circulation of Americans after the introduction of mandatory fortification. Its summary (para 264) infers this is due to oral doses above 260 mcg/d, despite SACN noting (para 259) a small pilot study where doses of 100 mcg/d were given 1 hour apart &amp; folic acid appeared after the second dose in all subjects.</p>	<p>notes that both these RCTs were not designed to test the effect of folic acid on methotrexate efficacy &amp; that there were a number of differences between the studies, including disease duration and use of non-steroidal anti-inflammatory drugs. One of the studies also did not have a placebo group.</p> <p>This estimate was based on a combined data from 3 studies based on measurements of serum concentrations of vitamin B12 (defined as &lt;150pmol/L or 200pmol/L and homocysteine &gt;20 µmol/L). A study in the US<sup>10</sup> reported the prevalence of low vitamin B12 status in elderly persons as 3% using a cut-off for serum B12 of &lt;148pmol/L and 7% with a cut-off of 185 pmol/L.</p> <p>SACN's conclusion that a only a high fortification level could benefit those suffering from food malabsorption was based on a dose finding study<sup>11</sup> of oral supplementation with vitamin B12.</p> <p>There is conclusive evidence from RCTs that folic acid can reduce NTD risk. SACN did not consider the evidence for vitamin B12 and NTD</p>

Respondent	Option	Comments	FSA Response
		<p>Recently hypothesised that human liver is initial site of folic acid biotransformation and that this may become saturated with regular daily intakes of quite modest doses of folic acid. This may result in its chronic appearance in the systemic blood system and may have implications inter alia for (i) DNA methylation &amp; modulation of gene expression, cancer, anti-folate chemotherapy (ii) the interrelationship with the effects of vitamin B12 deficiency (iii) immune function (iv) hyperplasia (v) embryo selection (vi) multiple births following IVF treatment. Because there is such a paucity of good quality research addressing the putative effects of unmetabolised folic acid in relation to the above, do not believe a soundly-based benefit/risk analysis could currently be undertaken.</p>	<p>reduction.</p> <p>SACN's conclusion was based on the balance of the evidence in this area. The new paper which appeared after the SACN report is an observational study and as such has inherent limitations. This paper has been criticised by researchers from the Centers for Disease Control and Prevention in the USA. See first entry in table for their comments regarding the limitations of this study.</p> <p>The pilot study described by SACN was too small (n=4) to draw conclusions. Another study<sup>12</sup> (n=19) published after the SACN report examined the effect of consuming bread fortified with folic acid at 3 different levels (400, 200, 100 mcg) over 1 week at each level. After presaturation with 400 mcg/d supplements of folic acid for 14 wks, the dose was administered in 2 equal-sized pieces of bread, 4 hours apart. Unmetabolised folic acid was detected after the 14-week supplementation period. It was not found in either the 100 or 200 mcg doses tested but was present at the highest level (400 mcg).</p> <p>SACN noted that the long term effects are unknown and recommend measures for careful monitoring of emerging evidence on the effects of long-term exposure. They also</p>

Respondent	Option	Comments	FSA Response
			<p>recommend that there should be no substantial increase in mean intakes in the folate status of the population. This is why SACN's recommendation includes the proviso that mandatory fortification should only be reduced if it is accompanied by controls on voluntary fortification. This will ensure a more even distribution of folic acid across the UK population and decrease the numbers with high intakes.</p>

**COST BENEFIT ANALYSIS RESULTS TABLES (AS STATED IN THE PARTIAL RIA)****Important notes regarding the following four summary results tables (Tables 1-4):**

1. Each of the following four tables contains a different set of assumptions behind it: the fortification of wholemeal flour is either included or excluded, and the continuation of the voluntary fortification of breakfast cereals and fat spreads is either included or excluded.
2. All numbers in each table have been calculated and then rounded to the nearest pound or unit, and are measured relative to a baseline that includes all current sources of folate and folic acid (including estimates of overage).
3. Please also note that Economics Branch are considering feedback relating to increased benefits to those calculated below as: reduced costs of NTD-sufferer home/vehicle adaptations are yet to be included; as well as the potential to account for an intrinsic value of living element into this work (as the developing Value of Life literature now suggests). Consideration as to the salience and feasibility of quantifying any additional cost of welfare losses to consumers strongly averse to mandatory folic acid fortification is also under review; not fortifying wholemeal flour reduces this salience.

**Important note regarding which table (and policy option) is most salient:**

4. Assuming that wholemeal flour is not fortified in order to preserve consumer choice:
5. Following their conclusions regarding carcinogenicity, SACN recommend restricting voluntary fortification, thus delivering no likely increase in consumers with a folic acid intake above the upper limit (UL) of 1mg/day. This minimises the potential for any carcinogenic effects as a result of the mandatory fortification of flour. The cost-benefit results for this scenario are presented in Table 1; note that the net monetary benefits (and reduced NTD prevalence) presented in this table are less than in Table 2, which assumes no restriction of voluntary fortification.

6. However, the Agency (and SACN) considers that the restriction of voluntary fortification is the best balance to strike given the uncertainty surrounding carcinogenic effects. Indeed, the Agency considers it appropriate to invoke the Precautionary Principle when seeking to avoid increased folic acid consumptions above the defined upper limit, which is defined in the Green Book<sup>1</sup> as: “The concept that precautionary action can be taken to mitigate a perceived risk. Action may be justified even if the probability of that risk occurring is small, because the outcome might be very adverse”. The UK Interdepartmental Liaison Group on Risk Assessment (UK-ILGRA)<sup>2</sup> considers that, amongst other things, the Precautionary Principle should be invoked when the level of scientific uncertainty about the consequences or likelihood of the risk is such that the best available scientific evidence cannot assess the risk with sufficient confidence to inform decision-making.
7. Table 1, which assumes that wholemeal flour is not fortified and excludes the fortification of breakfast cereals and fat spreads, is therefore the most appropriate table to consider.

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<sup>1</sup> See <http://greenbook.treasury.gov.uk/glossary.htm>

<sup>2</sup> See <http://www.hse.gov.uk/aboutus/meetings/ilgra>

**Table 1: RESULTS TABLE ASSUMING WHOLEMEAL FLOUR IS NOT FORTIFIED, AND EXCLUDING FOLIC ACID FROM VOLUNTARILY FORTIFIED BREAKFAST CEREALS AND FAT SPREADS**

Fortification rate (micrograms per 100g flour)	Category of life saved	Number of cases within this category	Monetary benefit per individual in this category	Total monetary benefit for all individuals of this category
300	Still birth / neo natal death	11	£881,940	£9,340,338
	Spina bifida with standard life expectancy	8	£486,816	£3,707,875
	Terminations	59	£542	£31,866
			<b>Total benefit:</b>	<b>£13,080,079</b>

Fortification rate (micrograms per 100g flour)	Total number of lives saved	Total monetary benefit associated with these lives saved	Total costs	Net benefit
0	-70	-£11,890,981	£0	-£11,890,981
100	-14	-£2,378,196	£178,520	-£2,556,716
200	35	£5,945,490	£347,040	£5,598,450
300	77	<b>£13,080,079</b>	<b>£515,560</b>	<b>£12,564,519</b>
450	126	£21,403,766	£768,340	£20,635,426

**Table 2: RESULTS TABLE ASSUMING WHOLEMEAL FLOUR IS NOT FORTIFIED, AND INCLUDING FOLIC ACID FROM VOLUNTARILY FORTIFIED BREAKFAST CEREALS AND FAT SPREADS**

Fortification rate (micrograms per 100g flour)	Category of life saved	Number of cases within this category	Monetary benefit per individual in this category	Total monetary benefit for all individuals in this category
300	Still birth / neo natal death	16	£881,940	£13,828,553
	Spina bifida with standard life expectancy	11	£486,816	£5,489,581
	Terminations	87	£542	£47,178

**Total benefit: £19,365,312**

Fortification rate (micrograms per 100g flour)	Total number of lives saved	Total monetary benefit associated with these lives saved	Total costs	Net benefit
BASELINE - 0	0	£0	£0	£0
100	42	£7,134,589	£178,520	£6,956,069
200	82	£13,929,435	£347,040	£13,582,395
300	114	<b>£19,365,312</b>	<b>£515,560</b>	<b>£18,849,752</b>
450	163	£27,688,998	£768,340	£26,920,658

**Table 3: RESULTS TABLE ASSUMING WHOLEMEAL FLOUR IS FORTIFIED AND EXCLUDING FOLIC ACID FROM VOLUNTARILY FORTIFIED BREAKFAST CEREALS AND FAT SPREADS**

Fortification rate (micrograms per 100g flour)	Category of life saved	Number of cases within this category	Monetary benefit per individual in this category	Total monetary benefit for all individuals of this category
300	Still birth / neo natal death	12	£881,940	£10,189,460
	Spina bifida with standard life expectancy	8	£486,816	£4,044,955
	Terminations	64	£542	£34,763

**Total benefit: £14,269,177**

Fortification rate (micrograms per 100g flour)	Total number of lives saved	Total monetary benefit associated with these lives saved	Total costs	Net benefit
0	-70	-£11,890,981	£0	-£11,890,981
100	-7	-£1,189,098	£187,447	-£1,376,545
200	42	£7,134,589	£364,893	£6,769,695
300	84	<b>£14,269,177</b>	<b>£542,340</b>	<b>£13,726,837</b>
450	140	£23,781,962	£808,510	£22,973,452

**Table 4: RESULTS TABLE ASSUMING WHOLEMEAL FLOUR IS FORTIFIED AND INCLUDING FOLIC ACID FROM VOLUNTARILY FORTIFIED BREAKFAST CEREALS AND FAT SPREADS**

<b>Fortification rate (micrograms per 100g flour)</b>	<b>Category of life saved</b>	<b>Number of cases within this category</b>	<b>Monetary benefit per individual in this category</b>	<b>Total monetary benefit for all individuals in this category</b>
300	Still birth / neo natal death	17	£881,940	£15,284,190
	Spina bifida with standard life expectancy	12	£486,816	£6,067,432
	Terminations	96	£542	£52,144
			<b>Total benefit:</b>	<b>£21,403,766</b>

<b>Fortification rate (micrograms per 100g flour)</b>	<b>Total number of lives saved</b>	<b>Total monetary benefit associated with these lives saved</b>	<b>Total costs</b>	<b>Net benefit</b>
BASELINE - 0	0	£0	£0	£0
100	47	£7,983,944	£187,447	£7,796,498
200	91	£15,458,275	£364,893	£15,093,382
300	126	<b>£21,403,766</b>	<b>£542,340</b>	<b>£20,861,426</b>
450	175	£29,727,452	£808,510	£28,918,942

