FOOD STANDARDS
Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

8-04
20 October 2004

INITIAL ASSESSMENT REPORT

PROPOSAL P295

CONSIDERATION OF MANDATORY FORTIFICATION WITH FOLIC ACID

DEADLINE FOR PUBLIC SUBMISSIONS to FSANZ in relation to this matter:
17 December 2004
(See 'Invitation for Public Submissions' for details)

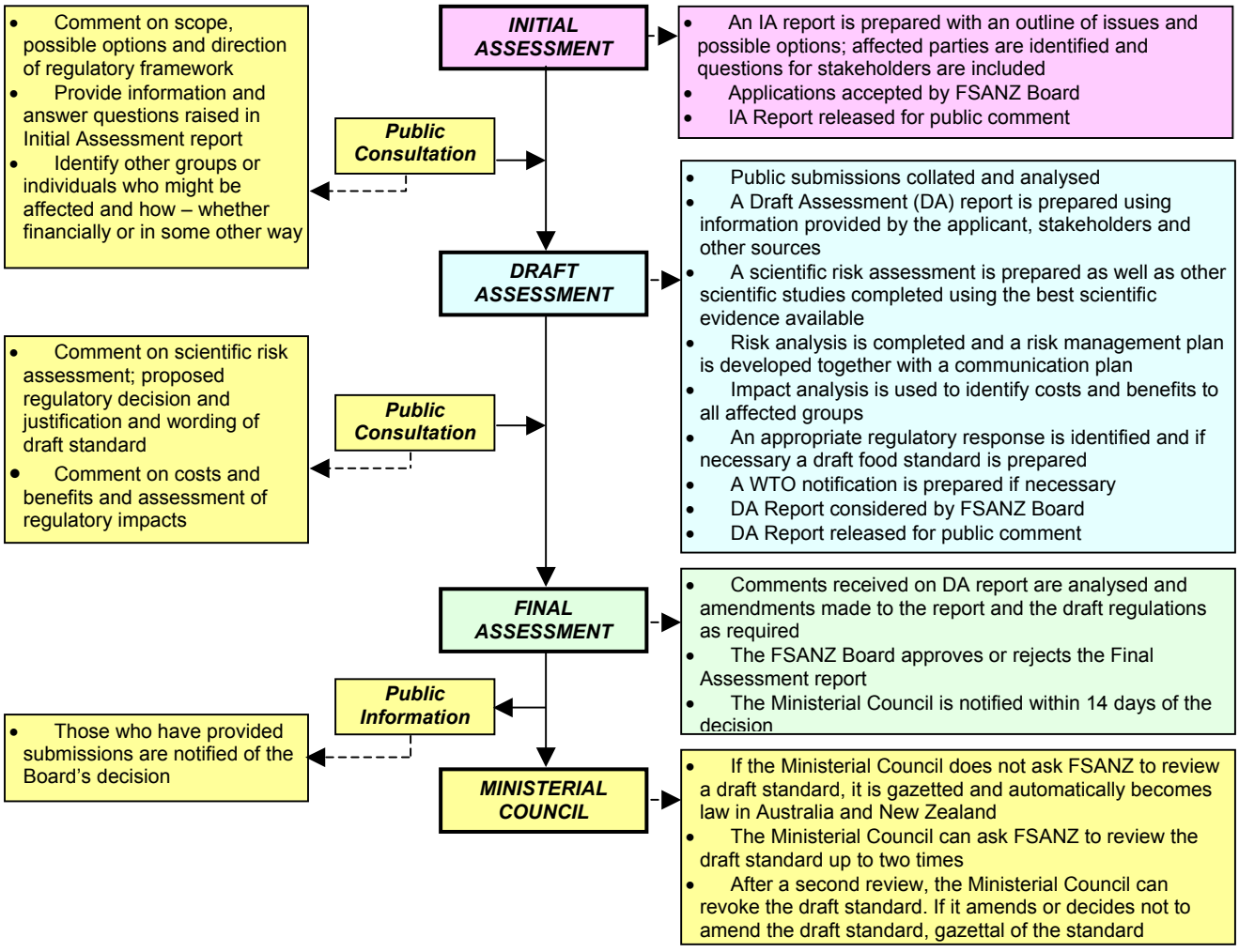
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

FSANZ's role is to protect the health and safety of people in Australia and New Zealand through the maintenance of a safe food supply. FSANZ is a partnership between ten Governments: the Australian Government; Australian States and Territories; and New Zealand. It is a statutory authority under Commonwealth law and is an independent, expert body.

FSANZ is responsible for developing, varying and reviewing standards and for developing codes of conduct with industry for food available in Australia and New Zealand covering labelling, composition and contaminants. In Australia, FSANZ also develops food standards for food safety, maximum residue limits, primary production and processing and a range of other functions including the coordination of national food surveillance and recall systems, conducting research and assessing policies about imported food.

The FSANZ Board approves new standards or variations to food standards in accordance with policy guidelines set by the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) made up of Australian Government, State and Territory and New Zealand Health Ministers as lead Ministers, with representation from other portfolios. Approved standards are then notified to the Ministerial Council. The Ministerial Council may then request that FSANZ review a proposed or existing standard. If the Ministerial Council does not request that FSANZ review the draft standard, or amends a draft standard, the standard is adopted by reference under the food laws of the Australian Government, States, Territories and New Zealand. The Ministerial Council can, independently of a notification from FSANZ, request that FSANZ review a standard.

The process for amending the *Australia New Zealand Food Standards Code* is prescribed in the *Food Standards Australia New Zealand Act 1991* (FSANZ Act). The diagram below represents the different stages in the process including when periods of public consultation occur. This process varies for matters that are urgent or minor in significance or complexity.



INVITATION FOR PUBLIC SUBMISSIONS

FSANZ has prepared an Initial Assessment Report of Proposal P295, which includes the identification and discussion of key issues. FSANZ invites public comment on this Initial Assessment Report for the purpose of considering a possible amendment to the Code for approval by the FSANZ Board.

Written submissions are invited from interested individuals and organisations to assist FSANZ in preparing the Draft Assessment for this Proposal. Submissions should, where possible, address the objectives of FSANZ as set out in section 10 of the FSANZ Act.

Information providing details of potential costs and benefits of the proposed change to the Code from stakeholders is highly desirable. Claims made in submissions should be supported wherever possible by referencing or including relevant studies, research findings, trials, surveys etc. Technical information should be in sufficient detail to allow independent scientific assessment.

The processes of FSANZ are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of FSANZ and made available for inspection. If you wish any information contained in a submission to remain confidential to FSANZ, you should clearly identify the sensitive information and provide justification for treating it as commercial-in-confidence. Section 39 of the FSANZ Act requires FSANZ to treat in-confidence, trade secrets relating to food and any other information relating to food, the commercial value of which would be, or could reasonably be expected to be, destroyed or diminished by disclosure.

Submissions must be made in writing and should clearly be marked with the word 'Submission' and quote the correct project number and name. Submissions may be sent to one of the following addresses:

Food Standards Australia New Zealand
PO Box 7186
Canberra BC ACT 2610
AUSTRALIA
Tel (02) 6271 2222
www.foodstandards.gov.au

Food Standards Australia New Zealand
PO Box 10559
The Terrace WELLINGTON 6036
NEW ZEALAND
Tel (04) 473 9942
www.foodstandards.govt.nz

Submissions should be received by FSANZ **by 17 December 2004**.

Submissions received after this date may not be considered, unless the Project Coordinator has given prior agreement for an extension.

While FSANZ accepts submissions in hard copy to our offices, it is more convenient and quicker to receive submissions electronically through the FSANZ website using the Standards Development tab and then through Documents for Public Comment. Questions relating to making submissions or the application process can be directed to the Standards Management Officer at the above address or by emailing slo@foodstandards.gov.au.

Assessment reports are available for viewing and downloading from the FSANZ website. Alternatively, requests for paper copies of reports or other general inquiries can be directed to FSANZ's Information Officer at either of the above addresses or by emailing info@foodstandards.gov.au.

CONTENTS

Executive Summary

Background

In May 2004, the Australia and New Zealand Food Regulation Ministerial Council (the Ministerial Council) asked FSANZ to investigate mandatory fortification with folic acid as a possible means of reducing the incidence of neural tube defects (NTDs). The Ministerial Council also issued a Policy Guideline on *Fortification of Food with Vitamins and Minerals* to guide FSANZ's consideration of the issues.

Regulatory Problem

NTDs are severe congenital malformations of the central nervous system and result from the failure of the neural tube to close during early embryonic development. The two major types of NTDs are anencephaly and spina bifida. Babies affected with anencephaly usually die within first few days of life. Babies with spina bifida usually survive but require extensive medical and surgical care and the majority of these children suffer from a lifelong moderate or severe handicap.

It is estimated that approximately 11.5 total births and terminations per 10,000 total births are affected by NTDs in Australia and that 9.1 total births and terminations per 10,000 total births are affected by NTDs in New Zealand[1].

There is considerable evidence showing that increased folate intakes can reduce the risk of NTDs. A dose response appears to exist between folate status and the risk of NTDs, with up to approximately 70% of NTDs preventable by increasing folate status.

It is difficult to obtain the recommended intake of folate through diet alone, with women of child-bearing age consuming only about half the amount recommended.

Since 1993, both Australia and New Zealand have instigated a health policy recommending women take folic acid supplements during the peri-conceptional period[2]. In Australia, various education initiatives have been undertaken by a number of jurisdictions to encourage women of child-bearing age to increase their dietary folate and/or take folic acid supplements. Despite these campaigns, current advice for supplemental folic acid is not followed by a majority of women in the target group. Reasons for this include:

- a large percentage of pregnancies are unplanned;
- lack of knowledge among women about the benefits of folic acid;
- knowledge not always equating to behaviour change; and
- numerous barriers to supplement usage, such as cost, access and compliance issues.

[1] Australian data is based on 1996-1997 data and New Zealand data is from 1999. Please note that this data is not directly comparable due to differences in reporting between the countries including whether ~~still birth~~stillbirths and termination are included. This is discussed in more detail in Section 5.
[2] Periconceptional period is 4 weeks prior and 12 weeks after conception

Since 1995 in Australia and 1996 in New Zealand, certain foods have been able to be fortified with folic acid. Standard 1.3.2 of the *Australia New Zealand Food Standards Code* (the Code) permits folic acid to be voluntarily added to a maximum claim of 100 μg per reference quantity to a number of cereal-based foods, fruit and vegetables juices and drinks, yeast and meat extracts.

Despite this, total folate intakes in women of child-bearing age have not increased significantly and are still well below recommended intakes.

Objective

The specific objective of this Proposal is to determine the most effective mechanism to increase total folate intake in peri-conceptional women to reduce the incidence of NTDs from current levels in the Australian and New Zealand population.

The risks and benefits to the general population of increased dietary folate intake will be taken into consideration when making this determination.

Relevant Issues

One of the key issues for consideration is the optimal folate status for decreasing NTDs. Overseas studies suggest that 900 nmol/L is the optimal level for reducing the occurrence of NTDs. However, no equivalent studies have been undertaken in Australia or New Zealand. It is yet to be determined whether the folate intakes and folate status are sufficiently well described and the reference values appropriate for Australia and New Zealand to predict the possible number of NTD cases saved through increased folate intake. Risk reduction models and overseas experience appears to show that the magnitude of the risk reduction is inversely related to the folate status of the target group, which means that a greater reduction in NTD risk would be predicted for target groups with poorer folate status.

Another key issue is the impact that any increased folate intake may have on the general population. While oral folic acid is generally considered to be safe for the majority of the population (even at high doses (>1 mg/day)), studies suggest that there may be risks to certain groups, particularly older people.

In particular, concern has been expressed about high doses of folic acid having the potential to mask the haematological signs of vitamin B_{12} deficiency. Vitamin B_{12} deficiency causes anaemia and can cause neurological damage (peripheral neuropathy, spinal cord damage and cerebral dysfunction), which may be irreversible if not treated early. The key issue in relation to potential masking of B_{12} deficiency is whether further fortification would produce a masking effect and whether the medical profession depends on the patient's haematological profile to make a diagnosis of vitamin B_{12} deficiency neurological disorder.

Impact of strategies on increasing folate intakes

While it is difficult to attribute any increase in folate intake (or change in incidence of NTDs) to any particular strategy that has been implemented, the studies examined in the preparation of this Initial Assessment Report tend to indicate that in Australia and New Zealand:

- there has only been a small increase in consumption of folate rich foods and folic acid supplements by the target population (between 3 and 24%); and
- voluntary fortification has led to a small improvement in dietary intake of folate in women of child-bearing age in both Australia and New Zealand with mean folate intake increases of 11% in Australia and 13% in New Zealand.

Experiences of other countries regarding mandatory folic acid fortification

In the U.S., mandatory fortification of certain foods was introduced in 1996. The introduction of mandatory fortification appears to have led to:

- an increase in dietary intake of folate across all sectors of the community;
- increase in measures of folate status for all sectors of the community;
- a decrease of 27% in the rate of NTDs following mandatory fortification (compared to the voluntary fortification period); and
- no reported increase in the prevalence of the masking of vitamin B_{12} deficiency or increased incidence of twinning.

In the United Kingdom, voluntary fortification has been in place since the late 1980's and there is limited data available about the contribution that voluntary folic acid fortification has made on UK folic acid intakes. The major issue in the UK has been concerns regarding the masking of B_{12} deficiency and the potential impact on the elderly population. The UK government has requested a detailed investigation of this issue prior to making a decision regarding mandatory fortification of certain foods with folic acid.

Regulatory Options and Impact Analysis

In order to further decrease the incidence of NTDs from current rates, FSANZ is considering the four following options:

1. Maintenance of the Status Quo (i.e. voluntary folate permissions for some foods).
2. Increased permissions for voluntary folate fortification.
3. Mandatory folate fortification.
4. Increased health promotion and education strategies to increase folate intakes. This is a non-regulatory option and could be selected as the sole strategy to further reduce the incidence of NTDs or be implemented in conjunction with any of the other three options.

The impact analysis provides initial consideration of the potential impact of each option on consumers and the community, industry and governments.

- FSANZ now seeks comment and information from stakeholders on the range of issues raised in this Report. Input from all sectors of the community, including consumers, industry, health professionals and government, is welcomed and encouraged. The submissions provided during this consultation will inform the Draft Assessment and assist FSANZ to determine the most appropriate means for increasing folate intake and decreasing the incidence of NTDs in Australia and New Zealand.

1. Introduction

There is convincing evidence that increased intakes of folic acid can reduce the risk of neural tube defects (NTDs). NTDs are a family of birth defects, which occur *in utero* during the development of the brain or spinal cord.

Over the past 10 years, a number of countries including Australia and New Zealand have adopted policies to increase the folate intake of women prior to and during pregnancy. The main primary prevention strategies have been, either singly or in combination: promotion of diets high in naturally-occurring folate; promotion of folic acid supplements during the peri-conceptional period; and fortification of the food supply with folic acid.

In May 2004, the Ministerial Council asked FSANZ to investigate mandatory fortification of food with folic acid as a possible means of reducing the incidence of NTDs. At that time, the Ministerial Council also issued a Policy Guideline on *Fortification of Food with Vitamins and Minerals* (Policy Guideline). This Guideline provides general direction to assist FSANZ determine the appropriate circumstances under which mandatory fortification should be implemented (see Attachment 1).

The purpose of this Initial Assessment Report is to:

- clearly articulate the regulatory problem sought to be addressed;
- identify the objectives of any regulatory action;
- identify any relevant issues associated with mandatory fortification of foods with folic acid (including addressing the issues included in the Ministerial Council Policy Guideline as detailed above);
- detail the potential impacts on all affected parties; and
- seek the views of stakeholders and any further available evidence on all of the above issues.

Glossaries of terms and acronyms used in this report are at Attachments 2 and 3.

2. Regulatory Problem

NTDs are severe congenital malformations of the central nervous system and result from the failure of the neural tube to close during early embryonic development. The two major types of NTDs are anencephaly and spina bifida (see Section 4). Babies affected with anencephaly usually die within first few days of life. Babies with spina bifida usually survive but require extensive medical care and the majority of these children suffer from a lifelong moderate or severe handicap.

It is estimated that up to 500 pregnancies in Australia (Lancaster, 2001) and approximately 30 live and stillbirths in New Zealand year (NZFSA/ NZMoH, 2004) are affected by NTDs each year. There is considerable evidence showing that increased folate intakes can reduce the risk of NTDs (NHMRC 1995). An inverse correlation exists between folate status and the risk of NTDs, with up to 70% of NTDs potentially preventable by increasing folate status (FSAI Nutrition Sub-committee 2003).

Since 1993, both Australia and New Zealand have instigated a health policy recommending women take folic acid supplements during the peri-conceptional period. In Australia, various education initiatives have been undertaken to encourage women of child-bearing age to increase their dietary folate and/or take folic acid supplements.

Despite these campaigns, current advice for supplemental folic acid is not followed by a majority of women in the target group. Reasons for this include:

- a large percentage of pregnancies are unplanned;
- lack of knowledge among women about the benefits of folic acid;
- knowledge not always equating to behavioural change; and
- numerous barriers to supplement usage, such as cost, access, and compliance issues.

It is difficult to achieve the recommended intake of folate through diet alone, with women of child-bearing age consuming only about half the amount recommended. Since 1995 in Australia and 1996 in New Zealand, regulations have permitted voluntary fortification of certain foods with folic acid. Preliminary results (albeit from 1998) show that mean folate intakes have increased only marginally and are significantly below recommended intakes, with not all fortified foods being consumed by the target population.

It appears that additional strategies are needed to increase dietary folate intakes in the target population to ensure a more effective prevention of NTD cases.

3. Objectives

The specific objective of this Proposal is to determine the most effective mechanism to increase total folate intake in peri-conceptional women to reduce the incidence of NTDs from current levels in the Australian and New Zealand population.

The risks and benefits to the general population of increased dietary folate intake will be taken into consideration when making this determination.

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives that are set out in section 10 of the FSANZ Act. These are:

- the protection of public health and safety;
- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

In developing and varying standards, FSANZ must also have regard to:

- the need for standards to be based on risk analysis using the best available scientific evidence;
- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council.

4. Background information

4.1 Regulation of folic acid in foods in Australia and New Zealand

In May 2004, the Ministerial Council adopted a *Policy Guideline on Fortification of Food with Vitamins and Minerals* (refer Attachment 1). The Policy Guideline covers both voluntary and mandatory fortification and contains several specific order Policy Principles in relation to the mandatory addition of vitamins and minerals to foods.

Since 1995 in Australia, and 1996 in New Zealand, folic acid has been permitted to be voluntarily added to a maximum claim of 50% RDI for adults (100 μg) per reference quantity of the following foods: flour; savoury biscuits; breads; breakfast cereals; pasta; fruit and vegetable juices and drinks; fruit cordial; beverages derived from legumes (Standard 1.3.2 of the *Australia New Zealand Food Standards Code* (the Code)). Folic acid may also be added to analogues of dairy foods and meat but in smaller amounts.

Since 1998, a health claim (describing the established link between adequate maternal dietary folate intake and a reduction in risk of NTDs developing in pregnancy) has been permitted on certain fortified and non-fortified foods as part of the Folate–NTD Health Claim Pilot (P170) and in accordance with Standard 1.1A.2 of the Code. The voluntary use of the folate-NTD health claim is permitted under certain conditions on listed food products. Food labels carrying the folate-NTD health claim must contain a footnote advising that the RDI of 200 μg referred to is for adults, whereas for women during the peri-conceptional period the recommended amount is 400 μg per day.

The temporary provision for the folate-NTD health claim has been extended four times and is now in effect until 13 February 2006.

4.2 International regulation of folic acids in foods

4.2.1 Codex Alimentarius

The Codex Alimentarius does not mandate the addition of particular nutrients to certain foods other than some special purpose foods.

However for generally consumed foods, the *General Principles for the Addition of Essential Nutrients to Foods* (Codex Alimentarius Commission 1991) provide that essential nutrients may be added to foods for the purposes of: restoration; nutritional equivalence of substitute foods; fortification; or ensuring the appropriate nutrient composition of a special purpose food.

4.2.2 Countries with fortification regulations

A number of countries have introduced mandatory requirements for folic acid fortification of foods in an effort to reduce the incidence of NTDs. These include Canada, the USA, Indonesia, and a number of South American and African countries.

Voluntary fortification only is also permitted for certain foods in a number of European countries (including United Kingdom, Ireland and Hungary) and in a number of Middle Eastern and Asian countries.

Further information about international experience of folic acid fortification (and the impact on NTD rates) is included in Section 5 and Attachment 6.

4.3 Folate

4.3.1 Folate terminology and forms

Folate is a water-soluble vitamin. The term *folate* is used generically to refer to the various forms of the vitamin, both naturally-occurring and synthetic, and its active derivatives (Department of Health 2000).

Natural forms of folate are found in a wide variety of foods including green leafy vegetables, cereals, fruits, grains, legumes, yeast extract, and liver. This type of folate is referred to as *naturally-occurring folate* in this document, to differentiate it from folic acid added to food in fortification. Naturally-occurring folate generally contains more than one, typically five to seven, glutamate moieties attached to pteroic acid (polyglutamate) (Ball 1998).

Folic acid, or pteroylmono-glutamic acid (PGA), is the most common synthetic form of folate and is the form used in food fortification and in the majority of supplements. As its name indicates, folic acid contains a single glutamate moiety attached to pteroic acid (Ball 1998). Folic acid is sometimes supplied in the form of disodium folate. Folic acid is rarely found occurring naturally in foods (National Health and Medical Research Council (NHMRC) 1995).

4.3.2 Recommended Intakes of Folate

The current Recommended Dietary Intake (RDI) for total folate for Australia and New Zealand range from 50-75 μg per day for infants to 200 μg per day for the general adult population. However, the RDIs for pregnant and lactating women are considerably higher, at 400 μg and 350 μg per day, respectively (NHMRC 1991).

There are potentially adverse health impacts resulting from excess intake of folate and this has lead to the establishment of Tolerable Upper Intake Levels (TUIL) for each group. The TUIL has been set using masking of vitamin B_{12} deficiency by folic acid as the most appropriate end point. Both the US and EC have established a TUIL of 1000 μg per day for adults with correspondingly lower levels established for children of different ages. The TUIL established for children by the US and the EC are similar, although not identical (Institute of Medicine 1998).

Currently Australia and New Zealand have not established TUIL. However, the National Health and Medical Research Council (NHMRC) and New Zealand Ministry of Health (NZMoH) are currently conducting a joint project to develop a suite of dietary reference values including revised Australian and New Zealand RDIs and new TUIL, expected to be released in late 2005.

4.3.3 Folate bioavailability

Bioavailability refers to the ability of the body to extract, absorb, and metabolise nutrients in food. The bioavailability of folate is not fully understood and there appear to be a number of factors that influence it.

It is difficult to predict the bioavailability of folate from a mixed diet, based on studies of individual foods (Brouwer et al, 2001; Gregory 1995; Sanderson et al, 2003).

Factors that influence folate availability from food include:

- composition of the food matrix (including the presence of antagonistic components most notably organic acids binding to other food components and encapsulation within plant cells leading to reduced exposure to digestive enzymes);
- amount of folate consumed;
- chemical form of folate; and
- host-related factors including nutrient and health status and genetic factors.

Naturally-occurring folate is generally considered to be less bioavailable than folic acid, but studies in this area are limited and somewhat inconsistent. Bioavailability of folic acid itself, when added to foods (e.g. fortification), appears to be lower than when it is consumed alone (e.g. in supplement form) (Brouwer et al, 2001; de Ambrosis et al, 2004). Differences in bioavailability of the various forms of folate are reflected in the term 'Dietary Folate Equivalents' (DFEs). Some data referenced in subsequent sections of this Report refer to DFEs, which are further explained in Attachment 2.

4.3.3 Folate metabolism

The majority of dietary folate is absorbed within the proximal region of the small intestine. Polyglutamate forms of folate have to be hydrolysed to the monoglutamates forms before they can be absorbed. Some components of food, low pH, some disease states and exposure to certain drugs and alcohol can inhibit this process and impair the absorption of polyglutamate food folate, accounting for the relatively low bioavailability of naturally-occurring folate.

Folate is used by the body in two important pathways: the DNA cycle and the methylation cycle (refer to Figure 1 in Section 5.2 for a simplified outline of the biochemistry involved). The DNA cycle is vital to cells as this is how purines and pyrimidines are synthesised. Therefore, folate is essential for *de novo* DNA biosynthesis and cell replication. The methylation cycle provides the cell with an adequate supply of S-adenosylmethionine, which acts as a methyl donor in a wide range of methylation reactions.

Folate is excreted in the urine, either as the metabolically active form or as breakdown products. In normal subjects urinary losses are < 10 ug/day (Expert Group on Vitamins and Minerals 2002). A small amount is also excreted in the bile and faeces.

4.4 Neural Tube Defects (NTDs)

NTDs are a family of congenital defects, which arise during the development of the brain and spinal cord *in utero*. In the very early stage of pregnancy, a band of cells along the dorsal surface of the embryo develop into a hollow tube called the neural tube, which eventually forms the spinal column and central nervous system. This process, called neurulation, reaches completion by day 22 to 28 after ovulation (Van der Put et al, 2001; Verity et al, 2003). Incomplete closure of the neural tube may lead to one or more of the following three neural tube defects:

- Spina bifida – This is a condition whereby incomplete closure of the neural tube results in the spinal cord being exposed or protruding through a gap in the spine. Over 80% of infants born with spina bifida survive into adulthood, but can develop leg paralysis or weakness, lack of bowel or bladder control and excess fluid around the brain (hydrocephalus).

- Anencephaly – This condition is characterised by a failure of the anterior neural tube to close, resulting in the total or partial absence of the cranial vault and brain tissue. Together spina bifida and anencephaly account for 90% of all cases of NTDs. Infants are usually stillborn or die shortly after birth.

- Encephalocoele – This condition is characterised by the meninges and/or brain tissue extruding through a defect in the skull. This is the least frequent of the neural tube defects (Lancaster and Hurst, 2001). The survival pattern of encephalocoele results in a low proportion of stillbirths, the majority of deaths occurring within the first year of life, and a long-term survival of around 50% (Kalucy et al, 1994).

The process of brain and spinal cord development can be disrupted by genetic and environmental factors. The risk of NTDs is increased by: certain single-gene disorders and chromosomal anomalies; maternal factors such as diabetes mellitus; use of anticonvulsant medication; and inadequate folate intake. The risk is also increased in women who have previously had a NTD-affected pregnancy (rate of NTDs in this high risk group ?100-500 per 10,000 births) (Cornel and Erickson in (NZMoH 2003). Differences in the incidence of NTDs have also been associated with geographical location, ethnicity, seasonal variation, maternal age, and socioeconomic status (Van der Put et al, 2001).

In Australia, the average NTD incidence rates reported for 1996-1997 were 11.5 births and terminations of pregnancy per 10,000 total births comprising:

- 4.6 per 10,000 total births for anencephaly;
- 5.7 per 10,000 total births for spina bifida; and
- 1.2 per 10,000 total births for encephalocoele (Lancaster and Hurst 2001).

Based on South Australian data accumulated over a number of decades and generalised to the Australian population, it appears that up to 500 pregnancies (births and terminations) are affected by a NTD each year (Lancaster and Hurst 2001).

In New Zealand approximately 30 live or stillbirths are affected by a NTD each year (NZFSA/ NZMoH 2004). In 1999, the prevalence rate per 10,000 was 9.1 total births (including live births, stillbirths and terminations) (NZMoH 2003).

Care needs to be taken in comparing NTD rates between Australia and New Zealand due to differences in definitions and data collections including uncertainty regarding the ascertainment of terminations included in the data. In most countries the occurrence of NTDs is between 5-30 per 10,000 births (Cornel and Erickson in (NZMoH 2003).

The rate of infants born with NTDs appears to have been declining in many countries since the 1980s (including Australia and New Zealand). The reasons for this are not entirely clear but cannot be fully explained by increased screening and terminations.

5. Relevant Issues

The purpose of this section is to detail all issues that are relevant to consideration of the best means to reduce the rates of NTDs.

The issues addressed in this section include the impact of folate intake during the peri-conceptional period and the impact of folate on the general population. Consideration of these issues assists in establishing the overall benefits and risks associated with increasing folate consumption and in determining the most appropriate regulatory option.

This section also examines the strategies that have been implemented in Australia and New Zealand in an attempt to reduce the risk of NTDs and the overall impact of these strategies.

Exploration of these issues is consistent with the requirements of the Ministerial Council that there be a comprehensive assessment of alternative strategies (including voluntary fortification and education programs) before a decision is made regarding mandatory fortification.

Finally, this section of the Initial Assessment Report examines international precedent in relation to fortification.

5.1 Impact of Folate Intake in the Peri-conceptional Period

5.1.1 Potential risks of inadequate folate intake

Patterns of nutritional deficiency have historically been correlated with an increased prevalence of NTDs around the world. In 1964, it was noted that women who delivered infants with NTDs had suspected folate deficiencies resulting from abnormal folate metabolism (Hibbard 1964).

Other early studies investigated the use of multi-vitamin supplementation (during the peri-conceptional period) in women with a previous history of NTD-affected pregnancies (that is, a recurrence of a NTD). These double-blind randomised controlled trials concluded that folate was the active agent in reducing the risk of NTDs (Laurence et al, 1981; Smithells et al, 1980).

Insufficient maternal folate intake has also been associated with increased risks of preterm delivery, infant low birth weight and foetal growth retardation (Scholl and Johnson 2000).

5.1.2 Potential benefits of increased folate intake

More recent studies suggest that folic acid supplementation can significantly reduce the risk of NTDs. Some of these studies have been population-based interventions (Berry et al, 1999) while others have been randomised controlled trials ((MRC Vitamin Study 1991), Czeizal and Dudas 1992). These studies demonstrated that folic acid supplementation at levels ranging from 400 μg to 4 mg per day significantly reduced the incidence of NTDs (up to 80%). These studies have been supported by a meta analysis of previous studies, which concluded that folate supplementation at rates of between 360 μg to 4 mg per day (during the peri-conceptional period) reduced the first occurrence and recurrence of NTDs (Lumley et al, 2001).

It should be noted that all of these studies are based on folic acid supplementation and not fortification of food with folic acid. Evidence is emerging that fortification of foods with folic acid can deliver comparable results (refer case studies in Attachment 6).

Subsequent research has demonstrated that the decrease in NTDs appears to be dependent on the baseline folate status and rate of NTDs (Berry et al, 1999).

5.1.3 Potential risks of increased folate intake

The potential risks associated with folic acid supplementation have also been examined. Folic acid supplementation has not been found to cause a significant increase in miscarriage, ectopic pregnancy or stillbirth. Although several studies have described a trend towards increased risk of multiple gestation (e.g. (Czeizel et al, 1994) and (Lumley et al, 2001)), this trend has not been observed in the US where there has been mandatory fortification of enriched cereal grains since 1996 ((Shaw et al, 2003); (Waller et al, 2003)).

5.2 Impact of Folate Intake on the General Population

5.2.1 Potential risks of inadequate folate intake

In developed countries, folate deficiency in the general population is rare, however, pregnant women, the elderly and low socioeconomic groups are at increased risk of folate deficiency (De Bree et al, 2002).

Very little information is available on the prevalence of folate deficiency in Australia and New Zealand. However, some studies suggest that the folate status levels are sub-optimal or deficient in only 2-5% of the population ((Metz et al, 2002), (Flood et al, 2004) and(Ferguson et al, 2000).

If there is inadequate folate in the diet, the activity of the methylation and DNA cycles is reduced. A decrease in the activity of the DNA cycle is most obvious in rapidly dividing cells. For example, decreases in red blood cell production, which result in megaloblastic hematopoiesis, with characteristic changes in bone marrow and peripheral blood and a progressive decline in erythrocyte, leukocyte and platelet counts. Failure of DNA synthesis can result in an increased susceptibility to infection, a decrease in blood coagulation, and secondary malabsorption (FAO/WHO expert consultation on human vitamin and mineral requirements 1998).

Changes in the activity of the methylation cycle may result in elevated levels of plasma homocysteine which has been recognised as a risk factor for cardiovascular disease (CVD) (Boushey et al, 1995). The most common cause of elevated plasma homocysteine levels in the general population is purported to be folate deficiency, consistent with its role as a cofactor in the conversion of homocysteine to methionine.

Chronic, severe folate deficiency has also (rarely) been associated with neurological disease (Manzoor and Runcie 1976). This may be due to the fact that folate is concentrated in nerve tissue compared to the plasma, providing nerve tissue with adequate supplies even when plasma folate levels have been inadequate for some time. For this reason, anaemia will often present clinically earlier than the neuropathy.

5.2.2 Potential benefits of increased folate intake

There may be potential benefits in that increased serum folate concentrations may lead to a lowering of the mean blood concentrations of homocysteine in the population and a decrease in the prevalence of severely elevated homocysteine concentrations (HLT Collaboration 1998; Jacques et al, 1999). It is possible that this will lead to a reduction in the incidence of CVD (Wald et al, 2002). However, there is still some uncertainty as to whether homocysteine levels are a causative agent of cardiovascular disease and if folic acid treatment will be an effective intervention (Eikelboom et al, 1999; O'Leary et al, 2004; Verhoef and Katan 2004).

5.2.3 Potential risks of increased folate intake

The available data show that no adverse effects are associated with the consumption of naturally-occurring folate as the folate levels in food are not high enough to pose a risk of toxicity (Institute of Medicine 1998).

While oral folic acid is generally considered to be safe for the majority of the population (even at high doses (>1 mg/day)), studies suggest that there may be risks to certain groups. In particular, concern has been expressed about high doses of folic acid having the potential to mask the haematological signs of vitamin B_{12} deficiency. Vitamin B_{12} deficiency causes anaemia and can cause neurological damage (peripheral neuropathy, spinal cord damage and cerebral dysfunction), which may be irreversible if not treated early.

The biochemical pathways of folate and vitamin B_{12} interact (see Figure 1) and it is this interaction which results in the masking effect. Folate intake can resolve the haematological symptoms and thus delay the appearance of neurological symptoms and diagnosis of vitamin B_{12} deficiency. The relationship between anaemia and the development of neurological symptoms is complex, with some cases of deficiencies exhibiting only the neurological symptoms (Campbell 1996; Lindenbaum et al, 1988; Savage and Lindenbaum 1995) cited in (European Commission 2000). Furthermore, in some cases folate intake has precipitated or exacerbated vitamin B_{12} deficiency-related neuropathy although this has not occurred in all cases (Dickinson 1995).

Vitamin B_{12} deficiency is most common in elderly people, mainly due to less efficient absorption of nutrients in the gut. In New Zealand it has been estimated that 10% of adults over 65 years of age have vitamin B_{12} deficiency (NZFSA/ NZMoH 2004). In the US and UK, it is estimated that approximately 10-15 % of people over 60 years of age are affected by vitamin B_{12} deficiency, which may eventually lead to megaloblastic anaemia (Baik and Russell 1999; Clarke et al, 2004). Vegans are also at particular risk of developing vitamin B_{12} deficiency due to the complete absence of animal foods in their diet.

The prevalence of vitamin B_{12} deficiency in the Australian and New Zealand general populations is not well defined. The limited studies undertaken tend to suggest that the level of vitamin B_{12} deficiency is between 1 and 22% ((Flicker et al, 2004), (Flood.V.M. et al, 2001) and (Ferguson et al, 2000). However, care should be taken in the interpretation of this data because the reference values that define deficiency (as used in the studies) vary.

Table 1: Australian and New Zealand Serum Vitamin B_{12} Levels

Study Group	Results	Author
Australia		
Perth 299 men aged over 74 years	14 % were deficient[1]	(Flicker et al, 2004)
Perth 273 women aged over 69 years	6% were deficient[1]	(Flicker et al, 2004)
New South Wales 371 males and females aged over 49 years	22% had serum B_{12} levels below 185 pmol/L, suggesting deficiency	(Flood.V.M. et al, 2001)
New Zealand		
Dunedin 216 women (aged 18 – 45 years)	2% were vitamin B_{12} deficient[2]	(Ferguson et al, 2000)
Dunedin 140 boys (aged 14 – 19 years)	1% were vitamin B_{12} deficient[2]	(Ferguson et al, 2000)

[1] deficiency not defined in study, reference range 140 – 646 pmol/L
[2] defined as <60 pmol/L

What other data are available on the extent of vitamin B_{12} deficiency in Australia and New Zealand?

The first symptom of insufficient vitamin B_{12} is often, but not always, megaloblastic anaemia, followed by neuropathy. It is not clear what causes the neurological symptoms of vitamin B_{12} deficiency, however, they may be due to the interruption of the methylation cycle and the resultant reduction in methylated myelin basic protein (Expert Group on Vitamins and Minerals 2002; Savage and Lindenbaum 1995).

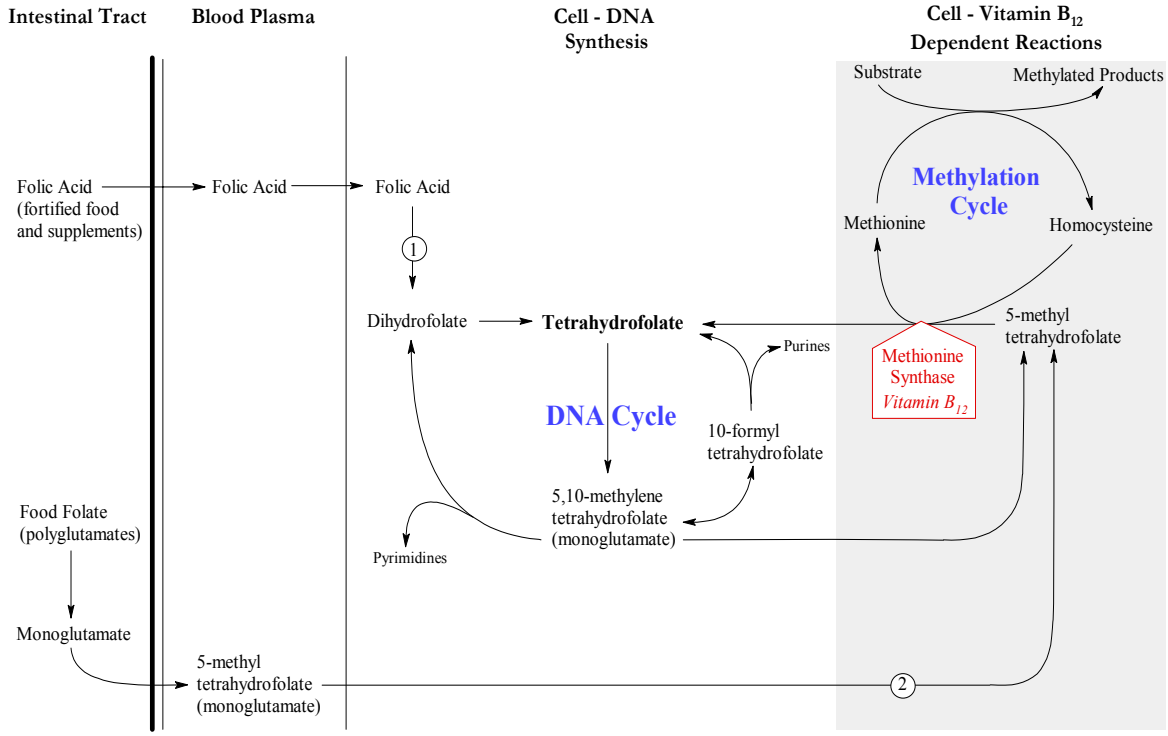
Therefore the key issue in relation to potential masking of B_{12} deficiency is whether further fortification would produce a masking effect and whether the medical profession depends on the patient's haematological profile to make a diagnosis of vitamin B_{12} deficiency neurological disorder.

- There do not appear to be any other significant risks associated with increased folate intake in the general population. However, some studies have suggested that:

- large oral doses of folic acid (>1 mg) may lead to mental changes, sleep disturbances and gastrointestinal symptoms (Hunter et al, 1970);
- folic acid supplementation may have a negative effect on zinc status, although studies do not show a consistent trend (Expert Group on Vitamins and Minerals 2002); and
- there are risks associated with the interaction between folate and drugs used in the treatment of common conditions such as epilepsy, rheumatoid arthritis, cancer, and bronchial asthma (e.g. anticonvulsant drugs, folate antagonists and anti-inflammatory drugs). Some studies suggest that increased folic acid intakes may influence the effectiveness of these drugs.

Furthermore, the consequences of long-term high-level intakes of folate are not clearly established (Expert Group on Vitamins and Minerals 2002).

Figure 1: DNA Biochemical Pathways Influenced by Folic Acid/Folate Intake



5.3 Optimal levels of folate intake and status to reduce the rates of NTDs

As the association between increased folate intake and reduced incidence of NTDs became established, both Australia and New Zealand instigated health policies recommending women take folic acid supplements during the peri-conceptional period. These policies have been introduced since 1993:

- The Australian NHMRC recommended that[3]: low risk women (no family history of NTDs, not on anticonvulsant medications) planning a pregnancy or likely to become pregnant should take folic acid supplementation at 0.5 mg daily, particularly in the month before, and in the first 3 months of pregnancy; and women with a family history of neural tube defects should be advised to take folic acid at 5 mg[4] per day during the peri-conceptional period.

- Current New Zealand policy recommends that women planning a pregnancy take 800 µg[5] [6]of folic acid daily for the month prior to conception and 3 months after, to reduce the risk of NTDs. Women at high risk of having a baby with an NTD are advised to take 5 mg folic acid per day for the same period (NZMoH 1999).

[3] This policy has since been rescinded by the NHMRC.
[4] 4 mg folic acid tablets were not available in Australia at this time.
[5] In New Zealand 800 µg is recommended as a 400 µg folic acid supplement is not available in New Zealand (NZMoH 2003).
[6] In 2004 the NZFSA consulted on proposed changes to the Dietary Supplements Regulations 1985, including an increase in the maximum permitted level of folic acid in a dietary supplement from 300 µg to 500µg (NZFSA 2004).

Since these policies were introduced in Australia and New Zealand, further studies have been undertaken overseas examining the relationship between folic acid intake, folate status in the body and NTD risk. Reference amounts for optimal folic acid intake, and optimal serum or red blood cell folate levels in this context have been established by overseas studies:

- Cohort studies found that women who had NTD-affected pregnancies had lower red blood cell (RBC) folate, serum folate and vitamin B_{12} levels compared to controls. As a result of these studies, RBC folate concentrations over 900 nmol/L were established as the optimal level for reducing the occurrence of NTDs (Daly et al, 1995; Kirke et al, 1993; Wald et al, 2001). This is assumed to be a maximal level, as NTDs which occur in women with high levels of RBC folate are assumed to be caused by other factors (Daly et al, 1995).

- The risk of having a NTD-affected pregnancy has been inversely associated with folate levels in a continuous and dose-dependent manner (Daly et al, 1995; Wald et al, 2001). In addition, risk reduction models based on clinical trials show that the magnitude of the risk reduction is inversely proportional to the folate status of the target group. This means that for a given dose of folic acid, a greater reduction in NTD risk would be predicted for target groups with poorer initial folate status (Wald et al, 2001).

- A UK study modelling the effect of food fortification on the population, found that the maximal protective effect against NTDs would be gained if a fortification program were chosen such that the entire target group received an intake of 400 μg folic acid per day. On average, this would result in RBC folate levels above the 900 nmol/L optimal level, which would prevent at least 60% of NTDs from occurring (Daly et al., 1997).

- No equivalent studies have been undertaken in Australia or New Zealand.

- It is yet to be determined whether the folate intakes and folate status are sufficiently well described and the reference values appropriate for Australia and New Zealand to predict the possible number of NTD cases saved through increased folate intake under the various options proposed. However, the overseas experience suggests that a reduction in the number of NTD cases is inversely proportional to the initial number of cases. This will require detailed consideration at Draft Assessment.

5.4 Strategies used in Australia and New Zealand to increase folate intake and reduce incidence of NTDs

The Policy Guideline adopted by the Ministerial Council provides that any consideration of mandatory fortification must include a comprehensive assessment of alternative strategies.

The purpose of this section is to identify the alternative strategies that have been employed in Australia and New Zealand to date. The subsequent section examines the impact that these strategies have had on reducing the incidence of NTD-affected pregnancies.

The main primary prevention strategies that have been employed in an attempt to reduce the risk of inadequate folate during the peri-conceptional period (and the attendant risk of NTDs) have been:

- promotion of diets high in naturally-occurring folate and promotion of folic acid supplements during the peri-conceptional period; and/or
- voluntary fortification of the food supply with folic acid; and
- a health claim in relation to both fortified and non-fortified foods.

These strategies, including their respective impacts and reported advantages and disadvantages are detailed in Attachment 4 but each of the strategies, together with the impact of each strategy, is summarised below.

5.4.1 Promotion of diets high in naturally-occurring folate and promotion of folic acid supplementation during the peri-conceptional period

Three national campaigns have been implemented in Australia, together with a number of State-based campaigns, to promote increased consumption of folate rich foods and folic acid supplementation. There have not been any publicly funded campaigns in New Zealand.

It is well recognised that it is difficult to obtain a sufficient intake of folate to further reduce the incidence of NTDs from naturally-occurring folate in food and it is also generally reported that campaigns focusing on increasing intake of folate rich foods have not produced significant improvements in folate intake and have not conferred significant protective effects against NTDs (Brown et al 1997 in (Chan et al, 2001)

Australia and New Zealand have policies promoting the use of folic acid supplements and have promoted the use of supplements in conjunction with campaigns promoting the consumption of folate rich foods. It is recognised that to be effective, sufficiently high dosage supplements must be taken consistently during the peri-conceptional period. However, research suggests that only a small proportion of women take the supplements during the recommended period, although evidence from New Zealand and Western Australia suggests that this proportion increased following public health campaigns, but not higher than approximately 40% (Bower et al 2002, Ferguson et al 2000; Schader and Corwin 1999). It is unclear whether this rate could be further increased by additional promotional effort.

A significant issue in relation to supplementation is the fact that approximately 45-50% of pregnancies in Australia and New Zealand are unplanned, and the neural tube develops before many women know they are pregnant (Schader and Corwin 1999 cited in (NZMoH 2003; The Alan Guttmacher Institute 1999).

What other data are available on the extent of current folate supplement use by the target group in Australia and New Zealand?

5.4.2 Voluntary fortification of the food supply with folic acid

Voluntary fortification of food with folic acid commenced in Australia in 1995 and in New Zealand in 1996. Information from 1999 indicates that in Australia at that time 104 folate-fortified products were available, while information from New Zealand indicates that at the end of 2001, there were 81 folate-fortified foods. In both countries breakfast cereals are the predominant folate fortified food. There does not appear to be more recent data available on the extent or type of folate-fortified food.

The impact of voluntary fortification on dietary intake of folate can be estimated using modelling of consumption patterns, although an accurate determination is hampered by the lack of up-to-date information on the available fortified foods. However, it has been estimated that voluntary fortification has lead to a small improvement in mean dietary intakes of folate in women of child-bearing age in both Australia and New Zealand with an 11% increase in Australia (from 213 μg to 235 μg) and a 13% increase in New Zealand (from 203 μg to 234 μg) (Abraham and Webb 2001; Newton et al, 2001). However, the mean intakes were significantly lower than recommended intake levels (of 400 μg) in both countries. This is described further at Attachment 4.

What foods are currently fortified with folic acid and are these foods marketed to the target group?

5.4.3 Health claim for folate containing foods

In 1998 the former ANZFA approved a health claim that referred to the relationship between consumption of folate rich foods and reduced incidence of NTDs. The claim was approved as part of a pilot project exploring a possible management framework for regulating health claims. The evaluation of the pilot project provided information on the role of claims in promoting the consumption of folate rich foods. The evaluation found that the claim on folate rich foods produced some increase in the awareness and changes in eating behaviour of women (up to 29%). However, there appeared to be no change in sales of folate rich foods carrying the claim (ANZFA 2000).

5.5 Overall impact of existing strategies

Each of the strategies detailed above has operated in conjunction with one another. As such it is very difficult to analyse the relative impact of each. However, some comments can be made about the overall impact of these strategies.

There are a number of different means by which to measure the impact of these strategies including changes:

- in awareness of folate;
- to levels of awareness of the folate-NTD association;
- to dietary behaviour;
- in folate status in women (red blood cell and mean serum folate); and
- in overall rates of NTDs.

Relevant data in relation to these is shown at Attachment 5.

5.5.1 Impact of these strategies on awareness of folate

Knowledge regarding folate and its importance is integral to dietary change and folic acid supplement use. To increase folate consumption and reduce the risk of an NTD-affected pregnancy, women of child-bearing age need to be aware of the association between folate and neural tube defects, know when to increase folate intake, the amount required and how to obtain this (Abraham and Webb 2001).

In Australia, between November 1998 and November 1999, during an extensive education campaign in relation to the health claims pilot, the national proportion of women of child-bearing age who had heard of folate, increased from 82% to 88% (Abraham and Webb 2001). Respondents from WA and SA (States that had active folate awareness campaigns), were more likely to have heard of folate than respondents from other states.

New Zealand has not conducted any publicly funded health campaigns but a survey of women in Christchurch undertaken in 1999, found that 91% of Christchurch women had heard of folate ((NZMoH 2003).

5.5.2 Impact of these strategies on awareness of folate-NTD association

The evaluations of State-based public awareness campaigns have shown that the campaigns have generally been effective in increasing women's knowledge of the role of folate, although the figures vary between surveys and regions as outlined at Attachment 4. The evaluation of the national Folate-NTD Health Claim Pilot found that between 1998 and 1999 there was an increase (from 40% to 46%) in the proportion of women who were aware of the association between folate and birth defects (ANZFA, 2000). These results also indicate awareness increased with age, education level and household income (Abraham and Webb 2001; ANZFA 2000)

There is also evidence that population based folate promotion campaigns have not been as effective for certain groups, such as Indigenous Australians. For example, only 55% of Indigenous women in Western Australia reported knowledge of the importance of folate, 21% less than non-Indigenous women in the same State (Bower et al, 2004).

5.5.3 Impact of these strategies on behavioural change

Sales data have been used to support reported folate consumption behaviour. The ANZFA evaluation of the folate health claim pilot indicated that there had been no significant change in sales of foods high in folate or with added folate between 1998-99 (ANZFA 2000).

The surveys conducted (as detailed at Attachment 5) tend to suggest that there has only been a small increase in consumption of folate rich foods and folic acid supplements by the target population (3-24%)(Abraham and Webb 2001).

5.5.4 Impact of these strategies on folate status

Folate status is most commonly assessed by measurement of folate in serum and red blood cells. While the introduction of voluntary fortification of certain foods with folic acid is presumed to have had a modest positive effect on serum folate levels and red blood cell folate levels, this is difficult to measure because of the absence of baseline data for the pre-fortification period.

5.5.4.1 Serum folate status

Serum folate levels indicate folate status at the time of the blood sample. Higher maternal serum folate levels have been associated with a lower risk of NTD-affected pregnancies (Kirke et al, 1993).

There are limited data that measure the impact on serum folate levels of strategies to increase folate intake in Australia and New Zealand (Ferguson et al 2000; Metz et al 2002; Flicker et al 2004). The mean serum folate levels measures to date are variable, ranging from 12.9 nmol/L (median value) to 25.3 nmol/L.

Only one large study of Victorian adults aged 15-45 measured serum folate before and after voluntary fortification. This study found that the mean serum folate concentration had increased by approximately 19% for women and 16% for men, after the introduction of voluntary fortification. However, it should be noted that no details were available on the level of folic acid supplement use and as such the change in serum folate levels cannot necessarily be attributed to voluntary fortification. The proportion of people with low serum folate levels decreased from 8.5% to 4.1% since fortification (Metz et al, 2002).

5.5.4.2 Red blood cell folate status

Red blood cell (RBC) folate status is recognised as a more reliable indicator of long-term folate status, as it is not easily affected by daily fluctuations due to food consumption (Booth et al., 1998). A very low risk of NTDs has been associated with maternal RBC folate levels greater than or equal to 900 nmol/L (Daly et al, 1995).

There do not appear to be any studies examining RBC folate levels pre and post the implementation of strategies such as campaigns and voluntary fortification. Information on the levels of RBC folate in Australia and New Zealand comes from three studies (refer Table 1 below), which suggests that the mean RBC folate concentrations vary from 486 nmol/L to 791 nmol/L (both median values) (Booth et al 1998; Ferguson et al 2000; Queensland Health 2002).

It should be noted that in relation to the New Zealand study, 97% of participants had RBC folate concentrations within acceptable levels. One third of women were found to have RBC folate concentrations greater than or equal to the target of 900 nmol/L, in the post-voluntary fortification period. Less than 5% of women and boys exhibited suboptimal RBC folate concentrations (Ferguson et al, 2000).

Comparison of these data with international optimal references of 900 nmol/L, suggests that there may be potential for an increase in folate status to further reduce rates of NTDs.

Table 2: Mean RBC Folate Concentrations in Australia and New Zealand

Study	Year of assay	Vitamin supplement use	Pre-voluntary fortification (nmol/L)	Post-voluntary fortification (nmol/L)	Author
Australia					
1176 adult blood donors (16-70 years) 111 reference group (18-65 years)	1995	No	468* 615*		(Booth et al, 1998)
540 females (25-75 years) 468 males (25-75 years) 322 females (25-75 years) 158 males (25-75 years)	2000	No No Yes† Yes†		626 602 777 706	(Queensland Health 2002)
New Zealand					
216 women (18–45 years) 140 boys (14-19 years)		Yes†† Yes		787* 791*	(Ferguson et al, 2000)

*Median RBC folate concentration
†Vitamin use during 24 hours prior to survey. Type not specified.
††Combined data from users and non-users of all vitamin supplements. Duration of use or type not specified.

What other data are available on serum folate or RBC folate status of Australians and New Zealanders?

Are data on folate status required to assess health and safety impact of increases in folic acid intake? If so, are the quoted or other identified data sources sufficient? If not, what data would be necessary?

5.5.5 Impact of strategies on NTD rates

5.5.1 In Australia

Since the late 1980s, a marked reduction in the number of actual births affected by an NTD has occurred, directly attributable to improved methods of prenatal detection and subsequent termination (Lancaster and Hurst 2001). The change in total NTD rates (comprising births and terminations where available) for both Australia and New Zealand since the introduction of voluntary fortification and education strategies is reflected in Table 3 below.

Table 3. Incidence[7] of NTDs in Australia and New Zealand

Jurisdiction	Rate per 10,000 births			
	Level of ascertainment of births and terminations	**Pre-voluntary fortification 1991-1995**	**Post-voluntary fortification 1996-1997**	**Percentage change**
Australia				
South Australia	*Complete ascertainment of births and terminations*	17.7	15.9	↓10.1%
Victoria	*Near-complete ascertainment of births and terminations.*	17.0	19.2	↑11.5%
Western Australia		16.2	10.4	↓35.8%
Australian Capital Territory	*Complete ascertainment of births. Incomplete ascertainment of terminations*	13.5	16.7	↑19.2%
New South Wales		9.0	8.0	↓11.1%
Northern Territory		12.9	11.4	↓11.6%
Queensland		7.9	7.1	↓10.1%
Average Australian Rate		**12.4**	**11.5**	**↓7.3%**
New Zealand				
		1980	**1999**	
	*Incomplete ascertainment of births and terminations**	12.0	9.1	↓24.2%

* New Zealand data is obtained from a variety of sources: the New Zealand Birth Defects Monitoring Programme (NZBDMP) (live births 1996-2000); the New Zealand Health Information Service (stillbirths 1996-2000); Statistics New Zealand using data from the Abortion Supervisory Committee (therapeutic terminations 1998-2000) (NZMoH 2003).

Care should be taken in interpreting the above results and drawing any conclusions when examining the impact of interventions using national data because:

- The number of NTD-affected pregnancies is under-reported in most States and Territories, due to differences in legislative requirements in the reporting of terminations (Lancaster and Hurst 2001). South Australia is the only State to have mandatory reporting of terminations of pregnancies; Western Australia has established the accuracy of data gathered by the Western Australian Birth Defects Registry (Bower et al, 2000). However, other States and Territories report terminations of NTD-affected pregnancies on a voluntary basis (Lancaster and Hurst 2001).

- As South Australia and Western Australia have the most stringent requirements regarding the notification of terminations, the decreases observed in these States are considered "true rates". The observed decrease in the incidence of NTDs is believed to be due to the effect of the current folic acid fortification policy combined with various health promotion activities (Lancaster and Hurst 2001).

- Certain population groups are more at risk of having a NTD-affected pregnancy. For example, data from the Western Australian Bibbulung Gnarneep study (2004) combined with those of the Western Australian Birth Defects registry were used to report the number of NTD-affected births and terminations in a group of Indigenous women, the majority of who lived in rural and remote areas.

[7] Incidence is the preferred term for Australian data, and prevalence for New Zealand data

This study found that, although there had been an overall decrease in the rate of NTDs for Indigenous women (from 31.9/10,000 in 1993-1995 to 25.6/10,000 in 1996-2000), they were almost twice as likely to have an NTD-affected pregnancy than non-Indigenous women (i.e. 25.6/10,000 for Indigenous women compared to 12.9/10,000 for non-Indigenous women in 1996-2000) (Bower et al, 2004).

5.5.2 In New Zealand

As shown in the table above, the prevalence of NTD-affected births in New Zealand was 12 NTD cases per 10,000 births in 1980 (Ferguson et al., 2000). In 1999, the prevalence was 9.1 per 10,000 live births, stillbirths and terminations (NZMoH 2003).

Care should be taken in drawing any conclusions from these results for the following reasons:

- Due to a change in the requirement of notification of live and stillbirths which occurred in 1992, these events are likely to have been previously under-reported and misclassified (NZMoH 2003).

- There have been suggestions that the prevalence of NTD-affected births is lower amongst Maori people compared to non-Maori people, however recalculation of these figures to include stillbirths has led to prevalence rates similar to that of non-Maori people. Maori people are reported to have an NTD-affected birth incidence of 6.7 (live and still) births per 10,000. Pacific peoples have been reported as having an NTD-affected birth prevalence of 3.5 per 10,000 births, lower than that of both Maori and Non-Maori people (NZMoH 2003).

What, if any, other more recent data are available on true incidence/prevalence of NTDs in Australia and New Zealand?

5.6 Overseas experience regarding mandatory fortification

Overseas experience in similarly developed countries provides an important source of information to guide consideration of mandatory fortification with folic acid in Australia and New Zealand. A number of countries require mandatory fortification of certain foods with folic acid. These include Canada and the United States, the majority of South American countries, and countries from Africa and Asia. The majority of these countries require folic acid fortification in cereal foods. Further details of countries that have mandatory fortification of certain foods are included at Attachment 6.

Unfortunately most of these countries do not appear to hold data relating to changes to NTD rates pre and post mandatory fortification. This will however be investigated further by FSANZ at Draft Assessment.

The United States has the most data available on the impact of mandatory folate fortification. In addition, the United Kingdom is currently considering several issues that are involved in the consideration of mandatory folate fortification. The details are given in the 2 case studies below.

5.6.1 United States of America

Mandatory folate fortification of enriched cereal grain products at 140 µg/100g was first introduced in 1996 and fully implemented by 1998. Fortified products included wheat flour; bread, rolls and buns; corn grits and meal; and rice and macaroni products. Because these were staple foods and ingredients, mandatory fortification increased the folate content of more than one third of the available foods.

Studies found the introduction of mandatory fortification resulted in an average increase of almost 200 µg folic acid from the diet across all sectors in the community. This was more than had been predicted possibly because of a higher than anticipated overage level adopted by industry. Such an increase in intake has led to a significant positive increase in measures of folate status for all US population groups including women of childbearing age. It has also reduced the prevalence of folate deficiency.

After the complete implementation of mandatory folate fortification, prenatally ascertained NTD-affected pregnancies decreased by an average of 27% (approximately 1,000 cases). The Centers for Disease Control attribute this decrease to mandatory folate fortification. Concerns about the potential masking of vitamin B_{12} deficiency and increased rates of twinning appear to have been unfounded.

Further details of mandatory fortification in the US are included at Attachment 6.

5.6.2 United Kingdom

Voluntary fortification of bread-making flour and breakfast cereals has been in place since the mid to late 1980s. In 2000, the Committee on the Medical Aspects of Food and Nutrition (COMA) concluded that on scientific, medical and public health grounds, universal fortification of flour with folic acid at 240 ug/100g in food products as consumed would reduce NTD-affected pregnancies by 41% without resulting in unacceptably high intakes in other population groups.

However, it was subsequently considered that such fortification could result in intakes above the upper safe level for some older people, which could result in masking undetected vitamin B_{12} deficiency for those at risk. New evidence will be gathered and assessed on the possible adverse health impact of fortification on older people as well as the broader potential health benefits to the community before a final decision on fortification is made.

5.7 Practical Issues Associated with Fortification

The selection of appropriate food vehicle(s) for fortification is an important consideration. A number of organisations (Codex Alimentarius Commission 1991; Darnton-Hill 1998; Nutrivit 2000) have published criteria for selecting appropriate food vehicle(s), including the need for the selected vehicle to:

- be regularly consumed by the population at risk in stable, predictable amounts (upper and lower intake levels known);
- be available to the target population regardless of socio-economic status;
- supply optimal amounts of micronutrient without risk of excessive consumption or toxic effects;

- retain high level stability and bioavailability of the added micronutrient under standard local conditions of storage and use;
- be economically feasible;
- be centrally processed so that quality control can be effectively implemented; and;
- not interact with the fortificant or undergo changes to taste, colour or appearance as a result of fortification.

To date, international examples of food vehicles selected for fortification with folic acid are predominantly cereals foods, as shown in Attachment 6.

Another important consideration is to determine the appropriate quantity of fortificant(s) that should be added to the food vehicle(s), in order to deliver an effective public health outcome.

FSANZ will further investigate possible foods that could be subject to fortification (and the level of fortification to be required) in the Draft Assessment.

Consideration will also be given to the practical impacts of fortification in terms of manufacturing processes, for example:

- the purchase and storage of the permitted form of the fortificant(s);
- adjustment to processing and manufacturing practices to ensure the successful addition of the fortificant(s) to their product;
- analytical testing to confirm the appropriate levels of fortificant(s) in their product; and
- modification to labels to reflect the changing composition of the food.

Some of these issues will also apply to manufacturers using fortified ingredients.

6. Regulatory Options

In order to determine the most effective mechanism to increase dietary folate intake in peri-conceptional women to reduce the incidence of NTDs from current levels in the Australian and New Zealand population, FSANZ is considering the following four options:

1. Maintenance of the *status quo* (i.e. voluntary folate permissions for some foods);
2. Extension of permissions for voluntary folate fortification;
3. Mandatory folate fortification; and
4. Increased health promotion and education strategies to increase folate intakes.

6.1 Option 1 – Maintenance of the *status quo*

Maintenance of the *status quo* would see the continuation of the existing permissions for the voluntary addition of folic acid to certain foods, to a level of 50% RDI per reference quantity, as well as the continuation of the folate-NTD health claim until February 2006. Health promotion and education strategies to increase folate intakes in women of childbearing age would also be presumed to continue on an ad hoc basis.

6.2 Option 2 – Extension of permissions for voluntary folate fortification

This would permit industry to voluntarily add folic acid to an increased number of food categories. The additional food categories selected would be based on their ability to effectively deliver and sustain an increase in the folate status of the target population. The decision about whether to include folic acid in these additional food categories would ultimately rest with industry.

6.3 Option 3 – Mandatory folate fortification

Option 3 would require the mandatory addition of folic acid to a prescribed food vehicle(s). The prescribed food vehicle(s) would be selected based on its ability to effectively deliver and sustain an increase in the folate status of the target population (while minimising costs and unintended consequences to the population as a whole). In ascertaining suitable vehicle(s), whole product categories may not necessarily be affected, for example folic acid may be added to white bread only as opposed to all bread categories or added to low fat milk and not full fat milk.

6.4 Option 4 – Increased health promotion and education strategies to increase folate intakes

Option 4 is a non-regulatory option and could be selected as the sole strategy to further reduce the incidence of NTDs or be implemented in conjunction with any of the other three options. It is envisaged that Option 4 would require a considerable increase in the current health promotion and education strategies in order to further increase folate intakes in the target population. These initiatives would be aimed at encouraging women of child-bearing age to eat a diet rich in folate and to take folic acid supplements during the peri-conceptional period.

7. Impact Analysis

7.1 Affected Parties

The parties most likely to be affected by this Proposal are:

- **Consumers and the Community,** including women of child-bearing age, subpopulations at risk of vitamin B_{12} deficiency, as well as the general population;

- **Industry,** including manufacturers who currently have permissions to voluntarily fortify their product(s) with folic acid, manufacturers who wish to obtain further permissions to voluntarily fortify their product(s) with folic acid, manufacturers of potential food vehicles eligible for mandatory fortification, importers and exporters as well as manufacturers and retailers of folic acid supplements; and

- the **Governments** of Australia and New Zealand, including State and Territory Governments which are responsible for the delivery of education strategies.

7.2 Impact Analysis

7.2.1 Option 1 – Maintenance of the Status Quo (i.e. voluntary folate permission of some foods)

7.2.1.1 Impacts on consumers and the community

During the peri-conceptional period, the majority of women would continue consuming diets with insufficient folate because of the difficulty of consuming the recommended amount of dietary folate in food and the limitations of effective supplement usage (particularly because 40-50% of pregnancies in Australia and New Zealand are unplanned).

While the rates of NTDs in Australia and New Zealand have been steadily decreasing, it is unknown if a further reduction in the incidence of NTDs can occur if the *status quo* is maintained.

This option requires the target population to know the value of folate rich foods and to consciously select such foods, which may therefore disadvantage those that are not knowledgeable about folate.

Under this option there is no assurance to the community that there is sufficient folate in the food supply to minimise the risk of NTDs (conversely there is minimal risk to the community in terms of any potential adverse impacts of folate in the diet). The potential opportunity to further reduce the emotional, social and economic impact of NTDs would not be realised.

For the non-target population, maintenance of the status quo would have minimal impact.

7.2.1.2 Impacts on industry

For industry, only certain foods currently have permissions for the voluntary addition of folic acid. This allows particular food manufacturers to develop 'niche' products and to be able to differentiate their products from competitors. Manufacturer's who wish to fortify foods that are not currently permitted to be fortified would not be able to do so and could not realise the marketing advantage that this may confer.

Overall, this option would have minimal impact on industry

7.2.1.3 Impacts on governments

The potential opportunity to reduce the costs to government associated with the treatment and management of NTDs would be lost.

Are there any other impacts on consumers, the community, health professionals, industry and governments as a result of maintaining the status quo?

How do rates of NTDs in Australia and New Zealand compare internationally?

Is there any evidence to suggest that rates of NTDs could continue to decline while maintaining the status quo? For example, is there any evidence from other countries that sustained education programs and voluntary fortification eventually leads to sustained behavioural change in the target group (increased folate intake) and accompanying decreases in NTDs?

7.2.2 Option 2 - Extension of permissions for voluntary folate fortification

7.2.2.1 Impacts on consumers and the community

Extending permissions for voluntary fortification to new food categories could increase the folate status of the population and potentially result in a further reduction in the incidence of NTDs. However, this would only be likely to occur if industry takes up these new permissions and increases the number of fortified foods available.

Extending permissions for voluntary folate fortification may result in consumers having more choice and access to folate-rich foods. New fortified products could be developed specifically for the target population, making it easier for this group to increase their dietary folate intakes. The impact on consumers will depend on the extent to which industry embraces additional fortification options and the extent to which consumers in the target population consciously select folate-fortified foods.

There is potential for consumers to be confused as the range of fortified foods could change overtime, for example, as fortified products are developed, modified or discontinued.

If consumers do not wish to consume folate-fortified food, under this option they can choose not to.

This option requires the target population to know the value of folate rich foods and to consciously select such foods, and therefore this option may disadvantage those that are not knowledgeable about folate.

The main risk to the community from increasing folic acid intakes in the population is the potential to mask vitamin B_{12} deficiency in the older population and vegans. The magnitude of this risk would depend in large part on the extent to which industry chooses to fortify foods and whether the foods that are fortified are foods that are specifically for the target population.

7.2.2.2 Impacts on industry

Extending permissions for voluntary folate fortification would allow industry to develop new innovative products and provide opportunities for product differentiation. Manufacturers that chose to fortify their products with folic acid would benefit from normal commercial returns. Manufacturers would not be forced to bear the costs associated with mandatory fortification.

7.2.2.3 Impacts on governments

There would be no additional enforcement responsibility and hence no resource costs under this option for Governments**.** If a reduction in NTDs did occur, Governments would benefit from lower public health costs.

What reduction in NTD rates is possible from increased voluntary fortification?

Will all the benefits of increased voluntary fortification outweigh all the costs?

Can voluntary fortification ensure an effective level of folic acid in the food supply in order to maximise a reduction in the incidence of NTDs? Please give your reasons.

What food products are suitable for extending permissions for voluntary folate fortification? Could a sole food vehicle containing folic acid be more successful in decreasing the incidence of NTDs than several products fortified with folic acid?

7.2.3 Option 3 - Mandatory folate fortification

7.2.3.1 Impacts on consumers and the community

Mandatory fortification would facilitate the passive uptake of increased dietary folate for the whole population. Assuming the selection of appropriate vehicles for fortification, all women in the target population, regardless of education or socio-economic status, would have access to additional folic acid in their diets. This would occur without the need to change food selections or remembering to take a supplement. It would also provide more protection for women with unplanned pregnancies.

Under this option, the non-target population would be consuming higher amounts of folic acid. Consumers may be concerned about long-term consumption of higher amounts of a synthetic form of folate (folic acid).

Other potential benefits may flow to the general population from increasing folate status. For example, early studies suggest that folate is linked to a reduced risk of cardiovascular disease.

Mandatory fortification may restrict consumers' freedom to choose unfortified foods. The extent of this, however, would depend of the food vehicle(s) selected for fortification.

Consumers may choose to avoid foods fortified with folic acid and this may have other unintended nutritional consequences. The cost of mandatory fortification may be passed onto consumers and, depending on the extent of the price increase, may also impact on food selections.

Under this option, the risk of vitamin B_{12} masking may increase as folate intakes increase, particularly for the elderly and for vegans. Health professionals will need to be aware of the increased potential for vitamin B_{12} masking and may need to undertake further clinical procedures in at-risk populations. Health professionals may also need to modify their education campaigns to reflect the changing sources of dietary folate.

The long-term consequences of higher amounts of folic acid in the diet are unknown and as such the future impact on the community is not clear.

7.2.3.2 Impacts on industry

Mandatory folate fortification would create a 'level playing field' for all manufacturers of the prescribed food vehicle(s). However, this would limit the marketing opportunity to differentiate products (from those of competitors) and so recoup some of the costs associated with adding folic acid.

Mandatory fortification may also impact on manufacturers and retailers of folic acid supplements, especially if consumers perceive that they no longer require supplements due to the increased amounts of folic acid in the food supply.

Depending on the food vehicle(s) chosen for fortification, mandatory folic acid fortification may impact on importers and exporters if they need to alter their product in order to comply with domestic and/or overseas regulations.

Manufacturers of the prescribed food vehicle(s) for fortification would face increased costs including:

- analytical testing costs to confirm the appropriate levels of folic acid in their product;
- production related costs, including the cost of adding folic acid; and
- the cost of changing labels.

However, based on international experience, the increased costs are unlikely to impact significantly on overall operating costs.

7.2.3.4 Impacts on governments

If a reduction in NTDs did occur, Governments would benefit from lower public health costs. This may however be partially offset by any costs associated with vitamin B_{12} masking, including potential increased costs associated with the diagnosis of vitamin B_{12} deficiencies and the treatment of neurological conditions.

There would be additional enforcement and monitoring responsibilities and hence resource costs under this option to ensure that manufacturers comply with the mandatory fortification requirements. There would also be costs associated with monitoring NTD rates to assess the effectiveness of this option (as required by the Ministerial Council Policy Guideline).

What reduction in NTD rates is possible from mandatory fortification?

Will all the benefits of mandatory fortification outweigh all the costs?

Would consumers be concerned about a lack of consumer choice if mandatory folic acid fortification were instigated?

How important is consumer choice if it was determined that mandatory folic acid fortification could deliver net public health benefits?

What would be an appropriate food vehicle(s) for mandatory fortification?

From industry's perspective, what are the advantages and disadvantages of mandatory folic acid fortification?

What would be the overall cost of adding folic acid to a food product and the likely impact on the price to consumers?

What would be the expected impact on foods currently fortified with folic acid if mandatory fortification was instigated?

What monitoring should be undertaken to assess the effectiveness of mandatory fortification and which government agencies are responsible for, and will undertake, such monitoring?

7.2.4 Option 4 - Increased health promotion and education strategies to increase folate intakes.

7.2.4.1 Impacts on consumers and the community

To date education campaigns have been undertaken on an ad hoc basis. This could be enhanced by co-ordinated strategies in Australia and New Zealand that specifically target women of child-bearing age.

The impacts on the target population would depend entirely on the nature of the strategies and the responsiveness of the target population to these strategies. The benefit of this option is that no risks would be posed to the general population.

7.2.4.2 Impacts on industry

There would be minimal impact on industry from this option. However, manufacturers and retailers of supplements may benefit from the increased sales of folic acid supplements.

7.2.4.3 Impacts on governments

Governments would need to provide additional funds and resources to further improve and sustain health promotion and education strategies to increase folate intakes. If a reduction in NTDs did occur, Governments would benefit from lower public health costs.

How effective can health promotion campaigns be in reducing the incidence of NTDs?

Is there any evidence that a targeted campaign to increase folic acid supplement use during the peri-conceptional period would be more effective than the other three regulatory options in reducing the incidence of NTDs?

Should health promotion campaigns be the sole strategy to reduce the incidence of NTDs or used in conjunction with the other regulatory options?

Are health authorities interested in increasing their investment in education strategies?

What costs would be involved in running a large-scale health promotion strategy to increase the folate status of the population?

8. Consultation

8.1 Public Consultation

This Initial Assessment Report seeks early input on a range of specific issues known to be of interest to various stakeholders on the likely regulatory impact of this Proposal. The views of stakeholders will assist in the development of a Draft Assessment and a preferred approach to further reduce the incidence of NTDs in Australia and New Zealand. Further public comment will be sought at Draft Assessment, including any proposed draft variation/s to the Code.

In addition to the statutory requirement for two rounds of public consultation, it is envisaged that FSANZ will convene a Standards Development Advisory Committee (SDAC) comprising a broad range of stakeholders. This committee will help identify the views and opinions FSANZ will need to consider in progressing this Proposal. It is also envisaged that a Folate Scientific Advisory Group (FSAG) will be established in order to provide advice on scientific matters.

Given the significant potential public health, social and economic impact of this Proposal, FSANZ also proposes to undertake a series of targeted consultations to inform and engage interested stakeholders and the general public. Given the increased risk of NTDs in the Aboriginal and Torres Strait Islander population, FSANZ will specifically consult on the impacts of this Proposal for this group. As opportunities arise and as recommended by the SDAC and FSAG, FSANZ expects to conduct key stakeholder meetings, present at relevant conferences and seminars, engage in targeted public forums and be proactive in sharing information with the wider community.

Please note that in July 2004 the New Zealand Food Safety Authority (NZFSA)/New Zealand Ministry of Health (NZMoH) released a consultation document on solutions to reduce the incidence of NTDs in New Zealand. There was much interest in the consultation document with 51 submissions received. The report acknowledged that FSANZ would also be undertaking public consultation as part of the food standards setting process.

The submissions to the New Zealand paper will be considered during the FSANZ standards setting process through a formal submission from NZFSA. However, both FSANZ and NZFSA wish to reiterate to stakeholders that any issues that overlap between documents, or that are of particular importance or relevance to individual submitters, should be emphasised in a separate submission to this Initial Assessment Report.

8.2 World Trade Organization (WTO)

As members of the World Trade Organization (WTO), Australia and New Zealand are obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

This issue will be fully considered at the Draft Assessment stage and, if necessary, notification will be recommended to the agencies responsible in accordance with Australia's and New Zealand's obligations under the WTO Technical Barrier to Trade and Sanitary and Phytosanitary Measure Agreements. This will enable other WTO member countries to comment on proposed changes to Standards where they may have a significant impact on them.

9. Conclusion

Since the discovery of the positive effect of folic acid on reducing the risk of an NTD-affected pregnancy, the relationship between folic acid intake, folate status and NTD risk has been defined in the literature. Reference amounts for optimal folic acid intake and optimal serum or RBC folate levels in this context have been established.

Baseline folate intake data, although somewhat dated, are available for Australian and New Zealand populations groups that can be used to estimate dietary folate intakes from potential fortification scenarios to compare against dietary targets. Some data are available on folate supplement usage as well as data that describe folate status of the target group. However, risk reduction models and experience overseas appears to show that the magnitude of the risk reduction is inversely related to the folate status of the target group, which means that a greater reduction in NTD risk would be predicted for target groups with poorer folate status.

It is yet to be determined whether the folate intakes and folate status are sufficiently well described and the reference values appropriate for Australia and New Zealand to predict the possible numbers of NTD cases saved under each of the proposed options. However preliminary perusal of these data sources suggests that there is potential for an increase in folic acid intake to reduce the current rates of NTDs in both countries.

This Initial Assessment Report outlines four options FSANZ is considering to determine the most effective strategy to further increase the intake of folate. These options range from maintaining the status quo to changes in mandatory or voluntary fortification and/or increased health promotion and education activities.

FSANZ now seeks comment and information from stakeholders on the range of issues raised in this Report. Input from all sectors of the community, including consumers, industry, health professionals and government, is welcomed and encouraged. The submissions provided during this consultation will inform the Draft Assessment Report. Stakeholders will be given further opportunity to comment if the preferred option is regulatory (i.e. options 2 or 3) and a Draft Assessment Report is subsequently released.

Information regarding how to make a submission to Proposal P295 is included in the section 'Invitation for Public Submissions' on page 3 of this Report.

10. Implementation and review

During the Draft Assessment stage, FSANZ, following consultation with other relevant bodies and authorities, will make a decision on which regulatory option is preferred. Depending on the preferred option, the Proposal may or not proceed at Draft Assessment.

In terms of review, the Ministerial Council Policy Guideline states:

> *Any agreement to require fortification should require that it be monitored and formally reviewed to assess the effectiveness of, and continuing need for, the mandating of fortification*.

If a regulatory option of mandating folic acid fortification is chosen, FSANZ can take responsibility for monitoring food industry response and food composition. However the monitoring of folate status and NTD rates would need to be undertaken by other more appropriate authorities.

ATTACHMENTS

1. The Australia and New Zealand Food Regulation Ministerial Council Policy Guideline on Fortification of Food with Vitamins and Minerals
2. Glossary of Terms
3. Glossary of Acronyms
4. Strategies used in Australia and New Zealand to increase folate and reduce incidence of NTDs
5. Folate health promotion campaigns in Australia and Impact of folate health promotion campaigns
6. International experience of mandatory fortification
7. References

Attachment 1

POLICY GUIDELINE
FORTIFICATION[1] OF FOOD WITH VITAMINS AND MINERALS

This Policy Guideline provides guidance on development of permissions for the addition of vitamins and minerals to food.

The Policy Guideline does not apply to special purpose foods the formulation and presentation of which are governed by specific standards in Part 2.9 of the Australia New Zealand Food Standards Code (the Food Standards Code).

The policy should only apply to new applications and proposals. There is no intention to review the current permissions.

The policy does not apply to products that should be or are regulated as therapeutic goods. This should not lead to a situation were generally recognised foods, through fortification, become like or are taken to be therapeutic goods.

The policy assumes the continuation of a requirement for an explicit permission for the addition of a particular vitamin or mineral to particular categories of foods to be included within the Food Standards Code. Currently the majority of permissions are contained in Standard 1.3.2 – Vitamins and Minerals.

Regard should be had to the policy in development of regulatory measures applying to the mixing of foods where one, or both of the foods may be fortified.

The policy for regulation of health and nutrition claims on fortified food is covered by the Policy Guideline on Nutrition, Health and Related Claims. Claims should be permitted on fortified foods, providing that all conditions for the claim are met in accordance with the relevant Standard.

'High Order' Policy Principles

The Food Standards Australia New Zealand Act 1991 (the Act) establishes a number of objectives for FSANZ in developing or reviewing of food standards.

1. The objectives (in descending priority order) of the Authority in developing or reviewing food regulatory measures and variations of food regulatory measures are:
   (a) the protection of public health and safety
   (b) the provision of adequate information relating to food to enable consumers to make informed choices; and
   (c) the prevention of misleading or deceptive conduct.

2. In developing or reviewing food regulatory measures and variations of food regulatory measures the Authority must also have regard to the following:

[1] Within the context of this policy Fortification is to be taken to mean all additions of vitamins and minerals to food including for reasons of equivalence or restoration.

(a) the need for standards to be based on risk analysis using the best available scientific evidence;
(b) the promotion of consistency between domestic and international food standards;
(c) the desirability of an efficient and internationally competitive food industry;
(d) the promotion of fair trading in food; and
(e) any written policy guidelines formulated by the Council for the purposes of this paragraph and notified to the Authority.

These objectives apply to the development of standards regulating the addition of vitamins and minerals to food.

A number of other policies are also relevant to the development of food standards including the Council Of Australian Governments document 'Principles and Guidelines for national Standard Setting and Regulatory Action by Australia and New Zealand Food Regulatory Ministerial Council and Standard Setting Bodies (1995, amended 1997)(Australia only), New Zealand Code of Good Regulatory Practice (November 1997), the Agreement between the Government of Australia and the Government of New Zealand concerning a Joint Food Standards System and relevant World Trade Organisation agreements.

Specific Order Policy Principles - Mandatory Fortification

The mandatory addition of vitamins and minerals to food should:

- Be required only in response to demonstrated significant population health need taking into account both the severity and the prevalence of the health problem to be addressed.
- Be required only if it is assessed as the most effective public health strategy to address the health problem.
- Be consistent as far as is possible with the national nutrition policies and guidelines of Australia and New Zealand.
- Ensure that the added vitamins and minerals are present in the food at levels that will not result in detrimental excesses or imbalances of vitamins and minerals in the context of total intake across the general population.
- Ensure that the mandatory fortification delivers effective amounts of added vitamins and minerals with the specific effect to the target population to meet the health objective.

Additional Policy Guidance - Mandatory Fortification

Assessment of alternative strategies – consideration must be comprehensive and include for example assessment of voluntary fortification and education programs.

Requirement to label – no mandatory requirement to label as fortified however, consideration should be given, on a case by case basis, to a requirement to include information in Nutrition Information Panel.

Monitor/Review – any agreement to require fortification should require that it be monitored and formally reviewed to assess the effectiveness of, and continuing need for, the mandating of fortification.

Specific order policy principles – Voluntary fortification

- The voluntary addition of vitamins and minerals to food should be permitted only:
  - Where there is a need for increasing the intake of a vitamin or mineral in one or more population groups demonstrated by actual clinical or sub-clinical evidence of deficiency or by data indicating low levels of intake.

  or
  - Where data indicates that deficiencies in the intake of a vitamin or mineral in one or more population groups are likely to develop because of changes taking place in food habits.

  or
  - Where there is generally accepted scientific evidence that an increase in the intake of a vitamin and/or mineral can deliver a health benefit.

  or
  - To enable the nutritional profile of foods to be maintained at pre-processing levels as far as possible after processing (through modified restoration[2]).

  or
  - To enable the nutritional profile of specific substitute foods to be aligned with the primary food (through nutritional equivalence).
- The permitted fortification has the potential to address the deficit or deliver the benefit to a population group that consumes the fortified food according to its reasonable intended use.
- Permission to fortify should not promote consumption patterns inconsistent with the nutrition policies and guidelines of Australia and New Zealand.
- Permission to fortify should not promote increased consumption of foods high in salt, sugar or fat.
- Fortification will not be permitted in alcoholic beverages.
- Permissions to fortify should ensure that the added vitamins and minerals are present in the food at levels which will not have the potential to result in detrimental excesses or imbalances of vitamins and minerals in the context of total intake across the general population.
- The fortification of a food, and the amounts of fortificant in the food, should not mislead the consumer as to the nutritional quality of the fortified food.

[2] The principle of Modified Restoration as derived from The FSANZ document *Regulatory principles for the addition of vitamins and minerals to foods*. (Canberra, 2002) is as follows:
Vitamins and minerals may be added, subject to no identified risks to public health and safety, at moderate levels (generally 10-25% Recommended Dietary Intake (RDI) per reference quantity) to some foods providing that the vitamin or mineral is present in the nutrient profile, prior to processing, for a marker food in the food group to which the basic food belongs. The vitamin or mineral must be naturally present at a level which would contribute at least 5% of the RDI in a reference quantity of the food. This regulatory principle is based on the restoration or higher fortification of the vitamin or mineral to at least pre-processed levels in order to improve the nutritional content of some commonly consumed basic foods.

Additional Policy Guidance - Voluntary Fortification

Labelling – There should be no specific labelling requirements for fortified food, with the same principles applying as to non-fortified foods. An added vitamin or mineral is required to be listed in the Nutrition Information Panel only if a claim is made about it and the vitamin or mineral is present at a level for which a claim would not be misleading. An added vitamin or mineral must be listed in the ingredient list under current labelling requirements.

Monitoring/Review - A permission to voluntary fortify should require that it be monitored and formally reviewed in terms of adoption by industry and the impact on the general intake of the vitamin/mineral.

Attachment 2

GLOSSARY OF TERMS

Term	Description
Ascertainment	The method by which persons with a trait or disease are selected or found by an investigator.
Bioavailability	A measure of the body's ability to extract, absorb and metabolize a nutrient.
Births	NTDs detected in live born infants in the first 28 days and stillbirths of at least 20 weeks' gestation and terminations that occur at gestational ages of 20 weeks or more are collectively termed "births". Spontaneous abortions which occur prior to 20 weeks gestation are not included.
(Dietary) folic acid supplement	Tablet containing folic acid.
Dietary folate equivalents (DFEs)	The bioavailability of folate ranges from 100% for synthetic folic acid to 50% for food folate. Consequently, the US Food and Drug Authority now recommends that folate requirements be expressed in terms of Dietary Folate Equivalents (DFEs). Estimates of DFEs in US fortified foods are calculated by the following equation: µg of DFE = µg of food folate + (1.7 x µg of synthetic folic acid)
Enriched	In the US, this term refers to the addition of a nutrient to a food that has been lost during the course of food processing or during normal storage and handling, up to the nutrient's level in the food before the processing, storage and handling. This process is commonly referred to as 'restoration' in the Australian and New Zealand context.
Folate	Folates are water-soluble vitamins. The term *folate* is used generically to refer to the various forms of the vitamins, both naturally-occurring and synthetic, and their active derivatives.
Folate, naturally-occurring	Natural forms of folate are found in a wide variety of foods including green leafy vegetables, cereals, fruits, grains, legumes, yeast extract, and liver. This type of folate is referred to as *naturally-occurring* to differentiate it from folic acid added to food in fortification.
Folic acid	Folic acid (pteroylmonoglutamic acid) is the most common form of synthetic folate. It occurs rarely in foods but is the form most often used in vitamin supplements and in fortified foods.
Fortified / fortification	The addition of an essential nutrient to a food for the purpose of meeting a health need in the population or specific population groups.

Health claim	A message that makes a direct link between eating a certain food or food component and the reduced risk of a specific disease.
Homocysteine	A sulphur-containing amino acid. Plasma homocysteine concentration increases when folate is deficient. Consequently it can be used as an ancillary indicator of folate status.
Homocystinuria	The collective term for several inborn errors of metabolism of homocysteine metabolism.
Incidence (of neural tube defects)	The number of new cases of neural tube defects that are reported in the population of individuals at risk during a specified time period. It is expressed as a rate where: $\text{Incidence} = \frac{\text{number of cases of neural tube defects during a given period of time}}{\text{total population at risk}}$ NB: the term prevalence is often used interchangeably with incidence. Both measures are affected by under-reporting of terminations
In utero	'In the uterus' or during pregnancy.
Mandatory fortification	As specified in the *Australia New Zealand Food Standards Code*, food manufacturers must add an essential nutrient (e.g. thiamin) to a specified food at a specified rate.
Megaloblastic anemia	An anemia in which the maturation of the precursors (megaloblasts) of red blood corpuscles in the bone marrow is impaired; these precursor cells enter the blood stream at a larger size (macrocytic) than normal blood cells, yet they contain a full complement of haemoglobin.
Meta-analysis	Results from several studies, identified in a systematic review, that have been combined and summarised quantitatively (NHMRC 2000).
Neural tube defects	Neural tube defects (NTDs) are a family of congenital defects that arise during the development of the brain and spinal cord *in utero*. NTDs include three specific abnormalities in the development of the central nervous system: Spina bifida is a condition whereby incomplete closure of the neural tube results in the spinal cord being exposed or protruding through a gap in the spine. Over 80% of infants born with spina bifida survive into adulthood, but can develop leg paralysis or weakness, lack of bowel or bladder control and excess fluid around the brain (hydrocephalus). Anencephaly is characterised by a failure of the anterior neural tube to close, resulting in the total or partial absence of the cranial vault and brain tissue. Anencephaly is incompatible with life; affected infants are usually stillborn or die shortly after birth. Encephalocoele is characterised by the meninges and/or brain tissue extruding through a defect in the skull.

Periconceptional period	Around conception; includes the 4-week period before, and 12-week period after conception. It is the recommended period of time during which a woman of childbearing age should increase her folate intake to minimise the risk of NTDs occurring with a pregnancy.
Randomised controlled trial	An experimental comparison study in which participants are allocated to treatment/intervention or control/placebo using a random mechanism. Participants have an equal chance of being allocated to an intervention or control group and therefore allocation bias is eliminated (NHMRC 2000).
Recommended Dietary Intake (RDI)	A RDI is the intake of an essential nutrient, whereby 95% of the Australian and New Zealand populations meet their requirement for the nutrient.
Red blood cell (RBC) folate	Since folate is taken up only by the developing erythrocyte in the bone marrow and not by the circulating mature red blood cell during its 120-day lifespan, red cell folate concentration is a better indicator of long-term status than serum or plasma folate.
Target population	Women of childbearing age.
Terminations	Terminations include induced abortions occurring before 20 weeks' gestation, for example as a result of detection of a NTD by prenatal screening, either by diagnostic ultrasound and/or maternal serum screening.
Voluntary fortification	As specified in the *Australia New Zealand Food Standards Code*, food manufacturers have the choice of adding an essential nutrient (e.g. folate) to a specified food up to specified rate.
Women of child-bearing age	Women aged 15–49 years.

Adapted from (Abraham and Webb 2001).

Attachment 3

GLOSSARY OF ACRONYMS

ANZFA	Australia New Zealand Food Authority
Codex	Codex Alimentarius Commission
CDC	Centers for Disease Control
COMA	Committee on Medical Aspects of Food and Nutrition
CVD	Cardiovascular disease
DFEs	Dietary Folate Equivalents
EC	European Commission
EU	European Union
FAO	Food and Agriculture Organization
FSA	Food Standards Agency
FSANZ	Food Standards Australia New Zealand
LOAEL	Lowest-Observed-Adverse-Effect Level
Ministerial Council	Australia and New Zealand Food Regulation Ministerial Council
NHANES	National Health and Nutrition Examination Surveys (US)
NDNS	National Diet and Nutrition Survey (UK)
NHMRC	National Health and Medical Research Council
NNS	National Nutrition Survey
NOAEL	No-Observed-Adverse-Effect Level
NTDs	Neural Tube Defects
NZFSA	New Zealand Food Safety Authority
NZMoH	New Zealand Ministry of Health
RBC	Red Blood Cell
RDI	Recommended Dietary Intake
SACN	Scientific Advisory Committee on Nutrition
The Code	Australia New Zealand Food Standards Code
TUIL	Tolerable Upper Intake Levels
UK	United Kingdom
USFDA	United States Food and Drug Administration
USA	United States of America
WHO	World Health Organization
WTO	World Trade Organization

Attachment 4

SUMMARY OF STRATEGIES USED IN AUSTRALIA AND NEW ZEALAND TO INCREASE FOLATE AND REDUCE INCIDENCE OF NTDS

This Attachment summarises the four primary prevention strategies that have been employed in Australia and New Zealand to increase total folate intakes and reduce the rates of NTDs. The reported advantages and disadvantages of the respective strategies are described in addition to the impact of these. Further detail on the impact of particular strategies is provided at Attachment 5.

1 Overview of folate campaigns implemented in Australia and New Zealand

In Australia, between 1994 and 1999 three health promotion campaigns were implemented nationally in addition to State-based campaigns in WA, SA, NSW, Victoria and Tasmania. There has been no publicly funded awareness campaigns regarding folate and women of child-bearing age in New Zealand (NZMoH 2003). The Australian campaigns have generally targeted women of child-bearing age and health professionals. In general, the main objectives of the campaigns have been to: increase awareness of the association between folate and NTDs; promote dietary sources of naturally-occurring folate and folic acid supplements; and increase folate intake. It should be noted that most of the campaigns promoted both increased consumption of folate rich foods and folic acid supplementation.

SUMMARY OF NATIONAL FOLATE HEALTH PROMOTION CAMPAIGNS IN AUSTRALIA TO 2001

Organisation	Name and description of program	Date	Target group	Aim/ objective/ main message
Pharmacy Guild of Australia in conjunction with Commonwealth Department of Health and Aged Care	Folate Initiative *Folate – make it part of your day'* distribution of education material & 35,000 free starter packs of folic acid tablets	Launched February 1996	Women planning a pregnancy	To promote folic acid supplements and folate rich foods (naturally-occurring and fortified)
Kellogg/Northcott Society folate education program	Folate education promoted through television, print and on-pack messages	July through November 1998	Women in child-bearing years	To promote the importance of folate for women in child-bearing years; to promote foods with added folic acid
Australia New Zealand Food Authority (ANZFA)	*Folate-NTD health claim Pilot* Health claim on food labels, ANZFA approved logo, promotional material	1998	Women considering becoming pregnant; food industry	To trial the use of health claim management system, To assess the impact of a folate-NTD health claim

Adapted from (Abraham and Webb 2001).

SUMMARY OF STATE FOLATE HEALTH PROMOTION CAMPAIGNS IN AUSTRALIA

Jurisdiction	Name and description of program	Date	Target group	Aim/ objective/ main message
Health Department of WA (coordinated by Institute of Child Health Research)	Folate Program Phase 1: *Folate and neural tube defects prevention project* education materials provided to health professionals	July 1992-December 1994	Women of child-bearing age (20-40 yrs); health professionals	To increase awareness amongst health professionals of association between folate and NTDs; To increase women's folate intake through diet and supplements (0.5 mg) to help prevent NTDs
South Australia Department of Human Services	*"Folate before pregnancy"* information packs provided to health professionals	October 1994-August 1995	Health professionals; women of reproductive age	To promote dietary sources of folate and folic acid supplements during the peri-conceptional period
NSW Health	*How diet can prevent birth defects* pamphlet	1995	Women from multicultural backgrounds planning a pregnancy	To promote folic acid supplements (0.5 mg) and increase naturally-occurring folate during the peri-conceptional period
Health Department of WA	Folate Program Phase 2: *Folate awareness campaign*	Launched November 1996	Women of child-bearing age (18-44 yrs)	Similar to 1992-1994, with supplements promoted more extensively than diet
Victorian Department of Human Services in conjunction with Family Planning Victoria	*Victorian Folate Campaign*: consumer and professional education strategies to inform of benefits of folate in preventing NTDs; pre-pregnancy checklist	launched 1999	Women of child-bearing age (15-45 yrs); health professionals; women with previous NTD affected pregnancy; teenagers; Koori women and women from multicultural backgrounds	To promote consumption of food fortified with folic acid plus foods high in naturally-occurring folate plus supplements
Tasmanian Department of Health and Human Services	GP and health profession training	unknown	Family Child Youth Health nurses GPs	To raise awareness of folate-NTD link; to promote good food sources of folate.

Adapted from (Abraham and Webb 2001; Chan et al, 2001)

2. Promotion of diets high in naturally-occurring folate

Reported advantages and disadvantages of promoting diets high in naturally-occurring folate

The difficulty of achieving the required folate in pregnancy through dietary modification has been widely acknowledged. Skeaff and Mann (1998) state that the folate-NTD relationship is the first well documented public health situation where the amount of nutrient required is more than that which can be practically eaten by choosing foods wisely (Skeaff and Mann 1998).

The NHMRC Expert Panel on Folate Fortification noted that the likelihood of achieving a reduction in NTDs through nutrition education alone was limited, and that the ability of nutrition education programs to reach those at most need was questionable (NHMRC 1995). Likewise the New Zealand Ministry of Health stated that promotion of diets high in naturally-occurring folate is not recommended on its own as a policy option to increase folate (NZMoH 2003).

Despite these reservations, it has been suggested that the promotion of diets high in naturally-occurring folate has the advantage of:

- preserving consumer choice;
- being a preferred option of a proportion of the target group;
- conferring a low risk of adverse health effects, both in the target population and other population subgroups; and
- providing wider health benefits from nutrient dense foods such as vegetables and fruit (NZMoH 2003).

Impact of promoting diets high in naturally-occurring folate

It is difficult to identify the impact of campaigns specifically targeting increased consumption of folate rich foods. This is because most of the Australian campaigns have targeted both increased consumption of folate rich foods and folic acid supplementation. However, it is generally reported that public health campaigns specifically targeted at increasing only naturally-occurring folate in the diet have not produced significant dietary modification in the population (Bower et al, 2002) and have not been able to sufficiently increase RBC folate to the levels required to confer a protective effect against NTDs Brown et al 1997 cited in (Chan et al, 2001).

Reasons for this may include the following:

- Obtaining adequate folate from food sources in pregnancy is difficult, because commonly eaten foods, such as wholegrain cereals, fruit and vegetables, are only low to moderate sources of folate, and some excellent sources of folate such as liver are not recommended during pregnancy. In addition, morning sickness may limit the amount of food women are able to eat early in pregnancy; and

- Women who are not planning a pregnancy are unlikely to consume adequate amounts of folate during the peri-conceptional period. Data from National Nutrition Surveys indicates that women's mean 24 hour intake of folate from food is well below the recommended intake during pregnancy of 400 μg per day.

The evaluation of health promotion campaigns promoting increased naturally-occurring folate is shown at Attachment 5.

3. Promotion of folic acid supplementation during the peri-conceptional period

Reported advantages and disadvantages of promoting folic acid supplementation

Health promotion initiatives to increase the use of folic acid supplements have been implemented in a number of countries as a means to increase folic acid intake and reduce the incidence of NTDs. Both Australia and New Zealand have folic acid supplement policies. The promotion of supplements offers a number of advantages (NZMoH 2003; Skeaff et al, 2003). These include:

- being able to deliver the recommended amount of folic acid to the target population (in one tablet);
- causing no increase in the exposure and potential adverse effects in other population subgroups;
- synthetic folic acid has a greater bioavailability than naturally-occurring folate; and
- preservation of consumer choice.

Supplementation is of most benefit to women planning a pregnancy but to be effective supplements of sufficient dosage need to be taken consistently during the peri-conceptional period.

Supplementation has not been recommended as a sole strategy to reduce the incidence of NTDs due to its disadvantages, which include the following:

- approximately 40-50% of pregnancies in Australia and New Zealand are unplanned, and the neural tube develops before many women know they are pregnant (Schader and Corwin 1999 cited in (NZMoH 2003; The Alan Guttmacher Institute 1999);

- the policy relies upon the knowledge, motivation and compliance of women;

- cost of supplements may be a barrier for some population groups;

- folic acid supplementation may be affected by socioeconomic factors, such that women of higher socio-economic status are more likely to take the recommended folic acid supplements (de Walle et al, 1999);

- folic acid supplementation may also be affected by cultural factors, such that women of Culturally and Linguistically Diverse backgrounds have lower uptake levels of folic acid supplement use (Watson and MacDonald 1999 cited in (NZMoH 2003); and

- use of folic acid supplements appears to be affected by age, with women aged 15 to 24 years less likely to use supplements than women over 25 years of age (ABS 1995 cited in (Abraham and Webb 2001).

Impact of promotion of folic acid supplementation

Only a small proportion of women take folic acid supplements, as shown below.

SUPPLEMENT USE BY FEMALES IN AUSTRALIA AND NEW ZEALAND

Survey	Folic acid use	Population group	Proportion of sample reporting taking supplements	Median dose of folic acid supplement
Australia				
National Nutrition Survey (ABS 1995 in (Abraham and Webb 2001)	Consumed a folic acid supplement on the day prior to survey	Females (15-49 years)	2%	unknown
Population Survey Monitor (ABS 1995 in Abraham and Webb, 2001)	Took supplements containing folic acid on the day prior to survey	Females (18-44 years)	10.5%	200 μg*
New Zealand				
National Nutrition Survey 1997 (Russell et al, 1999)	Consumed folic acid dietary supplements in last year	Females 15-24 years 25-44 years	 0% 2%	unknown

Adapted from (Abraham and Webb 2001; NZMoH 2003; Russell et al, 1999)
* dosage on containers of supplements checked by interviewers

However, there is some evidence that this proportion is increased following health promotion campaigns encouraging folic acid supplementation (refer Table below). For example, the wholesale sales of 0.5 mg folic acid supplements increased throughout Australia in the period 1995-1998. The most marked increases were in Western Australia, where a three-fold increase in sales of 0.5 mg folic acid supplements was reported following folate health promotion campaign (Bower et al 1997). Chan et al (Chan et al, 2001) report that the sales of 0.5 mg folic acid supplements doubled after the South Australian "Folate before pregnancy" campaign, and by a further 10% the following year.

USE OF FOLIC ACID SUPPLEMENTS PERICONCEPTIONALLY IN AUSTRALIA AND NEW ZEALAND

Survey	Percentage of women surveyed aware of importance of folate in the peri-conceptional period	Percentage of women taking folic acid supplements during the peri-conceptional period
WA Department of Health Folate Campaign evaluation (Bower et al 2002)	66%	28%*
Christchurch (Schader and Corwin 1999 in NZMoH 2003)	63%	17%
Dunedin (Ferguson et al 2000)		11% *

Adapted from (Abraham and Webb 2001; NZMoH 2003)
*Women who had been pregnant in the last 5 years

4. Voluntary fortification

Extent of folic acid fortification in Australia and New Zealand

Folic acid was first permitted to be added to certain foods in 1995 in Australia and in 1996 in New Zealand. Since then there has been no ongoing monitoring or surveillance of the extent of folic acid fortification in either country.

In the Australian context, the Australian Food and Nutrition Monitoring Unit published an *Interim evaluation of the voluntary folate fortification policy* in 2001 (Abraham and Webb 2001). This report used studies [8], and the number and variety of fortified foods available on supermarket shelves to assess the extent to which voluntary fortification had been implemented. The evaluation indicated that the introduction of folate-fortified products onto the market had been slow, and that few food products had been fortified since 1995 (Abraham and Webb 2001).

In Australia, by June 1999, there were 104 folate-fortified products available in Australia. The majority of these foods were breads (38) followed by breakfast cereals (34), fruit and vegetables juices (12), meal replacements (6), breakfast bars (4), supplementary foods (4), as well as a type of flour, pasta, yeast extract and a soy product. This data may have over-estimated the number of fortified products available, as it was based on manufacturers reports of intention to fortify specific products (Abraham and Webb 2001). Market share was also used to provide an indication of the impact of voluntary fortification with folic acid. The highest market share of a folate-fortified food was for breakfast cereal at 49%, however breakfast cereals were estimated to be eaten by only 34% of the target group (Abraham and Webb 2001; ANZFA 2000).

There has also been limited uptake of voluntary folic acid fortification in New Zealand. At the end of 2002, 81 foods were estimated[9] to be fortified with folic acid. More than half of these were breakfast cereals (44) which are consumed by an estimated 27% of women of child-bearing age (Newton et al cited in (NZMoH 2003). Other foods fortified with folic acid were breads, food drinks and a vegetable extract (NZMoH 2003).

Reported advantages and disadvantages of voluntary fortification

Voluntary fortification of food products with folic acid is reported to have the following advantages:

- if added to a food that is a staple for a high proportion of the target group by the majority of producers, the benefits could be available across the population, regardless of socio-economic factors or age; and
- it preserves consumer choice, as fortification is unlikely to be implemented universally by the food industry.

The reported disadvantages of voluntary folic acid fortification include the following:

[8] Information from the 1995-8 ANZFA Folate Monitoring Surveys and the ANZFA Folate Health Claim Pilot surveys was used in the evaluation of voluntary fortification.

[9] Based on the New Zealand Manufactured Foods Database, which relies on voluntary participation and does not include non-packaged foods.

- it requires high uptake by the food industry to impact on the folate intakes of the target group. There are indications that some sections of the food industry may be reluctant to fortify foods on a voluntary basis (NZMoH 2003);
- sustainability is affected by consumer demand for folic acid fortified foods, and thus there may not be certainty of supply;
- it is difficult to monitor fortification levels, and the number and type of foods that are fortified if the market is very dynamic; and
- high levels of folic acid may be consumed by the general population or non target groups (NZMoH 2003).

Impact of voluntary fortification on intake of folate

Folate intake prior to voluntary fortification in Australia

The 1995 Australian National Nutrition Survey (NNS) provides base-line data on food consumption shortly before the introduction of voluntary food fortification. For the 3,784 women aged 15-49 years surveyed:

- the mean 24-hour intake of folate from all foods was 229 μg per day, with mean intakes lowest for the 15-19 year old age group (219 μg per day) and highest for the 44-49 year old age group (244 μg per day) (Abraham and Webb 2001);
- almost one third (32.8%) consumed less than the RDI for non-pregnant females (200 μg per day), with females aged 15-19 least likely to meet that RDI (Abraham and Webb 2001);
- folate intakes were significantly reduced in those of low socio-economic status; where the mean 24-hour folate consumption was 214 μg for women (Giskes et al, 2002); and
- cereals and cereal products (including bread and breakfast cereals) and vegetables products and vegetable dishes accounted for more than 45% of total folate intake of women of child-bearing age (Abraham and Webb 2001).

Impact of voluntary fortification on folate intakes in Australia

Voluntary fortification of the food supply with folic acid commenced in Australia in 1996. Estimates of the folate intakes for women aged 15-49 years as of November 1998 based on food consumption recorded in the 1995 NNS showed that the mean dietary folate intakes had increased by 11% to 254 μg per day. When expressed as DFEs to account for the greater bioavailability of folic acid, dietary modelling estimated the mean folate intake had increased 19% to 272 μg per day post fortification (Abraham and Webb 2001).

The NHMRC Expert Panel on Folate Fortification (NHMRC 1995) set a level of 70% of women in the target population consuming more than 400 μg folate per day as criteria by which to judge the effectiveness of voluntary fortification. The Table below shows that at November 1998, the median folate intake of women aged 15-44 years was 235 μg, far short of the target set by the NHMRC Expert Panel (Abraham and Webb 2001). More recent data on the current range of foods fortified with folic acid or the resulting folate intakes is not available.

MEDIAN DIETARY FOLATE INTAKES OF WOMEN (15-45 YEARS) IN AUSTRALIA BEFORE AND AFTER VOLUNTARY FOLIC ACID FORTIFICATION (NOV 1998)

Age groups of women (years)	Median folate intake pre fortification [1] (1995) (μg/day)	Median folate intake November 1998 (μg/day)
15-19	195	229
20-24	216	240
25-29	219	239
30-34	206	235
35-39	210	227
40-44	217	231
45-49	221	247
15-49	213	235

Adapted from (Abraham and Webb 2001)
[1] derived from unweighted survey data

Folate intake prior to voluntary fortification in New Zealand

The most recent NNS in New Zealand was conducted in 1997, and included a sample of 1375 women aged 15-65+. While voluntary fortification was permitted as of January 1996, the extent to which folic acid fortified foods were included in this survey is unclear.

MEAN AND PERCENTILE FOLATE INTAKES FOR WOMEN (15-65+ YEARS) IN THE NEW ZEALAND 1997 NNS

Age group in years	Usual folate intakes (μg per day)				
	mean	10th	50th	90th	inadequate intake (%) [1]
15-18	203	125	194	292	22.2
19-24	202	125	195	290	21.2
25-44	220	141	213	307	13.4
45-64	228	151	222	313	9.8
65+	227	152	217	313	9.2
Total	**220**	**142**	**212**	**306**	**13.1**

Adapted from (Russell et al, 1999)
[1] adequacy evaluated by probability analysis, which compares nutrient intakes with the mean requirement distribution and calculates the likelihood that a particular nutrient would fail to meet this. The UK Dietary Reference Values were used in this analysis (EAR of 150 μg/day).

This survey also indicates:

- younger women had lower intakes, with a median intake of about 195 μg for females aged 15-24 years, compared to 213 μg per day for women aged 25-44 years;
- Maori women had slightly lower folate intakes than the non-Maori population, at 198 μg; and
- the main sources of folate in the diet of New Zealanders were vegetables (18%), bread (13%) and breakfast cereals (11%) (Russell et al, 1999).

Impact of voluntary fortification on folate intakes (in New Zealand)

To estimate the change in folic acid intake after voluntary fortification came into effect, dietary modelling was conducted by the University of Otago based on the NNS 1997. The modelling estimated a median increase of 17 μg folic acid per day (7.7%) for women of child-bearing age by August 2000.

Less than 4% of the women of child-bearing age were estimated to be achieving intakes of 400μg per day, and over 60% had not received any additional folic acid as a result of voluntary fortification (Newton et al 2001 cited in (NZMoH 2003).

The University of Otago in New Zealand has established base-line folate data for women of child-bearing age as well as adolescent boys, who are accepted as being of greatest risk of over-consumption of folic acid due to their high consumption of fortified foods (Ferguson et al, 2000). In 1999, median intakes of dietary folate per day in the Dunedin study population were 216 μg for women (aged 18 - 45 years) and 226 μg for adolescent boys (aged 14 – 19 years) (Ferguson et al, 2000)

5. Folate-NTDs health claim pilot

Description of the Folate-NTD Health Claim Pilot

In 1998, ANZFA (now FSANZ) approved a folate-NTD health claim pilot aimed at obtaining a clearer, more practical understanding of the regulatory, social and public health impacts of health claims. The pilot's main objectives were to trial the proposed management framework for health claims, and to promote public health through communication of the link between increased maternal folate consumption and a reduction in the incidence of NTDs.

The health claim was approved for folate-rich foods, both fortified and non-fortified, that met the specified nutrition criteria. The health claim statement recommended by ANZFA was '*This food contains folate*. A diet rich in folate may help prevent birth defects such as spina bifida'. A logo with the text '*ANZFA endorsed folate health claim*' was developed, along with a range of promotional materials, which were distributed to a variety of organisations [10]. The majority of the pilot education and monitoring activities were undertaken from November 1998 to May 1999 (ANZFA 2000).

Implementation by industry

The process evaluation of the pilot showed there was a slow uptake of the folate health claim on products and associated advertising. Uptake was particularly limited in New Zealand. There were also differences in uptake between food sectors and companies in both countries (ANZFA 2000).

While food products permitted to carry the folate-NTD health claim are listed in Standard 1.1A2 of the Code (see Section 4.1.2), there is no mechanism in place to determine which of the listed foods are carrying the folate-NTD health claim at any point in time.

In Australia, the evaluation of the pilot indicated that the number of foods labelled with the health claim was considerably less than the number of foods approved to carry the claim. By January 2000, ANZFA had approved the claim for use on more than 120 products, but at the end of 1999, the health claim was present on the labels of 15 breakfast cereals and 16 fruit and vegetable products (ANZFA 2000).

[10]Folate resource materials included a folate fact sheet, poster, and leaflets for doctors and pharmacists, and were provided to organisations including Nutrition Australia, Spina Bifida Association, Royal Australian College of General Practitioners, Family Planning Australia and pharmacies (Abraham and Webb 2001).

Reasons for this are unclear, but may include the lack of broad appeal of the folate health claim expressed by the food industry (Abraham and Webb 2001; ANZFA 2000). In New Zealand, almost 25% of fortified foods did not meet the specified nutrition criteria, or had not sought permission to use the folate-NTD health claim (Abraham and Webb 2001).

Impact of the health claim pilot

The outcome evaluation of the pilot was published by ANZFA in 2000 in a report entitled *evaluating the Folate-Neural Tube Defect Health Claim Pilot.* This report assessed the socio-cultural and other impacts of the pilot through a series of Australian surveys conducted before 1998 and after the pilot's implementation in 1999[11]. Factors investigated included changes in consumer knowledge and attitudes regarding the importance of folate, food sources of folate, and purchasing behaviour and dietary changes resulting from folate information (ANZFA 2000).

The outcome evaluation of the folate-NTD health claim found that:

- the number of women who had seen the folate-NTD health claim increased from 11% in 1998 to 29% in 1999;
- more women were able to specify particular foods carrying the health claim (9% in 1998 compared to 17% in 1999);
- about 25% of the women commented that folate information had encouraged them to eat foods containing folate; and
- there was no change in sales of products carrying the folate-NTD health claim for the period of 1998-1999 (ANZFA 2000).

[11] Surveys used to evaluate the Folate Health Claim Pilot included CSIRO National Nutrition Survey 1998-99; South Australian Health Monitor 1998-99; Eat Well Tasmania Survey 1998-99; and Australian Supermarket Institute Consumer Monitor Survey 1998-99 (ANZFA 2000).

Attachment 5

IMPACT OF FOLATE PROMOTION CAMPAIGNS

This Attachment provides further detail on the impact of individual folate health promotion campaigns aimed at women of child-bearing age. Data grouped in terms: of awareness and knowledge of folate-NTD association; knowledge of recommended timing, dose and sources of folate; and intention to increase folate intake and behavioural changes. There has been minimal folate promotion campaigns conducted in New Zealand, however data related to the factors outlines above has been included in the following Tables.

AWARENESS AND KNOWLEDGE OF FOLATE-NTD ASSOCIATION FROM AUSTRALIAN AND NEW ZEALAND SURVEYS

Survey	Awareness / knowledge determined	% pre-intervention	% post-intervention
Australia, national			
Kelloggs Newspoll (Williams et al., 2001)	Awareness of the role of folate in pregnancy in women (18-44 yrs)	21 (July 1998)	44 (May 1999)
ANZFA folate –NTD health claim [16] [17] (ANZFA 2000)	Women of child-bearing age who had heard of folate and knew of its link with birth defects.	40 (1998) (25-44%)[13]	46 (1999) (34-53%)[23]
ANZFA folate –NTD health claim (ANZFA 2000)	Women who had heard of folate but did not know why it was important	29 (1998)	23 (1999)
Australian States			
Western Australia (CIE, 2004)	Women of child-bearing age who had knowledge of the importance of folate in the peri-conceptional period	8.2 (1992)	67 (1995)
Western Australia (CIE, 2004)	GPs routinely advising women considering pregnancy about the importance of folate	15 (1992)	70 (1995)
South Australia (Chan et al, 2001(Chan et al, 2001).	Women of child-bearing age who had knowledge of the importance of folate in the peri-conceptional period	15 (1994)	60.5 (1998)
Western Australia (in Abraham and Webb, 2001)	Awareness of association between folate intake and spina bifida; Perth women (18-44 yrs) [14]	40 (1995)	44 (1997)
Victoria (Watson et al., 2001).	Awareness of folate and NTDs in women of child-bearing age	12.5 (1996)	30 (2000)
New Zealand			
Bourn and Newton 1998	Aware of relationship between folate and NTDs in women (25-44 years)	56	
Dunedin (Ferguson et al 2000)	Women interviewed that knew folate helped to prevent birth defects such as spina bifida	38	
Christchurch (Schader and Corwin 1999)	Women that knew folic acid reduces the risk of spina bifida	63%	

Adapted from (Abraham and Webb 2001; NZMoH 2003)

[16] Surveys used to evaluate the Folate Health Claim Pilot included CSIRO National Nutrition Survey 1998-99; South Australian Health Monitor 1998-99; Eat Well Tasmania Survey 1998-99; and Australian Supermarket Institute Consumer Monitor Survey 1998-99 (ANZFA 2000).

[12] analysis excluded women who did not intend to become pregnant or could not become pregnant

KNOWLEDGE OF RECOMMENDED TIMING, DOSE AND SOURCES OF FOLATE IN AUSTRALIAN AND NEW ZEALAND SURVEYS

Survey	Awareness / knowledge determined	Percentage pre-intervention	Percentage post-intervention
Recommended time and dose to increase folate to help prevent spina bifida			
WA Institute for Child Health Research (ICHR)	When is it important for women planning a pregnancy to increase folate to reduce their risk of spina bifida (prompted)		67% in March 1995
WA Department of Health evaluation of folate program	When is it important for women planning a pregnancy to increase folate to reduce their risk of spina bifida (chosen from a list)	38% in May 1995	28% in July 1997
Kelloggs Newspoll	Women having heard the recommendation that folate be taken 6 weeks before becoming pregnant to reduce the risk of spina bifida	36% in 1998	45% in Nov 1998 67% in May 1999
ICHR (WA)	Women who chose the recommended dose of folic acid (from a list)		19% in March 1995
How to increase folate consumption			
ANZFA 2000	Women with knowledge of which foods contain folate -green leafy vegetables -cereals	 40% in 1998 26% in 1998	 52% in 1999 49% in 1999
Kelloggs Newspoll	Women unable to name a food high in folate	14% in July 1998	17% in May 1999
ANZFA 2000	Women able to name supplements as a source of folate	1.4% in 1998	4% in 1999
Dunedin (Ferguson et al 2000)	Women able to name foods as good sources of folate - cereals and breads	70%	(not an evaluation of an intervention)

Adapted from (Abraham and Webb 2001; NZMoH 2003)

INTENTION TO INCREASE FOLATE INTAKE AND BEHAVIOUR CHANGES MEASURED IN AUSTRALIAN SURVEYS

Survey	Awareness / knowledge determined	Percentage pre-intervention	Percentage post-intervention
Intention to increase folate intake			
WA Department of Health	Women (18-44 yrs) who said they would increase the amount of folate in their diet if planning a pregnancy -by folate-rich foods -by supplements	62 % in 1992 55% 39%	64% in 1997 62% 57%
WA ICHR	Women who would increase the amount of folate in their diet if they were planning a pregnancy		84% in March 1995
Behavioural change			
SA (Chan et al, 2001)	Women who did not increase their folate intake as they thought they were already consuming enough		14.5%
ANZFA	Women indicating folate information had encouraged them to eat foods containing folate	22% in 1998	29% in 1999
CSIRO National Diet Survey	Women who changed their folate intake (in any way) as a result of receiving information about folate – Yes by: taking a supplement eating more fruit & vegetables eating more folate added foods	17% 29% in Nov 1998 **29%** 19%	 28% in Nov 1999 24% 14%

Adapted from (Abraham and Webb 2001)

Attachment 6

INTERNATIONAL CASE STUDIES OF MANDATORY FORTIFICATION WITH FOLIC ACID

1. Countries with mandatory folic acid fortification

Country	Year mandatory folic acid fortification introduced	Foods fortified with folic acid	Level of fortification mg/ kg
Africa			
Malawi	2002	Maize flour	2.06
South Africa		Maize meal	1.89-1.94
		wheat: flour white, brown	1.36, 1.24
		bread: white, brown	0.74
Zambia		Enriched maize meal	2.4
Middle East			
Saudi Arabia	2000	Enriched wheat, enriched treated flour	1.5
North America			
Canada	November 1998[15]	flour (white, enriched, enriched white); enriched bread; enriched pasta; enriched pre-cooked rice	1.5
USA	Phased in between 1996 and January 1998	Enriched cereal grain products including: enriched wheat flour; enriched bread, rolls & buns; enriched corn grits & corn meal; enriched farina; enriched rice; enriched macaroni products;	1.4
South America			
Argentina,	2002	wheat flour	2.2
Bolivia,	1996	wheat flour	1.5
Chile,	1997	wheat flour	2.0-2.4
Colombia,	1996	wheat flour	1.54
Costa Rica,	2002	wheat flour, corn flour, rice, milk	1.8, 1.3, 1.8,1.6
the Dominican Republic,	2003	wheat flour	1.8
Ecuador,	1996	wheat flour	0.6
El Salvador, Guatemala,	2002	wheat flour, corn flour	1.8, 1.3
Honduras,	2002	wheat flour, corn flour	1.8, 1.3
Mexico,	2002	wheat flour, corn flour	1.8, 1.3
Nicaragua,	1998	wheat flour, corn flour	0.4-0.8, 0.4-0.8
Panama,	2002	wheat flour, corn flour	1.8, 1.3
Paraguay.	2002	wheat flour, corn flour	1.8, 1.3
	1998	wheat flour	3.0
South East Asia			
Indonesia	unknown	Enriched wheat flour	2.0

Adapted from: (Canadian Government 1998; Roche Vitamins Europe 2003; USFDA 1996b)

[15] Canada introduced voluntary fortification regulations in December 1996, and phased into mandatory fortification by November 1999 (Canadian Government 1998).

2. Impact of mandatory fortification in the United States

Background

In December 1996, the US Food and Drug Administration reviewed its voluntary regulations for folic acid fortification and required that *enriched*[16] cereal grains products be fortified on a mandatory basis at 140 μg folic acid per 100 g cereal grain product by January 1998 (USFDA 1996b). In addition, ready to eat breakfast cereals were permitted to be voluntarily fortified with folic acid up to 400 μg per serve.

This decision was based on modelling and public consultation on the proposal to amend the standards of identity for enriched cereal grain products to require folic acid fortification. Modelling was undertaken for cereal grains, dairy products and fruit juices, at levels of 70, 140 and 350 μg per 100 g, using the 1987-8 national food consumption data and the safe upper limit of 1 mg per day as recommended by the CDC. The amount of folic acid added to enriched cereal grains was chosen so that approximately 50% of all reproductive-age women would receive a total of 400 μg of folate from all sources (CDC 1992) and increase the typical folate intake by approximately 100 μg per day (Jacques et al., 1999). The selected fortification level of 140 μg was considered to be a compromise between safety and prevention of NTDs (CDC 1992; Daly et al, 1997). This amount of fortification was estimated to reduce the incidence of NTDs by up to 41%, (Daly et al, 1997; Wald et al, 2001).

The cereal foods enriched with folic acid included enriched: wheat flour; bread, rolls and buns; corn grits and cornmeal; farina; rice and macaroni products. These food vehicles were chosen on the basis of being staple food products for most of the US population (including 90% of the target group), and a long history of being successful vehicles for fortification (USFDA 1996a). Unenriched cereal-grain products are not fortified with folic acid to allow for consumer choice (USFDA 1996b), although these constitute a minority of the entire available product.

Implementation by industry

Mandatory fortification of folic acid in cereal grains commenced in 1996 and was basically complete by mid 1997(Jacques et al, 1999). As a result, it was estimated that the folate content of more than one third of available foods had increased (Lewis et al 1999 cited in (NZMoH 2003).

It appears that the actual folate content of fortified foods was greater than had been assumed in predicting folate intakes under mandatory fortification. Initial studies comparing the analysed folate content of enriched cereal-grain products to the levels required by Federal regulations showed that mandatorily fortified foods contained up to 160-175% of their predicted folate content (Choumenkovitch et al, 2002; Rader et al, 2000). Similar results were found with fortified breakfast cereals (Whittaker et al, 2001b).

[16] In the US, enriched refers to the addition of a nutrient to a food that has been lost during the course of food processing or during normal storage and handling, up to the nutrient's level in the food before the processing, storage and handling.

The high levels of total folate were thought to be due to overages used by manufacturers to ensure food products contained at least the amount of nutrient specified on the label throughout shelf life, as well as higher than expected levels of naturally-occurring folate and/or problems with the analysis method used (Rader et al, 2000; Whittaker et al, 2001a).

Public health impact of mandatory fortification

Impact on dietary intake

Overall studies found an average increase of almost 200 μg of folate per day across all sectors of the community, including the target group of reproductive-age women (Choumenkovitch et al, 2002; Quinlivan and Gregory 2003).

The Framingham Offspring cohort study showed that among non-supplement users in the cohort, the prevalence of older individuals who consumed less than the recommended daily intake of folate (defined as 320 μg DFE per day) decreased from 48.6% prior to the FDA-mandated folic acid fortification to 7.0% post-mandatory fortification. Consumption of greater than 1 mg folic acid occurred only in individuals who regularly consumed supplements containing folic acid (frequency of use was not defined). The proportion of individuals who exceeded this limit rose from 1.3% prior to fortification to 11.3% after mandatory fortification (Choumenkovitch et al, 2002).

Impact on folate status

The US CDC compared folate status data from the National Health and Nutrition Examination Surveys: one conducted prior to any fortification of the food supply, between 1988 and 1994 (NHANES III); the other after mandatory fortification in 1999 (NHANES 1999).

The mean serum folate concentration in participating women aged 15-44 years increased by 157%, from 14.3 nmol/L during NHANES III to 36.7 nmol/L in NHANES 1999. For non-supplement users, the mean serum folate concentration increased by 167%, from 10.7 nmol/L to 28.6 nmol/L over this time (CDC 2000).

In the above group of subjects, mean red blood cell folate concentration, indicating long-term folate status, increased from 410.1 nmol/L to 713.8 nmol/L, an average increase of 74% (data not adjusted for supplement use). In addition, women with the lowest initial folate values showed the greatest improvement in folate status (CDC 2000).

Looking at a wider sector of the US population, serum folate data from a US clinical laboratory were analysed from 1994 to 1998. The majority of men and women were aged between 12 and 70. Median serum folate values increased by 50% from 28.6 nmol/L in 1994 (prior to fortification) to 42.4 nmol/L in 1998 (post-mandatory fortification) (Lawrence et al, 1999). These values were not corrected for vitamin supplement intake.

Among non-supplement users of the Framingham Offspring cohort, the mean serum folate concentrations increased from 10.4 nmol/L (pre-mandatory fortification) to 22.7 nmol/L (post-mandatory fortification), an increase of 117% in the study population**.**

The mandatory folic acid fortification program has virtually eliminated the presence of low folate concentrations (defined as serum folate levels below 7 nmol/L) from the cohort of older adults, with a decrease from 22% to 1.7% of the cohort exhibiting low folate status since mandatory fortification (Jacques et al, 1999).

Overall, the mandatory fortification of the food supply with folic acid has led to a significant positive increase of serum and red blood cell folate levels for all sectors of the US population, including the target group.

Impact on NTD rate

As detailed in the previous section, an average decrease of 27% in prenatally ascertained NTD-affected pregnancies (true incidence) was found after the introduction of mandatory folate fortification, which CDC attributes to the introduction of mandatory folate fortification. Overall, the total number of NTD-affected pregnancies declined from 4,000 prior to the folic acid mandate to 3,000 after mandatory fortification. In addition, various economic models have shown that mandatory fortification results in favourable benefit-to-cost ratios (Grosse 2004; Horton 2003; Romano et al, 1995).

Potential adverse effects

Studies addressed:

- Masking of vitamin B_{12} deficiency - A study of 1,573 mainly African American women and men from a Veterans Affairs Centre found that the proportion of people who had poor vitamin B_{12} status without anaemia did not change significantly from the pre fortification period (39.2%) to after full implementation of mandatory fortification (37.6%). This study concluded that mandatory fortification did not increase the prevalence of masking of vitamin B_{12} deficiency (Mills et al, 2003). The introduction of mandatory fortification was found to increase the number of people who would be considered at-risk for masking of vitamin B_{12} deficiency, however, this value still remains below 1% and no actual cases of masking were reported in the US.

- Twinning - Out of more than 2.5 million births in California, there has been no reported increase in the incidence of twinning after the mandatory fortification of the US food supply relative to the pre-fortification period (Shaw et al, 2003). Similar results were found when comparing data from over 1 million births in Texas. A general increase in the prevalence of twinning has been noted to have occurred over the past decade, which was attributed to factors such as increasing maternal age at parity, rather than the fortification program (Waller et al, 2003).

3. Consideration of mandatory fortification in the United Kingdom

Background

Since the mid- to late 1980s, the United Kingdom (UK) has adopted a voluntary approach to fortification of foods with folic acid. Though few products are fortified, an estimated 80-90% of breakfast cereals are fortified with varying levels of folic acid. The UK also continues to promote the uptake of folic acid supplements and to encourage consumption of folate-rich foods by women of childbearing age.

In January 2000, a report titled *Folic Acid and Prevention of Disease* was published by the Department of Health, England (Department of Health 2000). This report (COMA report), concluded that on scientific, medical and public health grounds, universal fortification of flour with folic acid at 240 μg/ 100 g in food products as consumed would have a significant effect in preventing NTD-affected births and pregnancies, without resulting in unacceptably high intakes in any other population groups. However, the report also concluded that higher folic acid intakes might affect vitamin B_{12} deficiency, particularly in the 50+ age group, and make the signs of deficiency less easy to detect by delaying onset of anaemia.

The UK Health Departments and Food Standards Agency (FSA) consulted on the COMA report and held a joint stakeholder meeting to discuss the issues identified. In 2002, the FSA Board discussed the issue of mandatory fortification in detail. In considering the issue, the FSA looked at evidence of the impact of varying the fortification rate on the intakes of UK population groups, in particular, the potential risk of high intakes of folic acid among older groups of the population to mask vitamin B_{12} deficiency. This deficiency affects about 5% of people aged 65-74 years, and over 10% of those aged 75 years or older (Clarke et al, 2004). The FSA Board concluded by a majority, and provided advice to Health Ministers, not to currently recommend the mandatory fortification approach (Food Standards Agency (FSA) 2002).

Health Ministers accepted the proffered advice due to outstanding concerns about vitamin B_{12} deficiency. However, they agreed that the Scientific Advisory Committee on Nutrition (SACN) would assess the wider impact of fortification and emerging evidence, including the benefits and risks to older people and other population groups. Ministers also wished to consider options to increase usage of peri-conceptional supplements, increase dietary intakes of folate and to identify the prevalence of vitamin B12 deficiency.

Public health impacts of voluntary fortification

There has been no formal assessment of voluntary folic acid fortification and there remains very little fortification of food products. Whilst it is useful to examine folate status, it is difficult to assess whether any of the observations can be attributed solely to fortification practices and/or a greater public awareness of folic acid following the conduct of nutrition education campaigns in the mid 1990s.

Folate intakes

It is difficult to estimate the contribution to folic acid intakes by voluntary folic acid fortification as there is no information on changes to folic acid intakes over time. The COMA report quotes information from the National Diet and Nutrition Survey (NDNS) of 4 to 18 year olds (Gregory et al, 2000), which found that the breakfast cereal category contributed to 25% and 20% of male and female folic acid intakes respectively. If extrapolated to the wider population, such information indicates that voluntary fortification is already contributing to a sizable proportion of folic acid intakes by the UK population. However, total intakes of folate for women of childbearing age remain below the amount required to prevent NTDs.

Red Blood Cell (RBC) folate levels

Measurements of RBC status are collected as part of the NDNS programme which has looked at 4 age groups from toddlers aged 1½ years to the elderly aged 65 years and over in the past two decades. Each survey looks at a different age cohort and therefore does not allow for an assessment of RBC folate levels over time. Current mean RBC folate status of adults falls within normal ranges (422 nmol/L to 1463 nmol/L) (Department of Health 2000; Ruston et al, 2004). The older age group (50-64 years) had, on average, higher RBC folate levels than those free living elderly adults aged 65-74 years who were surveyed in the mid 1990s, although these two age groups are likely to have different dietary patterns and lifestyles.

NTD rates

The UK has monitored notified congenital anomaly statistics including NTD-affected pregnancies since 1964. Surveillance shows that the incidence of NTDs, which includes births, stillbirths, terminations and an adjustment for under reporting, has decreased from 36.6/10,000 births in the 1970s through to 5.8/10,000 births in 2000 (Food Standards Agency (FSA) 2002; NZMoH 2003). The UK statistics demonstrate that NTD rates have been in noticeable decline prior to voluntary fortification practices which commenced in 1987 (McDonnell et al, 1999).

Attachment 7

REFERENCES

Abraham,B. Webb,K.L. 2001. Interim evaluation of the voluntary folate fortification program. Canberra, Australian Food and Nutrition Monitoring Unit, Commonwealth of Australia.

ANZFA. 2000. Evaluating the folate-neural tube defect health claim pilot; process evaluation of the management framework and outcome evaluation. Canberra, ANZFA.

Baik,H.W. Russell,R.M. 1999. Vitamin B12 deficiency in the elderly. Annu.Rev Nutr 19, 357-377. PM:10448529

Ball,G.F.M. 1998. Bioavailability and analysis of vitamins in foods. 444, 474. London, Chapman and Hall.

Booth,C., Clark,T., Fenn,A. 1998. Folic acid, riboflavin, thiamin, and vitamin B-6 status of a group of first-time blood donors. Am J Clin Nutr 68, 1075-1080.

Boushey,C.J., Beresford,S.A., Omenn,G.S., Motulsky,A.G. 1995. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. JAMA 274 (13), 1049-1057. PM:7563456

Bower,C., Eades,S., Payne,J., D'Antione,H., Stanley,F. 2004. Trends in neural tube defects in Western Australia in Indigenous and non-Indigenous populations. Paediatr Perinat Epidemiol 18, 277-280.

Bower,C., Ryan,A., Rudy,E., Miller,M. 2002. Trends in neural tube defects in Western Australia. Aust N Z J Public Health 26, 150-151.

Bower,C., Silva,D., Henderson,T.R., Rudy,E. 2000. Ascertainment of birth defects: the effect on completeness of adding a new source of data. J Paediatr Child Health 36, 574-576.

Brouwer,I.A., van Dusseldorp,M., West,C.E., Steegers-Theunissen,R. 2001. Bioavailability and bioefficacy of folate and folic acid in man. Nutrition Research Reviews 14, 267-293.

Campbell,N.R. 1996. How safe are folic acid supplements? Arch.Intern.Med 156 (15), 1638-1644. PM:8694661

Canadian Government. 1998. Canada Gazette Part II. vol 32, No 24.

CDC. 1992. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. MMWR 41, 1-7.

CDC. 2000. Folate status in women of childbearing age - United States 1999. MMWR 49, 962-965.

Chan,A., Pickering,J., Hann,E.A., Netting,M., Buford,A., Johnson,A., Keane,R.J. 2001. 'Folate before pregnancy'; the impact on women and health professionals of a population-based health promotion campaign in South Australia. Medical Journal of Australia 174, 631-636.

Choumenkovitch,S.F., Selhub,J., Wilson,P.W.F., Rader,J.I., Rosenberg,I.H., Jacques,P.F. 2002. Folic acid intake from fortification in the United States exceeds predictions. J Nutr 132, 2792-2798.

Clarke,R., Grimley-Evans J., Schneede,J., Nexo,E., Bates,C., Fletcher,A., Prentice,A., Johnston,C., Ueland,P.M., Refsum,H., Sherliker,P., Birks,J., Whitlock,G., Breeze,E., Scott,J.M. 2004. Vitamin B12 and folate deficiency in later life. Age Ageing 33 (1), 34-41. PM:14695861

Codex Alimentarius Commission. 1991. General principles for the addition of essential nutrients to foods. CAC/GL 09-1987 (amended 1989, 1991). www.codexalimentarius.net/searchindex.doc

Czeizel,A.E., Metneki,J., Dudas,I. 1994. The higher rate of multiple births after periconceptional multivitamin supplementation: an analysis of causes. Acta Genet Med Gemllol (Roma) 43, 175-184.

Daly,D., Mills,J.L., Molloy,A.M., Conley,M., Lee,Y.J., Kirke,P.N., Weir,D.G., Scott,J.M. 1997. Minimum effective dose of folic acid for food fortification to prevent neural tube defects. Lancet 350, 1666-1669.

Daly,L.E., Kirke,P.N., Molloy,A.M., Weir,D.G., Scott,J.M. 1995. Folate levels and neural tube defects. Implications for prevention. JAMA 274, 1698-1702.

Darnton-Hill,I. 1998. Rationale and elements of a successful food-fortification program. Scrimshaw,N.S. 2 (19). Tokyo, United Nations University Press. Food and nutrition bulletin. http;//www.unu.edu/unupress/food/V192e/begin.htm

de Ambrosis,A., Arcot,J., Haber,P., Paterson,J., Smyth,G., Guilhais,M. 2004. Bioavailability of folic acid from fortified rice in humans using stable isotope techniques. Am J Clin Nutr 13, S57.

De Bree,A., Verschuren,W.M., Kromhout,D., Kluijtmans,L.A., Blom,H.J. 2002. Homocysteine determinants and the evidence to what extent homocysteine determines the risk of coronary heart disease. Pharmacol.Rev 54 (4), 599-618. PM:12429870

de Walle,H.E., van der Pal,K.M., den Berg,L.T.W., Jeeninga,W., Schouten,J.S.A.G., De Rover,C.M.B.S.E., Cornel,M.C. 1999. Effect of mass media campaign to reduce socioeconomic differences in women's awareness and behaviour concerning use of folic acid:cross sectional study. Br.Med J 319, 291-292.

Department of Health. 2000. Folic acid and the prevention of disease. Report Health and Social Subjects 50. London, The Stationary Office.

Dickinson,C.J. 1995. Does folic acid harm people with vitamin B12 deficiency. QMJ 88, 357-364.

Eikelboom,J.W., Lonn,E., Genest,J.J., Hankey,G., Yusuf,S. 1999. Homocyst(e)ine and cardiovascular disease; a critical review of the epidemiological evidence. Ann Inten Med 131, 363-375.

European Commission,S.C.o.F.S. 2000. Opinion of the scientific committee on food on the tolerable upper intake level of folate. http://europa.eu.int/comm/food/fs/sc/scf/out80e_en.pdf

Expert Group on Vitamins and Minerals,U. 2002. Review of folic acid. http://www.food.gov.uk/multimedia/pdfs/evm0018p.pdf

FAO/WHO expert consultation on human vitamin and mineral requirements. 1998. Folate and folic acid. ftp://ftp.fao.org/es/esn/nutrition/Vitrni/PDF/CHAPTER04.pdf

Ferguson,E.L., Skeaff,C.M., Bourne,D.M., Nixon,N., Parnell,W.R. 2000. Folate status of representative populations in Dunedin, issues for folate fortification. Department of Human Nutrition and Department of Food Science, University of Otago, New Zealand.

Flicker,L.A., Vasikaran,S.D., Thomas,J., Acres,J.G., Norman,P.E., Jamrozik,K., Lautenschlager,N.T., Leedman,P.J., Almeida,O.P. 2004. Homocysteine and vitamin status in older people in Perth. Med J Aust. 180 (10), 539-540. PM:15139834

Flood,V.M., Webb,K.L., Smith,W., Rochtchina,E., Mitchell,P. 2004. Prevalence of low serum folate, red cell folate, serum vitamin B12 and elevated homocysteine. Asia Pac.J Clin Nutr 13 (Suppl), S85. PM:15294590

Flood.V.M., Webb,K.L., Smith,W., Mitchell,P., Bantick,J.M., Macintyre,R., Sindhusake,D., Rubin,G.L. 2001. Folate fortification: potential impact on folate intake in an older population. Eur J Clin Nutr 55 (9), 793-800. PM:11528496

Food Standards Agency (FSA). 2002. Board Paper: Folic acid and the prevention of disease. http:/www.food.gov.uk/news/newsarchive/2002/may/62488

FSAI Nutrition Sub-committee. 2003. Report on the mandatory fortification of flour with folic acid for the prevention of neural tube defects. Dublin, Food Safety Authority of Ireland.

Giskes,K., Turrell,G., Patterson,C., Newman,B. 2002. Socioeconomic differences among Australians adults in consumption of fruit and vegetables and intakes of vitamins A,C and folate. J Hum Nutr Diet 15, 375-390.

Gregory,J., Lowe,S., Bates,C., Prentice,A., Jackson,L.V., Smithers,G., Wenlock,R., Farron,M. 2000. National Diet and Nutrition Survey: young people aged 4 to 18 years. Volume 1: Report of the diet and nutrition survey. London, TSO.

Gregory,J.E. 1995. The bioavailability of folate. Bailey,L. Folate in health and disease. 195-226. New York, Marcel Dekker Inc.

Grosse,S. 2004. Economic evaluation in maternal and child health: principles and cases.

Hibbard,B. 1964. The role of folic acid in pregnancy with particular reference to anaemia, abruption and abortion. J Ostet Gynaecol Br Commonw 71, 529-544.

HLT Collaboration. 1998. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. Homocysteine Lowering Trialist's Collaboration. Br.Med J 316, 894-898.

Horton. 2003. The economic impact of micronutrient deficiencies, Presentation at 54th Nestle Nutrition Workshop, San Paola, Brazil. 2003.

Hunter,R., Barnes,J., Oakeley,H.F., Matthews,D.M. 1970. Toxicity of folic acid given in pharmacological doses to healthy volunteers. Lancet 1 (7637), 61-63. PM:4188624

Institute of Medicine. 1998. Folate. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. (8), 198-305. Washington, D.C., National Academy Press.

Jacques,P.F., Selhub,J., Bostom,A.G., Wilson,P.W., Rosenberg,I.H. 1999. The effect of folic acid fortification on plasma folate and total homocyteine concentrations. The New England Journal of Medicine 340 (19), 1449-1454.

Kalucy,M., Bower,C., Stanley,F., Burton,P. 1994. Survival of infants with neural tube defects in Western Australia 1966-1990. Paediatr Perinat Epidemiol 8, 334-351.

Kirke,P.N., Molloy,A.M., Daly,L.E., Burke,H., Weir,D.G., Scott,J.M. 1993. Maternal plasma folate and vitamin B12 are independent risk factors for neural tube defects. Q J Med 86, 703-708.

Lancaster,P. Hurst,T. 2001. Trends in neural tube defects in Australia. Canberra, Australian Food and Nutrition Monitoring Unit, Commonwealth of Australia.

Laurence,K.M., James,N., Miller,M.H., Tennant,G.B., Campbell,H. 1981. Double-blind randomised controlled trial of folate treatment before conception to prevent recurrence of neural tube defects. Br.Med J 282, 1509-1511.

Lawrence,J.M., Petitti,D.B., Watkins,M., Umekubo,M.A. 1999. Trends in serum folate after foods fortification. Lancet 354, 915-916.

Lindenbaum,J., Healton,E.B., Savage,D.G., Brust,J.C., Garrett,T.J., Podell,E.R., Marcell,P.D., Stabler,S.P., Allen,R.H. 1988. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. N Engl.J Med 318 (26), 1720-1728. PM:3374544

Lumley,J., Watson,L., Watson,M., Bower,C. 2001. Periconceptional supplementation with folate and/or multivitamins for preventing neural tube defects. Cochrane Database Syst Rev 3 .

Manzoor,M. Runcie,J. 1976. Folate-responsive neuropathy: report of 10 cases. Br.Med J 1 (6019), 1176-1178. PM:1268613

McDonnell,R.J., Johnson,Z., Delaney,V., Dack,P. 1999. East Ireland 1980-1994: epidemiology of neural tube defects. J Epidemiol Community Health 53 (12), 782-788.

Metz,J., Sikaris,K.A., Maxwell,E.L., Levin,M.D. 2002. Changes in serum folate concentrations following voluntary food fortification in Australia. Med J Aust. 176 (2), 90-91. PM:11936300

Mills,J.L., Von Kohorn,I., Conley,M.A., Zeller,J.A., Cox,C., Williamson,R.E., Dufour,D.R. 2003. Low vitamin B12 concentrations in patients without anaemia: the effect of folic acid fortification of grain. Am J Clin Nutr 77, 1474-1477.

MRC Vitamin Study. 1991. Prevention of neural tube defects: results of the medical research council vitamin study. Lancet 338, -131.

National Health and Medical Research Council (NHMRC). 1995. Folate Fortification; Report of the Expert Panel on Folate Fortification. (Commonwealth of Australia). Canberra.

Newton,R., Green,T., Bourn,D. 2001. The effects of fortification of the New Zealand food supply on folate intakes. Dunedin, University of Otago.

NHMRC. 1991. Recommended dietary intakes for use in Australia. Canberra, Commonwealth of Australia.

NHMRC. 1995. Folate fortification; report of the expert panel on folate fortification. (Commonwealth of Australia). Canberra.

NHMRC. 2000. How to use the evidence; assessment and application of scientific evidence. Handbook series on preparing clinical practice guidelines. Canberra, NHMRC. http://www.nhmrc.gov.au/publications/synopses/cp65syn.htm

Nutrivit. 2000. Fortification basics: choosing a vehicle. http://www.nutrivit.org/vic/staple/index.htm

NZFSA. 2004. Proposed changes to the dietary supplements regulations 1985. NZFSA Public Discussion Paper No 01/04. Wellington, NZFSA.

NZFSA/ NZMoH. 2004. Reducing neural tube defects in New Zealand; a consultation document. consultation document No 2/04. Wellington, New Zealand Food Safety Authority/ Ministry of Health.

NZMoH. 1999. Folate, folic acid and health. Wellington, Ministry of Health.

NZMoH. 2003. Improving folate intake in New Zealand. Wellington, Ministry of Health.

O'Leary,C.M., Knuiman,M.W., Divitini,M.L. 2004. Homocysteine and cardiovascular disease: a 17-year follow-up study in Busselton. Eur J cardiovasc Prev Rehabil 11, 350-351.

Queensland Health. 2002. An overview of indicators of nutritional status of Queensland adults: collected as part of the AusDiab study. 9-21.

Quinlivan,E.P. Gregory,J.F. 2003. Effect of food fortification on folcc acid intake in the United States. Am J Clin Nutr 77, 221-225.

Rader,J.I., Weaver,C.M., Angyal,G. 2000. Total folate in enriched cereal-grain products in the United States following fortification. Food Chemistry 70, 275-289.

Roche Vitamins Europe. 2003. Mandatory food enrichment. Bolwley,A. Nutrivew . Basel, Switzerland, Roche Vitamins Europe Ltd. http://www.nutrivit.org/vic/staple/index.htm

Romano,P.S., Waitzman,N.J., Scheffler,R.M., Pi,R.D. 1995. Folic acid fortification of grain: an economic analysis. Am J Public Health 85 (5), 667-676. PM:7733427

Russell,D., Parnell,W., Wilson,N. 1999. NZ food: NZ people: key results of the 1997 national nutrition survey. Wellington, Ministry of Health.

Ruston,D., Hoare,J., Henderson,L., Gregory,J., Bates,C.J., Prentice,A., Birch,M., Swan,G., Farron,M. 2004. The national diet and nutrition survey: adults aged 19 to 64 years. London, Her Majesty's Stationery Office.

Sanderson,P., McNulty,H., Mastroiacovo,P., McDowell,I.F.W., Melse-Boonstra,A., Finglas,P.M., Gregory,J.F. 2003. Folate bioavailability. UK food standards agency workshop. British Journal of Nutrition 90, 473-479.

Savage,D.G. Lindenbaum,J. 1995. Folate-Cobalamin interactions. Bailey,L. Folate in Health and Disease. New York, Marcel Dekker, Inc.

Scholl,T.O. Johnson,W.G. 2000. Folic acid:influence on the outcome of pregnancy. Am J Clin Nutr 71 (5), 1295S-1303.

Shaw,G.M., Carmichaels,S.L., Nelson,V., Selvin,S., Schaffer,D.M. 2003. Food fortification and twinning among California infants. Am J Med Genet 119A, 137-140.

Skeaff,C.M. Mann,J. 1998. Should folate be added to flour to prevent neural tube defects. New Zealand Medical Journal 111, 417-418.

Skeaff,M., Green,T., Mann,J. 2003. Mandatory fortification of flour? Science, not miracles, should inform the decision. The New Zealand Medical Journal 116 (1168). http://www.nzma.org.nz/journal/116-1168/303

Smithells,R.W., Sheppard,S., Schorah,C.J., Seller,M.J., Nevin,N.C., Harris,R., Read,A.P., Fielding,D.W. 1980. Possible prevention of neural-tube defects by periconceptional vitamin supplementation. 339 349.

The Alan Guttmacher Institute. 1999. Sharing responsibility; women society and abortion worldwide. New York, AGI.

USFDA. 1996a. Folic acid fortification fact sheet. http://www.babybag.com/articles/wh-folic.htm . http://www.babybag.com/articles/wh-folic.htm

USFDA. 1996b. Food standards: amendment of standards of identity for enriched cereal grain products to require the addition of folic acid (final rule). US Food and Drug Administration. Federal Register vol 61 (44), 8781-8797.

Van der Put,N.M., van Straaten,H.W., Trijbels,F.J., Blom,H.J. 2001. Folate, homocysteine and neural tube defects: an overview. Exp.Biol Med (Maywood.) 226 (4), 243-270. PM:11368417

Verhoef,P. Katan,M.B. 2004. A healthy lifestyle lowers homocysteine, but should we care? Am J Clin Nutr 79, 713-714.

Verity,C., Firth,H., French-Constant,C. 2003. Congenital abnormalities of the nervous system. J Neurol Neurosurg Psychiatry 74, 3i-8.

Wald,D.K., Law,M.R., Morris,J.K., Wald,D.S. 2001. Quantifying the effect of folic acid. Lancet 358, 2069-2073.

Wald,N.J., Law,M.R., Morris,J.K. 2002. Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. Br.Med J 325, 1202.

Waller,D.K., Tita,A.T., Annegers,J.F. 2003. Rates of twinning before and after fortification of foods in the US with folic acid, Texas 1996 to 1998. Paediatr Perinat Epidemiol 17, 378-383.

Whittaker,P., Tufaro,P.R., Rader,J.I. 2001a. Iron and folate in fortified cereals. J Am Coll.Nutr 20 (3), 247-254. PM:11444421

Whittaker,P., Tufaro,P.R., Rader,J.I. 2001b. Iron and folate in fortified cereals. J Am Coll.Nutr 20 (3), 247-254. PM:11444421