The Role of Folate and Flour Fortification to Reduce the Risk of Neural Tube Defect-affected Pregnancies in Europe: An Advocacy Summary

Executive Summary

Neural tube defects (NTDs) affect an estimated 4500 pregnancies in the European Union (EU) and 320,000 newborns on an annual basis worldwide. According to 2006-2010 data from EUROCAT, a network of registries that provides surveillance for congenital anomalies in Europe, 76% of NTD-affected pregnancies in countries that report terminations were aborted. Folate (vitamin B9) plays an important role in cell division and in DNA synthesis and methylation. Thus, sufficient folate is essential during early pregnancy when embryonic growth and development occur rapidly. Though the causes of NTDs are not fully understood, many studies have shown that folic acid, the form of folate in supplements and fortified foods, decreases the risk of NTDs when consumed during the periconceptional period (two months before conception and throughout the first trimester of pregnancy). Fortifying flour with low levels of folic acid is a low-cost, effective means for reducing the risk of NTDs at a population level. Countries that utilize this public health initiative indicate that the birth prevalence of NTDs has dropped by an average of 46%. Flour fortification is highly feasible in Europe given that bread is easily accessible and consumed in abundance, the milling industry is technologically advanced and countries have experience monitoring food quality and safety. Mandatory flour fortification is preferable to market-based voluntary fortification because it maximizes the public health impact and is more easily regulated. The European Union Regulation No 1925/2006 states that mandatory fortification using specified vitamins and minerals is permitted for "certain ordinary foods" to address public health concerns. To facilitate a sustainable flour fortification program, it is imperative that representatives of the public, private and civic sectors actively participate in the planning process and commit themselves to implementation of the legislation. The Flour Fortification Initiative (FFI) and the International Federation for Spina Bifida and Hydrocephalus (IF) are two entities that support the primary prevention of NTDs through flour fortification around the world.

Neural Tube Defects (NTDs)

NTDs affect the central nervous system. During the first month of a healthy pregnancy, the neural plate folds into a tube, leading to the development of the spinal cord and the brain. When this process is not fully completed, it results in a NTD. Three of the most common NTDs are:

Spina bifida occurs when the spinal column fails to close properly. Spina bifida has many classifications that vary in terms of severity. Myelomeningocele is the most debilitating form. It is typically characterized by a sac filled with the spinal cord and nerves that protrude through an opening in the spine. Side effects of spina bifida are

unique to each individual, but lifetime hardships such as hydrocephalus (fluid on the brain), varying degrees of paralysis, and incontinence are common.

Anencephaly is easily diagnosed because parts of the infant's brain and skull are missing. Pregnancies affected by anencephaly are often miscarried, but children born with this NTD die shortly after birth.

Encephalocele affects the brain and is characterized by sac-like protrusions filled with cerebral fluid, membranes and sometimes brain tissues that result from the skull's failure to close completely. Encephalocele can occur in the back or front of the head. Individuals with this NTD may also have hydrocephalus, vision problems, seizures and developmental delays depending on the location of the defect.

Spina Bifida | Anencephaly | Encephalocele

Illustrations courtesy of The Centers for Disease Control and Prevention

The Role of Folate in Overall Health

The term folate (vitamin B9) encompasses both food folate, which is naturally found in food, and folic acid, which is added to fortified foods and supplements. Vitamin B9 is important for everyone. It is required for proper cellular development and division, DNA methylation, the metabolism of amino acids and the regulation of homocysteine in the blood. Folate deficiency can result in megaloblastic anemia, pregnancy complications and raised homocysteine levels. Folate's potential role in reducing the risk of orofacial clefts (a type of birth defect), autism, certain cancers, stroke, and cognitive decline in the elderly is of interest for researchers.

The Role of Folate in Pregnancy

Given that folate is essential for healthy cellular function and division, this vitamin is vital during the early stages of pregnancy when embryonic growth occurs rapidly. Folic acid decreases the likelihood that women will have a pregnancy affected by a NTD. As a preventive measure, the Institute of Medicine (IOM), a globally recognized independent nonprofit entity that provides advice to decision makers and the public, recommends women of reproductive age consume 400 µg/day of folic acid through fortified foods and/or supplements in addition to normal intake of food folate.

Folate Intake and Status in Europe

Europe is a very diverse region in terms of ethnicity, economic development and health indicators. Though the region has many different types of foods available, food accessibility, personal taste preferences and increasingly busy schedules can hinder proper nutrition.

The biomarkers serum (or plasma) folate and red blood cell (RBC) folate, measured through blood samples, are considered the gold standards for evaluating a population's folate status. Serum folate provides an indication of short-term folate status while RBC folate is reflective of long-term folate status. Given that these tests are costly and invasive, national data of this kind are infrequently available. Alternatively, food intake data are often analyzed to provide a proxy for the folate status of a population. In Europe, country-specific recommendations for folate intake among women of reproductive age range from 200 to 400 µg/day. This increases to 300-600 µg/day for pregnant women.

A working group of the European Food Safety Authority conducted a comprehensive review of studies that assessed serum folate, RBC folate and folate intake in European countries in 2009. It presented the mean/median dietary intake of folate across the countries as 122-339 µg/day for women and 151-345 µg/day for men. For the few studies that also took into account supplement consumption, the average combined folate intake was 220-478 µg/day for women and 338-395 µg/day for men. The European Nutrition and Health Report, published the same year, also provides folate intake data from the region. Among adult women, folate intake was below the utilized reference value of 400 µg/day for all countries highlighted in the Report, regardless of whether or not the study included supplementation. A few more-recent studies on these topics are referenced in the *Key Scientific Documents* section of this paper.

NTDs in Europe

The European Surveillance of Congenital Anomalies (EUROCAT) is a network of population-based registries that was started in 1979. Currently, 43 registries located in 23 countries collectively cover a total of 29% of births in Europe. Three primary objectives of this network include: tracking congenital anomalies in Europe, evaluating the effectiveness of primary prevention methods, and assessing the impact of prenatal screening.

EUROCAT collects data on NTDs, including terminations of pregnancy where legal. Using 2006-2010 data[1] from the European countries that report live births, fetal deaths and terminations, an estimated 76% of NTD-affected pregnancies were aborted. EUROCAT advises countries to implement strategies to optimize folate status by increasing the uptake of folic acid supplements periconceptionally and the availability of fortified foods. EUROCAT notes that mandatory fortification of staple

[1] Data obtained on 19 July 2013 and is subject to change as the registries share additional surveillance information.

foods is a viable means of preventing NTDs, which also addresses the socio-economic inequalities related to this congenital anomaly.

Country profiles are available in EUROCAT's 2009 folic acid special report titled *Prevention of Neural Tube Defects by Periconceptional Folic Acid Supplementation in Europe.*

Wheat Flour Fortification as an Effective Low-cost Public Health Intervention

Flour fortification is a cost-effective, globally accepted means of improving the nutrient intake of populations to reduce the consequences of micronutrient malnutrition. The most common micronutrients added to flour through fortification are folic acid and iron. Fortification costs approximately 0.16€ per person per year depending on the vitamins and minerals included in the flour. This additional cost can be passed on to the consumer by slightly increasing the cost of wheat flour and flour-based products, such as bread. A 2012 impact assessment conducted in the United Kingdom found that fortification costs the average bread consumer roughly 0.10£ (0.12€) annually. Sometimes flour milling companies absorb the cost as part of their corporate social responsibility initiatives, or governments financially support flour fortification programs to help curb the costs of vitamin and mineral deficiencies.

Women need optimum folate stores at the time of conception because the neural tube closes around the 28th day of pregnancy. Given that most women are not aware of their pregnancy by this time, folic acid supplementation will only benefit those who plan their pregnancies and/or take supplements on a daily basis. Unfortunately, an estimated 38-50% of pregnancies in Europe are unplanned and habitual supplementation is not common. Under a mandatory flour fortification program, individuals will receive low levels of this vital micronutrient while continuing their normal consumption practices, thereby reducing the risk of NTDs without requiring a behaviour change. Moreover, this initiative reaches those who do not plan their pregnancies or who may not have access to supplementation.

Promote Mandatory Flour Fortification

Mandatory flour fortification provides a nutritional benefit to individuals from all socioeconomic strata given that wheat-based products are routinely consumed in Europe and bread remains a relatively low-cost staple food. Mandatory flour fortification maximizes the benefits of folic acid while minimizing the risk of surpassing the designated Tolerable Upper Intake Level (UL) of 1 mg/day. According to the Institute of Medicine, the UL is the "highest level of a daily nutrient that is likely to pose *no risk* of adverse health effects to almost all individuals in the general population".

European countries permit voluntary fortification for a wide range of products. Under this market-based scheme, the levels of fortificants added are not consistently regulated. Thus, companies can alter the fortificant levels at any time and can even cease fortification without notifying the consumer. Health conscious consumers,

especially those who seek products with nutrition claims, run a greater risk of surpassing the UL under voluntary fortification programs given the high nutrient levels that are added to some food items. At the same time, voluntary fortification potentially misses consumers in certain vulnerable segments of society.

Mandatory fortification requires equitable financial inputs in terms of equipment and fortificants from all flour millers in the country, ensuring that no miller has a financial advantage over another. On the other hand, millers who fortify voluntarily as part of a corporate social responsibility plan or to increase their market-share, risk operating at an economic loss compared to their competitors.

Under mandatory fortification, country leaders develop standards which specify the amount and the type of fortificants that should be included in flour, taking into account the nutrition status of the population and its consumption patterns. Standards therefore free the flour millers from making arbitrary judgments about the nutritional needs of a population.

Lastly, mandatory fortification lends itself to a systematic quality control and monitoring system. Millers are aware of what is required of them, and the government regulators can easily inspect the mills, especially in Europe, where many countries have consolidated milling industries.

Flour Fortification around the World

In 2008, nearly 100 leading nutrition, pharmaceutical and cereal scientists and milling experts from the public and private sectors from around the world gathered for four days to harmonize advice for countries considering national wheat and/or maize flour fortification. The background papers from this meeting were published in the Food and Nutrition Bulletin in 2010.

Recommendations have been put forth by the World Health Organization (WHO) for fortifying wheat and maize flour with folic acid, iron, zinc, vitamin B12 and vitamin A. Other B vitamins are also commonly added to flour, and vitamin D and calcium are sometimes included. Flour fortification is viewed as an effective public health strategy for addressing micronutrient deficiencies and their consequences by the following additional entities: WHO, UNICEF, the Copenhagen Consensus Centre, the World Food Programme, the Centers for Disease Control and Prevention and numerous civic and nongovernmental organizations.

The European Union Regulation No 1925/2006 states that mandatory fortification using specified vitamins and minerals is permitted for “certain ordinary foods” to address public health concerns. However, most national governments in the European region have opted for voluntary fortification or supplementation programs in lieu of mandatory flour fortification. In the Western part of Europe, the United Kingdom is the only country that ascribes to mandatory flour fortification practices. As of July 2013, discussions about including folic acid in its standard were underway.

Central and Eastern Europe and the Commonwealth of Independent States more commonly utilize mandatory flour fortification as a means for improving the nutritional status of their populations. Kazakhstan, Kosovo, Kyrgyzstan, Turkmenistan, Uzbekistan and Moldova all have legislation requiring the addition of iron and folic acid to at least one kind of commonly consumed wheat flour. Some other countries in these regions are also considering the adoption of mandatory flour fortification.

The current legislative status of grain fortification programs throughout the world can be viewed using this map. As of July 2013, 73 countries had passed legislation requiring at least one type of commonly consumed wheat flour to be fortified with folic acid.

Making Flour Fortification Happen at the National Level: Public Private Civic Partnerships

Flour fortification at a national level requires the engagement and cooperation of the public, private, and civic sectors to be effective and sustainable. It is recommended that countries form National Fortification Alliances early during discussions about flour fortification because collaboration between government ministers, parliamentarians, flour milling companies, bakeries, and civic society is paramount. Each entity has its unique strengths and experiences, which lead to insightful contributions and a stronger fortification program. Though the public sector must pass the legislation to implement flour fortification, the standards indicating the levels and types of vitamins and minerals to be added to flour need input from both the public and private sector. Without strong support from the private sector and feasible standards, the legislation may exist, but flour fortification will not happen.

International Federation for Spina Bifida and Hydrocephalus

The International Federation for Spina Bifida and Hydrocephalus (IF) is driven by its mission to decrease the birth prevalence of spina bifida and hydrocephalus through primary prevention measures and to improve the quality of life for those living with these disabilities. In June 2005, the IF Board agreed on a policy statement supporting mandatory flour fortification and calling for action to promote this initiative throughout the world. This statement can be viewed in **Appendix 1**. A timeline of IF's involvement in flour fortification activities can be found in **Appendix 2**.

Flour Fortification Initiative

The Flour Fortification Initiative (FFI) collaborates with multi-sector partners worldwide to improve nutrition by working to accelerate fortification of industrially milled cereal grains. It provides technical assistance and supports activities to catalyze action at a national level, but it is not an implementing body. FFI includes representatives from the private, public and civic sectors who combine their expertise and resources to foster wheat and maize flour and rice fortification. A complete list of partners can be found here. Learn more by exploring FFI's website in detail.

Key Scientific Documents

**Abstracts for all journal articles are located in Annex 1 (a separate document)*

To provide a solid scientific basis for flour fortification and address some concerns cited about this public health intervention in Europe, the following articles by experts in the field are referenced below in addition to those hyperlinked in the body of the document.

Vitamin and mineral intakes in Europe:

1. Flynn A, Hiroven T, Mensink GBM et al. Intake of selected nutrients from foods, from fortification, and from supplements in various European countries. Food Nutr Res 2009;53(1-51).
2. Troesch B, Hoeft B, McBurney M et al. Dietary surveys indicate vitamin intakes below recommendations are common in representative Western countries. Br J Nutr 2012;108:(4)692–8.
3. Viñas BR, Barba LR, Ngo J et al. Projected Prevalence of Inadequate Nutrient Intakes in Europe. Ann Nutr Metab 2011;59:84-95.
4. Young Park J, Nicolas G, Freisling H et al. Comparison of standardized dietary folate intake across ten countries participating in the European Prospective Investigation into Cancer and Nutrition. Br J Nutr 2012;108(3):552-569.

Folate status (serum/plasma folate and RBC folate)

1. González-Gross M, Prinz-Langenohl R, Pietrzik. Folate Status in Germany 1997-2000. Int J Vitam Nutr Res 2002; 72(6):351-359.
2. Öner N, Vatansever U, Karasalihoglu S et al. The prevalence of folic acid deficiency among adolescent girls living in Edirne, Turkey. J Adolesc Health 2006;38:599-606.
3. Vandevijvere S, Amsalkhir S, Oyen HV, Moreno-Reyes R. Determinants of folate status in pregnant women: results from a national cross-sectional survey in Belgium. Eur J Clin Nutr 2012;66: 1172-1177.

Folic acid can prevent NTDs:

1. Laurence KM, James N, Miller M et al. Double-Blind Randomised Controlled Trial of Folate Treatment Before Conception to Prevent Recurrence of Neural Tube Defects. Br Med J. 1981;282(6275):1509-1511.
2. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. Lancet 1991;338:131-137.
3. Smithells RW, Shepard S, Schorah CJ et al. Possible prevention of neural-tube defects by periconceptional vitamin supplementation. Lancet 1980;1(8164):339-340.

Supplementation is underutilized

1. Baykan Z, Oztürk A, Poyrazoğlu S et al. Awareness, knowledge, and use of folic acid among women: a study from Turkey. Arch Gynecol Obstet 2011; 283(6):1249–53.
2. Bitzer J, von Stenglin A, Bannemerschult R. Women's awareness and periconceptional use of folic acid: data from a large European survey. Int J Women's Health 2013; 5:201-13.
3. Brough L, Rees GA, Crawford MA et al. Social and ethnic differences in folic acid use during preconception and early pregnancy in the UK: effect on maternal folate status. J Hum Nutr Diet 2009; 22(2):100–7.
4. Paulik E, Csasza J, Kozinszky Z et al. Preconceptional and prenatal predictors of folic acid intake in Hungarian pregnant women. Eur J Obstet Gynecol Reprod Biol 2009;145(1):49-52.
5. Pinto E, Barros H, dos Santos Silva I. Dietary intake and nutritional adequacy prior to conception and during pregnancy: a follow-up study in the north of Portugal. Public Health Nutr 2009;12(7): 922–31.

Flour fortification reduces the prevalence of neural tube defects:

1. Blencowe H, Cousens S, Modell B et al. Folic acid to reduce neonatal mortality from neural tube disorders. Intl J Epidemiol 2010;39:i110-i121.
2. Castillo-Lancelloti C, Tur JA, Uauy R. Impact of fortification of flour on neural tube defects: a systematic review. Public Health Nutr. 2012;July:1-11.

Encouraging flour fortification in Europe:

1. Busby A, Armstrong B, Dolk H et al. Preventing neural tube defects in Europe: A missed opportunity. Reprod Toxicol 2005; 20(3): 393-402.
2. Cwernichow S, Noisette N, Blacher J et al. Case for Folic Acid and Vitamin B_{12} Fortification in Europe. Semin Vasc Med 2005;5(2):156-62.
3. Pachón H, Kancherla V, Handforth B, Tyler V, Bauwens L. Folic acid fortification of wheat flour: A cost-effective public health intervention to prevent birth defects in Europe. Nutr Bull 2013; 308:201-9.

Folic acid does not cause cancer-even when consumed in an amount greater than the UL for a sustained period of time:

1. Clarke R, Halsey J, Lewington S. Effects of lowering homocysteine levels with B vitamins on cardiovascular disease, cancer, and cause-specific mortality meta-analysis of 8 randomized trials involving 37,485 individuals. Arch Intern Med 2010;170(18):1622–31.
3. Hankey GJ, Eikelboom JW, Lees KR et al. Treatment with B vitamins and incidence of cancer in patients with previous stroke or transient ischemic attack results of a randomized placebo-controlled trial. Stroke 2012;43(6):1572–7.
4. Vollset SE, Clarke R, Lewington S et al. (2013) Effects of folic acid supplementation on overall and 621 site-specific cancer incidence during the

randomised trails: meta-analyses of data on 50 000 622 individuals. Lancet 2013; doi: 10.1016/S0140-6736(12)62001-7. [Epub ahead of print].
5. Wein TN, Pike E, Wisløff T et al. Cancer risk with folic acid supplements: a systematic review and meta-analysis. BMJ Open 2012;2(1).

Folic acid and B12 deficiency

1. Dickinson CJ. Does folic acid harm people with vitamin B12 deficiency? QJM 1995;88(5):357–64.
2. Mills JL, Carter TC, Scott JM et al. Do high blood folate concentrations exacerbate metabolic abnormalities in people with low vitamin B12 status? Am J Clin Nutr 2011; 94(2):495–500.
3. Ministry for Primary Industries. Scientific evaluation of comments on submissions received on the future of folic acid fortification in New Zealand, MPI Technical Paper No: 2012/25. 2012. Internet: http://www.foodsafety.govt.nz/elibrary/industry/fortification-bread-folic-acid/scientific-evaluation-submissions-folic-acid.pdf (accessed November 9 2012).

Costing studies

1. Grosse SD, Waitzman NJ, Romano PS, Mulinaire J. Reevaluating the Benefits of Folic acid Fortification in the United States: Economic Analysis, Regulation and Public Health. Am J Public Health 2005;95(11):1917-22.
2. Jentink J, van de Vrie-Hoekstra N, de Jong-van den Berg L, Postma M. Economic evaluation of folic acid food fortification in the Netherlands. Eur J of Public Health 2008;18(3):270-4.
3. Llanos A, Hertrampf E, Cortes F, Pardo A et al. Cost-effectiveness of a folic acid fortification program in Chile. Health Policy 2007;83:295-303.
4. Sayed AR, Bourne D, Pattinson R, Nixon J et al. Decline in the Prevalence of Neural Tube Defects Following Folic acid Fortification and Its Cost-Benefit in South Africa. Birth Defects Res A Clin Mol Teratol 2008;82(4):211-6.
5. Yi Y, Lindemann M, Colligs A, Snowball C. Economic burden of neural tube defects and impact of prevention with folic acid: a literature review. Eur J Pediatr 2011;170(11):1391-1400.

Key Technical Resources for Flour Fortification

1. Flour Millers' Tool Kit
2. Guidelines on Fortification with Micronutrients
   Edited by Lindsay Allen, Bruno de Benoist, Omar Dary and Richard Hurrell
3. Regulations of Fortified Foods to Address Micronutrient Malnutrition: Legislation, Regulations and Enforcement
   Written by Rose Nathan

Relevant European Union Legislation

1. Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements

2. Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 lays down the general principles and requirements of food law, the procedures in matters of food safety and establishes the European Food Safety Authority
3. Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods
4. Regulation (EC) No 1170/2009 of 30 November 2009 amending Directive 2002/46/EC of the European Parliament and of Council and Regulation (EC) No 1925/2006 of the European Parliament and of the Council as regards the lists of vitamin and minerals and their forms that can be added to foods, including food supplements
5. Regulation (EC) No 307/2012 of 11 April 2012 establishes implementing rules for the application of article 8 of Regulation (EC) No 1925/2006 of the European Parliament and the Council on the addition of vitamins and minerals and certain other substances to foods

In-depth information about the directive and the regulations can be found on the website of the European Commission in the sections "Food Supplements", "Addition of Vitamins & Minerals" and "General Food Law – Introduction".

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APPENDIX 1:

INTERNATIONAL FEDERATION
FOR SPINA BIFIDA AND HYDROCEPHALUS

Consultative status special category with Economic and Social Council of the United Nations
Participatory status, Council of Europe

IF POLICY STATEMENT ON PREVENTION OF NEURAL TUBE DEFECTS AND MANDATORY FOOD FORTIFICATION

Adopted by the IF Annual General Meeting on 28 June 2005 in Minneapolis

IF calls for action to:

1. Promote the health benefits of the vitamin folic acid.
2. Ratify a policy calling on all countries to fortify staple food with the vitamin folic acid to reduce the incidence of neural tube defects (NTDs).
3. Encourage further research into the prevention of neural tube defects (including spina bifida).

Primary Prevention and folic acid

Maternal periconceptional use of folic acid has been found to reduce the risk of both recurrent and occurent NTDs (Locksminth and Diff, 1998; Watkins, 1998, Czeizel et al. 1999). This reduction occurs both in regions of high NTD rates and in regions of low NTD rates (Berr et al. 1999). [1] Lumley et al. found that reductions of up to 70% can be achieved with the correct dosage.[2]

Folic acid is the synthetic form of the vitamin folate, which is naturally found in foods. It is a simple, inexpensive supplement which reduces the incidence of NTDs in the foetus if taken by women prior to conception and for the first three months of pregnancy.

The recommended folate intake is 0.6mg per day[3] , but as a normal diet cannot provide this level, an extra 0.4mg per day is required through folic acid supplements. This should be taken for at least a month before becoming pregnant and for the first three months of pregnancy.

Increasingly, research shows that folate may be important not only in the prevention of spina bifida. Folate may reap unexpected benefits in the reduction of the incidence of other birth defects such as congenital anomalies of the heart, face, limbs and of cardiovascular diseases. [4] [5]

Further research on the nutritional habits of other regions of the world is needed to ensure that all levels of the society can benefit from the effects of food fortification.

Why Fortification?

Estimates suggest that over 300,000 babies[6] per year are developing a neural tube defect.

For more than twenty years it has been known that the vitamin folic acid can reduce significantly the incidence of neural tube defects.

Voluntary consumption of supplements of folic acid by couples planning a pregnancy is reaching only small part of the population.

Prevention through folic acid supplements alone is not enough, because large numbers of pregnancies are unplanned.

Health promotion and voluntary fortification are not reaching all segments of the target population, and it is very unlikely that any further gains can be made with health promotion of supplement use and dietary change[7]. The latter is notoriously difficult at the population level, and evidence worldwide is that it does not seem possible to increase periconceptional supplement use beyond about 40% of women.[8]

Voluntary Fortification

Voluntary fortification of products such as breakfast cereals is more expensive and will mostly reach the population that is also reached by prevention campaigns that promote supplements (i.e., educated western middle class families).

Mandatory Fortification

Food fortification with folic acid is the way of maximising the consumption of extra folate in the entire population.

Legislation for mandatory fortification of flour already exists in over 50 countries, including the U.S.A. and Canada.[9]

Mandatory fortification does not discriminate.

Follow-up studies in the U.S.A and Canada [10], [11] show the effect of mandatory flour fortification with folic acid.

IF proposes the creation of an international policy for mandatory food fortification to actively encourage all countries to adopt this measure.

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2. Lumley J, Watson L, Watson M, Bower C. Periconceptional supplementation with folate and/or multivitamins to prevent neural tube defects (Cochrane Review) [substantive update]. In: The Cochrane Library, Issue 3, 2001, Oxford: Update Software
3. DGE (Deutsche Gesellschaft für Ernährung), Östereichische Gesellschaft für Ernährung, Schweizerische Gesellschaft für Ernährungsforschung, Schweizerische Vereinigung für Ernährung (Eds.). Referenzwerte für Nährstoffzufuhr. Umschau Braus Verlag, Frankfurt am Main, 2000.
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8. A) de Walle HEK, de Jong-van den Berg LTW. Insufficient folic acid intake in the Netherlands: What about the future? Teratology 2002;66:40-43.
   B) CDC. Use of folic acid-containing supplements among women of childbearing age - United States 1997. MMWR 1998;47:131-134.
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APPENDIX 2:

Timeline of IF activities in support of flour fortification efforts

2005		Lobbying the European Members of Parliament requesting mandatory food fortification with folic acid
2005		Adoption of the IF Policy Statement on mandatory food fortification
2006		IF President, Pierre Mertens, presents: Preventing Spina Bifida through Folic Acid Flour Fortification at the 3rd National Week on Prevention of Spina Bifida organized by GASBI (Genitori Associati Spina Bifida Italia)
2007		IF Award for FFI
2007		FFI and IF host the European Meeting on Mandatory Flour Fortification in Brussels
2008		Public consultation regarding a European Action in the Field of Rare Diseases - IF response
2008		The original Toolkit for Flour Fortification in Europe presented during flour fortification workshop in Lisbon
2008		European Regional Flour Fortification Consultation, in association with the 3rd Annual International Association of Operative Millers (IAOM) Eurasia District Conference and Expo in Bucharest
2008		IF participates in the First African Flour Fortification Workshop in Arusha, Tanzania
2009		An update on folic acid flour fortification in Ireland was presented by a research partner during the IF EU workshop in Ballinasloe, Ireland
2009		IF participates in the FFI Africa Partners Meeting in Dakar, Senegal
2009		IF participates in the Smarter Futures project, together with BOSK, FFI and AkzoNobel, with financial aid from the Dutch Government (Schokland Fund/Millennium Agreements)
2009		IF president Pierre Mertens visits Ethiopia to advocate for flour fortification
2009		Through the Smarter Futures project, IF participates in the Training for Trainers meeting on flour fortification in Dakar, Senegal
2009		Partnership with Bayer Schering Pharma Women's Healthcare to raise awareness of the prevention of Neural Tube Defects (NTDs) in Europe

2010		Publication and presentation in the European Parliament of joint report with Bayer Schering Pharma Women's Healthcare: Act against Europe's most common birth defects: The right advice at the right time can reduce Neural Tube Defects now. Data for the report are supplied by EUROCAT.
2010		IF participates in the 2nd African Flour Fortification Meeting, in Cape Town, South Africa
2010		Start of the Bayer HealthCare Pharmaceuticals and IF postcard campaign to create awareness for the prevention of NTDs in Europe and to advocate for the promotion of folic acid supplementation and fortification
2011		Launch of the IF-Bayer HealthCare Pharmaceuticals follow-up report "Act against Europe's most common birth defects: one year on – Defining Neural Tube Defect prevention strategies in Europe", developed in cooperation with EURORDIS, EFCNI, EASPD and MediClara. Data for the report are supplied by EUROCAT.
2011		Lieven Bauwens, IF secretary general, becomes member of FFI's Executive Management Team
2011		IF EU Executive Workshop "Making our network stronger - Raising awareness on prevention"
2011		IF takes the floor on the 4th International Muhlenchemie Symposium 'Future of Flour'
2012		The Smarter Futures project begins to scale up in Africa with a commitment from the Ministry of Foreign Affairs of the Netherlands
2012		IF and FFI organize workshop at the 15th European Health Forum Gastein
2013		IF participates in the FORTIMAS:Fortification Monitoring and Surveillance meeting sponsored by Smarter Futures in Johannesburg, South Africa. The attendees helped developed a manual to track trends in 1) Household coverage of quality fortified flour and foods made with fortified flour and 2) Health outcomes that can reasonably be improved through fortification.