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

6-04
4 August 2004

DRAFT ASSESSMENT REPORT

APPLICATION A528

MAXIMUM IODINE LIMIT IN FORMULATED SUPPLEMENTARY FOODS FOR YOUNG CHILDREN

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

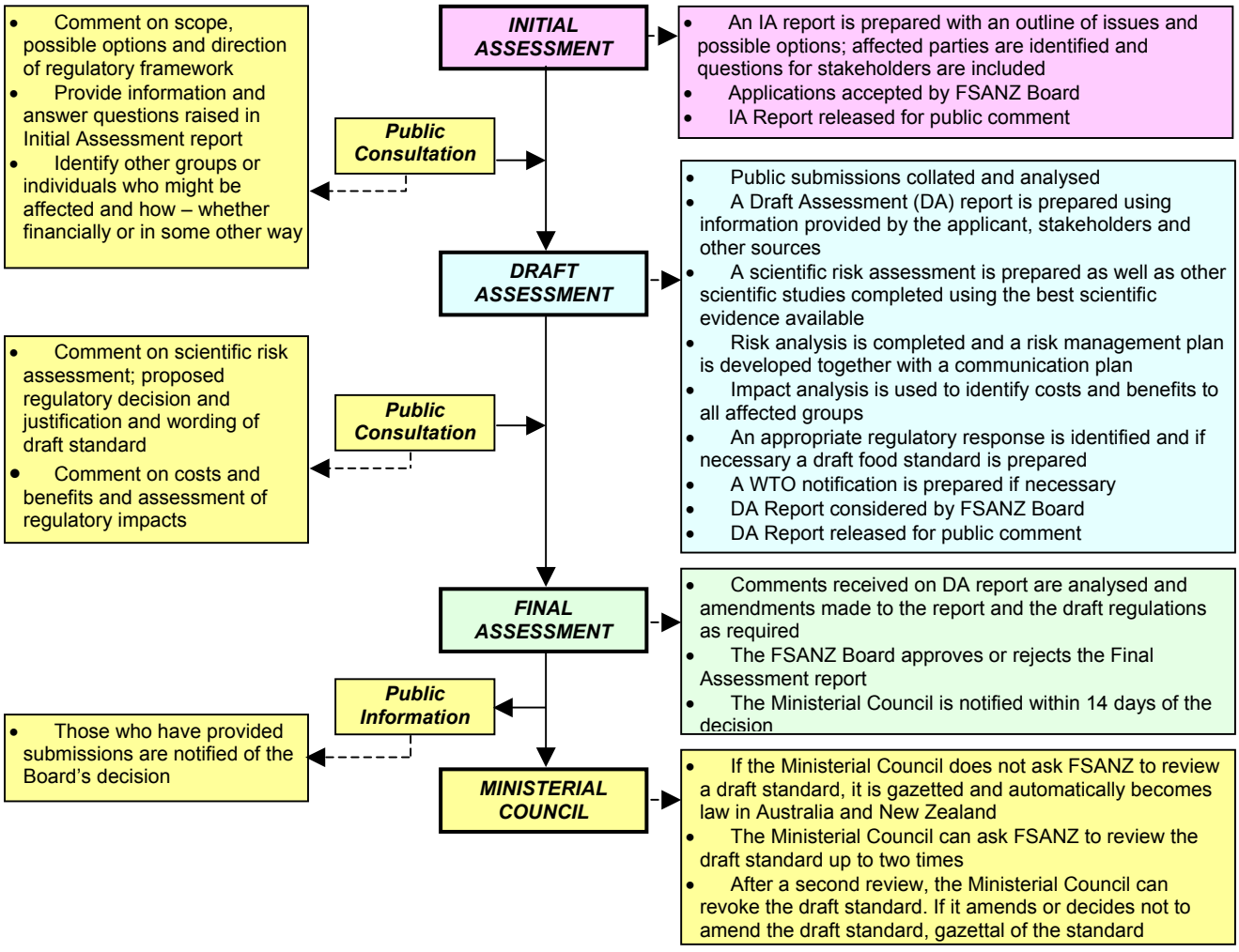
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

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 Commonwealth; 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 Commonwealth, 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 Commonwealth, 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 a Draft Assessment Report of Application A528, and prepared a draft variation to the *Australia New Zealand Food Standards Code* (the Code).

FSANZ invites public comment on this Draft Assessment Report based on regulation impact principles and the draft variation to the Code for the purpose of preparing an 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 Final Assessment for this Application. 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 15 September 2004**.

Submissions received after this date may not be considered, unless the Project Manager 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.

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Executive Summary and Statement of Reasons

Food Standards Australia New Zealand (FSANZ) received an Application from Wyeth Australia Pty Limited on 20 January 2004 seeking to amend Standard 2.9.3 – Formulated Meal Replacements and Formulated Supplementary Foods of the *Australia New Zealand Food Standards Code* (the Code) to increase the maximum permitted quantity of iodine per serving from 35 to 70 micrograms (μg) in formulated supplementary foods for young children (FSFYC). FSFYC are defined in the Code as formulated supplementary food for children aged 1 – 3 years.

This Draft Assessment Report discusses the issues involved in the proposed amendment and seeks comment from stakeholders, particularly in relation to expected regulatory impact(s), to assist FSANZ in making a Final Assessment of this Application.

Regulatory Problem

The Applicant has requested an increase in the maximum permitted quantity of iodine in FSFYC to accommodate levels of naturally occurring[1] iodine in ingredients used to manufacture FSFYC. Some manufacturers of FSFYC claim that on occasions the endogenous quantity of iodine can exceed the maximum permitted iodine quantity due to seasonal and geographical variation in the iodine content of ingredients. The Applicant suggests that their milk-based FSFYC could exceed the current upper limit of 35 μg iodine/serve approximately 30% of the time even if the iodine in the product is contributed solely from milk and milk ingredients. This being the case, the Applicant has requested that FSANZ consider the iodine variability that exists in raw materials, specifically milk, and to raise the upper limit of iodine permitted in FSFYC from 35 to 70 μg/serve.

Issues

This Draft Assessment Report discusses issues, including issues raised in submissions, which are considered important in meeting the objectives of this Application, in particular:

- the variability of iodine found in ingredients used to manufacture FSFYC;
- the iodine status of young children in Australia and New Zealand; and
- safety issues including upper limits and toxicological assessment.

Regulatory Options and Impact Analysis

Two options are considered for this Application at Draft Assessment. These are:

1. Maintaining the *status quo* by not increasing the maximum iodine quantity; or

2. Amending Standard 2.9.3 to increase the permitted maximum quantity of iodine in FSFYC from 35 to 70 μg per serving.

For each regulatory option, an impact analysis has been undertaken to assess potential costs and benefits to various stakeholder groups associated with its implementation.

[1] In this case 'naturally occurring' refers to the innate iodine content in addition to any adventitious contamination which may occur during the processing of ingredients e.g. iodophores in milk.

Consultation

The Initial Assessment Report for this Application was released for public comment from 17 March 2004 to 28 April 2004 (six weeks). A total of seven submissions were received, five in support of increasing the maximum permitted quantity of iodine in FSFYC, one opposed, and another who did not indicate support for either option (see Attachment 5). The issues raised in submissions are discussed in this report. FSANZ now seeks public comment on this Draft Assessment in order to proceed to Final Assessment.

Conclusion and Statement of Reasons

This Draft Assessment Report concludes that amending the Code to accommodate the natural variation of iodine in ingredients used to manufacture FSFYC does not pose a significant risk to public health and safety. Therefore it is recommended that Standard 2.9.3 be amended to increase the maximum permitted level of iodine in FSFYC from 35 to 70 μg per serving (Attachment 1) for the following reasons:

- the resultant increase in iodine status as a consequence of raising the maximum permitted quantity of iodine in FSFYC will not raise any safety concerns or cause any adverse nutritional risks in the target population;

- the proposed draft variation to the Code is consistent with the section 10 objectives of the FSANZ Act. Specifically, FSANZ has addressed the protection of public health and safety by undertaking a risk assessment using the best scientific data available;

- the proposed draft variation to the Code will increase compliance with the Code, reduce manufacturing costs, and prevent unnecessary trade barriers; and

- the regulation impact assessment concludes that the benefits from increasing the maximum permitted quantity of iodine in FSFYC outweigh any potential costs to affected parties.

If approved, the variation to the Code will come into effect on date of gazettal.

1. Introduction

Food Standards Australia New Zealand (FSANZ) received an Application from Wyeth Australia Pty Limited on 20 January 2004 seeking to amend Standard 2.9.3 – Formulated Meal Replacements and Formulated Supplementary Foods of the *Australia New Zealand Food Standards Code* (the Code) to increase the maximum permitted quantity of iodine from 35 to 70 micrograms (μg) per serving in formulated supplementary foods for young children (FSFYC).

In the Code, a formulated supplementary food is defined as a *food specifically designed as a supplement to a normal diet to address situations where intakes of energy or nutrients may not be adequate to meet an individual's requirements*. FSFYC are formulated supplementary foods for children aged 1 – 3 years.

This Draft Assessment Report discusses the issues involved in the proposed amendment and seeks comment from stakeholders, particularly in relation to expected regulatory impact(s), to assist FSANZ in making a Final Assessment of this Application.

2. Regulatory Problem

The Applicant has requested an increase in the maximum permitted quantity of iodine in FSFYC to accommodate levels of naturally occurring[2] iodine in ingredients used to manufacture FSFYC. Some manufacturers of FSFYC claim that on occasions the endogenous quantity of iodine can exceed the maximum permitted iodine quantity due to seasonal and geographical variation in the iodine content of ingredients. The Applicant suggests that their milk-based FSFYC could exceed the current upper limit of 35 μg iodine/serve approximately 30% of the time even if the iodine in the product is contributed solely from milk and milk ingredients. This being the case, the Applicant has requested that FSANZ consider the iodine variability that exists in raw materials, specifically milk, and to raise the upper limit of iodine permitted in FSFYC from 35 to 70 μg/serve.

3. Objectives

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives which 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:

[2] In this case 'naturally occurring' refers to the innate iodine content in addition to any adventitious contamination which may occur during the processing of ingredients e.g. iodophores in milk.

- 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

4.1 Current Regulation

Division 4 of Standard 2.9.3 sets out the compositional and labelling requirements for FSFYC. Subclause 6(1)(c) of Standard 2.9.3 prescribes the compositional requirements, including vitamins and minerals, of FSFYC as follows:

(1) Formulated supplementary foods for young children must contain in a serving no less than –

> *(c) 20 % of the RDI of no less than one of those vitamins or minerals listed in column 1 of Table 3 in the Schedule, provided the total quantity[3] of each vitamin or mineral in a serving does not exceed the quantity, where specified, set out in relation to that vitamin or mineral in column 2 of Table 3.*

Column 2 of Table 3 in the Schedule to Standard 2.9.3 specifically sets the maximum quantity per serving for iodine as 35 μg, which is 50% of the recommended dietary intake (RDI) for children aged 1 – 3 years[4].

Iodine is allowed to be added to FSFYC, in a permitted form, provided that the total quantity of both the naturally occurring and added amount does not exceed this prescribed maximum level [subclauses 6(2) and (3)]. Where a permitted vitamin or mineral is added, a maximum claim limit of 50% RDI also applies [subclause 7(2)(c)]. However, in relation to this Application, the issue relates to iodine naturally present in raw materials used to manufacture FSFYC, not iodine added during manufacture. Therefore the declaration of iodine, in this case, is subject to the generic nutrition labelling requirements in Standard 1.2.8 – Nutrition Information Requirements of the Code.

[3] In the Code 'total quantity' refer to both naturally occurring and added nutrients.
[4] Column 4 in the Schedule to Standard 1.1.1 – Preliminary Provisions – Application, Interpretation and General Prohibitions of the Code specifies the recommended dietary intake (RDI) for iodine in children aged 1 –3 years as 70 μg.

4.2 Current Market

The vast majority of FSFYC available in Australia and New Zealand are milk-based supplementary drinks known as 'toddler formula'. FSANZ is not aware of other products that are currently manufactured to the FSFYC provisions.

Toddler formula is generally promoted as a supplementary milk drink for young children aged 1 to 3 years. Product information advises that FSFYC should be prepared in water, although the Applicant has indicated that in most cases (approximately 70%) the product is made up in milk, using half the number of recommended scoops. In addition toddler formulas are sometimes promoted as being suitable as a replacement for milk in other foods e.g. custards.

There are only a small number of manufacturers/importers of FSFYC in Australia/New Zealand and on the whole, the market for these products is relatively small and discrete. Wyeth, Nestlé and Heinz Wattie's are the main manufacturers of FSFYC. The Applicant has indicated that the toddler drinks market has a turnover of 640,000 kg/year, with a growth rate in market sales of more than 40% for 2003. Wyeth is the market leader with a sales volume of 360,000 kg/year which represents 40% of the total market share.

4.3 Historical Changes to Regulations

In 1999, during the development of the *Australia New Zealand Food Standards Code*, FSANZ completed Proposal P199 – Formulated Meal Replacements and Formulated Supplementary Foods. This Proposal reviewed the regulations for formula dietary foods (Standard R4) and supplementary foods (Standard R9) of the Australian *Food Standards Code* and the equivalent regulations in the *New Zealand Food Regulations 1984.*

In considering the vitamin and mineral permissions for additions to formulated supplementary foods, Proposal P199 recommended a maximum claim limit of 50% RDI/serve on the basis that it is *inappropriate that a supplementary food supply the complete needs of given nutrients.*

In addition to the use of maximum claim limits for added vitamins and minerals, prescribed maximum quantities at the 50% RDI limit were also set for vitamin A, vitamin D and iodine (whether added or naturally occurring) in formulated supplementary foods (including FSFYC).

4.4 International Regulations

4.4.1 Codex Alimentarius

There is no specific Codex Standard for formulated supplementary foods for young children, although guidelines[5] exist on the nutritional and technical aspects of the production of FSFYC. These guidelines do not however specify an upper limit for iodine. In addition the Codex Standard for Follow-up Formula (CODEX STAN 72-1981), which includes formulas used for young children, does not specify a maximum limit for iodine.

[5] Guidelines on Formulated Supplementary Foods for Older Infants and Young Children (CAC/GL 08-1991)

4.4.2 Other international regulations

FSANZ has identified no other international regulations for FSFYC relevant to this Application except in Chinese food regulation[6] where a permitted range of iodine at 30 – 150 μg per 100g is prescribed.

4.5 Iodine in the Diet

4.5.1 Sources

Iodine in food occurs mostly as inorganic iodides or iodates (COMA 1999) and its levels in food are dependent on the environment of the food's origin, particularly the levels of iodine in the soil. Australia and New Zealand have low levels of iodine in their soils, which can often expose sections of the population to low iodine intakes (Gunton et al 1999). Internationally, the major natural sources of iodine in the diet (i.e. excluding fortified foods) are seafood, milk and eggs (FAO/WHO 2002). Meat and cereal are secondary sources.

4.5.2 Role

Iodine is an essential component of the thyroid hormones thyroxine (T4) and tri-iodothyronine (T3). T3 and T4 are synthesised within the thyroid gland where iodine is removed from the blood and concentrated before being linked to the hormones. Thyroid hormones are essential for the maintenance of metabolic rate, cellular metabolism and the integrity of connective tissue (Gibson 1990).

Dietary iodine is easily absorbed from the stomach and upper small intestine (Thomson 2002, Stanbury 1996), however this absorption can be reduced by the calcium, magnesium and iron content in food and water (SCF 2002). Additionally the utilisation of dietary iodine in the body is influenced by goitrogens. Goitrogens are found in the vegetables of the Brassica genus (Cruciferae family: cabbage, broccoli, turnips, Brussels sprouts) and interfere with the biosynthesis of the hormones T3 and T4. Heat from the cooking of these vegetables will inactivate most of the goitrogens that are present.

4.5.3 Recommended dietary intakes of iodine

The current Australian and New Zealand RDI for iodine of 70 μg/day for children 1-3 years is at the lower end of other comparable international RDIs (Table 1). The Applicant contends that if the maximum quantity of iodine permitted in FSFYC was raised to 70 μg (100% RDI) and a child consumed the recommended 2 serves per day then they would receive 140 μg/day from this source which they believe, whilst recognising this to be higher than the currently accepted Australian RDI, is within internationally accepted ranges.

[6] National Standard of the People's Republic of China (GB 10767 – 1997) Foods for Infants and Young Children.

Table 1: Current International Dietary Reference Intake Values for Iodine

Country	Age	Reference Intake (RDI/RDA* or equivalent)
AUSTRALIA AND NEW ZEALAND[7,8,9]	1-3 years	70 µg/day
UK[10]	1-3 years	70 µg/day
WHO[11]	0-59 months (0-5 years)	90 µg/day
Germany/Austria[12]	1-3 years	100 µg/day
Switzerland[12]	1-3 years	90 µg/day
USA and Canada Reference Intake Values for Iodine[13]	1-3 years	90 µg/day

*RDA=Recommended Dietary Allowance

4.5.4 Nutrient interactions

Some nutrients are known to compete with others for absorption and bioavailability. There is no literature to suggest that iodine competes with, or inhibits the bioavailability of any other nutrient. This suggests that an increase in dietary iodine intake is unlikely to impact on the nutrient absorption of the consumers of FSFYC.

4.6 Variability in Milk Iodine Levels

The Applicant has made specific reference to the variability of iodine in the milk and milk-based ingredients that are of prime importance in the manufacture of FSFYC. It is therefore important to identify the status of iodine within the base milk ingredients of FSFYC, and to determine if there is sound rationale for amending the Code as proposed by the Applicant.

4.6.1 Extent of iodine variability in milk

The Applicant has mentioned that except for iodine, all minerals are contained within milk as components of micelles. As micelle production is regulated during milk formation, the concentrations of these minerals are consistent no matter where the milk is sourced from (United States Board on Agriculture 1988). However, iodine is present as a free form in milk and is therefore subject to external influences.

The main external influences on the free form level of iodine in milk are geographical variations and seasonal diets, in addition to the use of iodophores as sanitising agents of milking equipment.

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[7] The National Health and Medical Research Council (NHMRC) is currently reviewing the RDIs for Australia and New Zealand in light of recent international recommendations.

[8] Truswell AS, Dreosti IE, English RM, Rutishauser IHE, Palmer N. (1990). *Recommended Nutrient Intakes. Australian Papers*. Sydney: Australian Professional Publications

[9] Thomson C. (2002). Australian *and New Zealand Nutrient Reference Values for Iodine, prepared for the New Zealand Ministry of Health*

[10] Report of the panel on dietary reference values of the committee on medical aspects of food policy. Dietary Reference values for food energy and nutrients for the United Kingdom 1991. Chapter 35 Iodine

[11] ICCIDD, UNICEF, WHO Assessment of Iodine Deficiency Disorders and Monitoring their elimination. 2nd Edition. Geneva: WHO publishing ,2001

[12] German Nutrition Society, Austrian Nutrition Society, Swiss Nutrition Society, Swiss Society for Nutrition Research. Reference values for nutrient intakes. Frankfurt am main: Umschau/Braus, 2000 (in Thomson 2002)

[13] Food and Nutrition Board IoM. Dietary reference intakes for vitamin A, vitamin K, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium and zinc. Washington, D.C.: National Academy Press, 2001

Geographical variations in milk iodine levels are due to differences in the soil iodine content of cattle grazing pastures. Seasonal variations occur when iodine rich stock feed is given to dairy cattle during winter to compensate for reduced access to grazing pastures (United Kingdom Food Safety Agency 2000).

Iodophores have been used in the past as sanitising agents for teats and milking equipment, and contributed significantly to the iodine content of milk. Australia, New Zealand and many other overseas countries have now moved away from the use of iodophores to other sanitising agents, resulting in a lowering of milk iodine contents. However, some nations (e.g. United Kingdom) still maintain the practice of iodophore use, which contributes to the global variability in milk iodine contents (Eastman 1999, McDonnell 2003, Dunn 1998).

Table 2 demonstrates some of the variability that can exist in milk iodine concentration on a global scale; only a selection of countries are provided due to the lack of information on international milk iodine concentrations. New Zealand data has been obtained from the 1997/98 Total Diet Survey results, while information on Australia is available for Tasmania, where periodic monitoring is undertaken by two major milk producers, and for the Northern Victorian District of the Goulburn Valley.

Table 2: Annual Iodine Concentrations in Milk (μG/L)

	Minimum	Maximum	Mean
Australia (Tasmania) (Personal communications: Seal J, 2004)	110	440	265
Australia (Victoria) (Nestlé submission in response to IAR A528)	31	361	155
New Zealand (Vannort R 2000)	44	184	85
United Kingdom (United Kingdom Food Standards Agency 2000)	184	426	315
Germany (Preiss 1997)	<100	150	115
International Mean (FAO/WHO 2002)	34	54	46

4.6.2 Impact of iodine variability in milk on FSFYC

The Applicant has stated that because the iodine in milk is highly variable, the use of milk and milk components can result in some FSFYC potentially exceeding the current iodine maximum limit as specified in the Code.

The milk used in the Applicant's FSFYC products is sourced from Ireland, United States/Canada, and Australia/New Zealand depending on the availability of milk at particular times of the year. The Applicant has provided information on the iodine variability of a FSFYC (Progress Toddler Gold®) produced in Ireland.

Table 3 is a summary of the statistical analysis of this data. Iodine levels range from a minimum of 21.3 μg/ 44 g serving to a maximum of 42.3 μg/44 g serving, with a mean of 28.9 μg/44 g serving.

Table 3: Statistical Analysis of the Iodine Levels in Progress 3rd Age Toddler Gold

CODE	µg I /100 g	µg I /44 g serving
Mean	65.6	28.9
Min	48.4	21.3
Max	93.9	41.3
Std Dev*	12.1	5.3
Mean + 3 std. dev*	101.8	44.8

* = Standard Deviation

The Applicant currently manufacturers its FSFYC in Ireland where the iodine level in this product can reach a maximum of 52 µg per 44 g serving. Production will soon be transferred to Singapore where the iodine level in the milk ingredients for this region can reach a maximum of 56 µg per 44 g serving.

To prevent iodine levels of FSFYC exceeding the maximum permitted quantity without an amendment to the Code, manufacturers would need to screen the iodine content in all ingredients derived from milk. The Applicant has indicated that this is not logistically feasible for manufacturers to undertake, as other attributes of milk ingredients set the quality benchmark for their use; e.g. milk protein levels.

4.7 Other Relevant FSANZ Work Activities

4.7.1 Application A493

FSANZ is currently assessing Application A493 – Iodine as a Processing Aid, whereby the Applicant is seeking permission to use elemental iodine as a washing agent for fruits, vegetables (including herbs), nuts and eggs with a maximum permitted residue level of good manufacturing practice (GMP). Application A493 is currently at Draft Assessment and if this Application is approved, the iodine residue from the sanitising wash will contribute to dietary iodine intake. Therefore, in undertaking dietary modelling FSANZ has considered Application A493 to determine the potential impact of both Applications on the iodine status of the population.

4.7.2 Mandatory iodine fortification

The Ministerial Council has recently (May 2004) requested that FSANZ commence work on assessing the need for mandatory fortification of the food supply with iodine. In undertaking this assessment, FSANZ will need to consider all indiscriminate sources of iodine in the food supply and may need to reassess iodine permissions in the future, if deemed necessary.

5. Risk Assessment

FSANZ has undertaken three separate assessments that can inform an overall assessment of risk. These assessments are the Safety Assessment, the Dietary Intake Assessment (including the combined Dietary Intake Assessment for both Applications A528 and A493) and the Nutrition Risk Assessment; and are provided in full detail at Attachments 2, 3 and 4 respectively. A summary of the findings from the three assessments can be found in the following sections.

5.1 Safety Assessment

5.1.1 Adverse effects from excess iodine intake

A large number of human experimental, clinical, and epidemiological studies have been reported on the consequences for human health from an excess iodine intake. Because both the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the US Agency for Toxic Substances and Disease Registry (ATSDR) have assessed these studies in detail, FSANZ has reviewed the outcomes of their reports along with each of the studies cited therein to gauge a picture of iodine toxicity. The reviewed material indicates that the primary effect of excess iodine is on the thyroid gland and regulation of thyroid hormone production and secretion.

Excess iodine can produce an enlargement of the thyroid gland (goitre) and/or affect the production of the thyroid hormones. A diminished production of thyroid hormones is referred to as hypothyroidism (and may be accompanied by goitre), while increased thyroid hormone synthesis and secretion by the thyroid gland is referred to as hyperthyroidism.

The effect on the thyroid depends on the current and previous iodine status of the individual and any current or previous thyroid dysfunction. For example, individuals with a history of iodine deficiency may be prone to the development of iodine-induced hyperthyroidism if iodine exposure increases later in life.

5.1.2 Identification of safe iodine intakes

The human response to excess iodine can vary. Some individuals can tolerate large intakes (up to 50 µg/kg/day) while others may respond adversely to levels close to recommended intakes (3-7 µg/kg/day). Individuals responding adversely to relatively low intake levels often have an underlying thyroid disorder or have a long history of iodine deficiency.

For the majority of healthy individuals, the most sensitive endpoint for iodine toxicity is sub-clinical hypothyroidism. Sub-clinical hypothyroidism is defined as an elevation in thyroid stimulating hormone (TSH) concentration, while at the same time serum thyroid hormone concentration is maintained within the normal range of values for healthy individuals.

Although not clinically adverse, such an effect, could lead to clinical hypothyroidism if it persists over a prolonged period of time. In healthy adults, sub-clinical hypothyroidism has been associated with acute intakes of 1700 µg/day (24 µg/kg body weight/day for a 71 kg person), and for children, has been associated with chronic intakes of 1150 µg/day (29 µg/kg/day for a 40 kg child).

5.1.3 Determination of an upper safe limit for children aged 1-3 years

Iodine intakes of approximately 1000 µg/day appear to be well tolerated by healthy adults. This level has been used by JECFA to establish a provisional maximum tolerable daily intake (PTDI) for iodine of 17 µg/kg bw/day from all sources. FSANZ has adopted this level as a safe intake level for the purpose of risk assessment. The PTDI has been established for all ages, and assuming a mean body weight of 16 kg, the age group of 1-3 year olds has an upper safe intake limit of 272 µg/day.

It needs to be noted, however, that individuals with thyroid disorders or a long history of iodine deficiency may respond adversely at levels of intake below the PTDI. Because iodine is an essential nutrient, a safe level cannot be set low enough to protect these individuals without potentially impacting on the health of the remaining population.

5.2 Dietary Intake Assessment

5.2.1 Background

Proposal P199 prescribed a maximum quantity for iodine at the 50% RDI limit (whether added or naturally occurring) in formulated supplementary foods (including FSFYC). When Proposal P199 was being developed, dietary modelling of iodine intakes for adults and children was not undertaken due to limited iodine food composition data. As a consequence, the maximum quantity for iodine may be considered conservative. Therefore, iodine food composition data now available allows for dietary modelling to more accurately determine upper safely limits for iodine.

5.2.2 Assessment of Application A528

The dietary intake assessment was conducted using dietary modelling techniques that combine food consumption data with food chemical concentration data to estimate the dietary intake of iodine. The dietary intake was estimated by combining usual patterns of food consumption, as derived from National Nutrition Survey (NNS) data, with proposed levels of use and naturally occurring concentrations of iodine in foods.

Dietary iodine intake was calculated for the population group of Australian children aged 2-3 years only because there are no Australian food consumption data for children aged below 2 years of age and no New Zealand food consumption data for New Zealand children aged 1-3 years.

Baseline intakes of iodine were calculated using naturally occurring concentrations of iodine in food, in addition to the iodine from FSFYC (that have a maximum permitted iodine quantity of 35 µg/serve if prepared according to directions).

A scenario examined a maximum permitted iodine level in FSFYC of 70 µg/serve (if prepared according to directions) – with iodine concentration adjustments for different preparation methods – in addition to intakes of naturally occurring iodine from all other food sources. The results of this modelling are shown in Table 4 below.

Table 4: Modelling of Iodine Intakes in Australian 2-3 Year Olds for Application A528

Scenario	Iodine Intake in Australian 2-3 year olds	
	Mean	95th Percentile
Baseline dietary pattern	5.4 µg/kg bw/day (83 µg/person/day)	9.9 µg/kg bw/day (165 µg/person/day)
Scenario 1 (increase of iodine in FSFYC to 70 µg/serve)	6.0 µg/kg bw/day (92 µg/person/day)	11.0 µg/kg bw/day (179 µg/person/day)

Mean and 95th percentile estimated dietary intakes of iodine in Scenario 1 were below the Provisional Tolerable Daily Intake (PTDI) for iodine (17 µg/kg bw/day) as identified in the safety assessment. Further details on the dietary iodine intake assessment can be found at Attachment 3.

5.2.3 Assessment of Applications A493 & A528

For the purpose of estimating the potential dietary intake of iodine, should the requested variations to the Code from both A493 and A528 be approved, three different scenarios were examined:

- Baseline: naturally occurring levels of iodine in addition to currently permitted maximum quantities of iodine, with adjustments for variations in preparation method of FSFYC;

- Scenario 1: this scenario applies a peeling factor to the iodine concentrations of those fruits and vegetables that may be consumed either peeled or unpeeled (e.g. apples) and that may be washed with an elemental iodine wash. This scenario reflects a more accurate estimate of the likely extent to which an elemental iodine wash (A493) will impact on iodine dietary intakes. Scenario 1 also takes into account the increase in the maximum iodine quantity in FSFYC from 35 to 70 µg/serve, with adjustments for variations in preparation method, by using an adjusted 'full fat milk equivalents' iodine concentration (A528). Scenario 1 is a more probable scenario;

- Scenario 2: this scenario assumes that fruits and vegetables that may be consumed either peeled or unpeeled (e.g. apples) are always eaten unpeeled after being treated with an elemental iodine wash (A493). Scenario 2 also takes into account the increase in the maximum iodine quantity in FSFYC from 35 to 70 µg/serve, with adjustments for variations in preparation method, by using an adjusted 'full fat milk equivalents' iodine concentration (A528). Scenario 2 is a worst-case scenario.

The modelling results for each of these scenarios are detailed in Table 5 below.

Table 5: Modelling of Iodine Intakes In Australian 2-3 Year Olds for Applications A528 and A493 Combined

Scenario	Iodine Intake in Australian 2-3 year olds	
	Mean	95th Percentile
Baseline dietary pattern	5.4 µg/kg bw/day (83 µg/person/day)	9.9 µg/kg bw/day (165 µg/person/day)
Scenario 1 (peeling included)	8.7 µg/kg bw/day (133.9 µg/person/day)	16.1 µg/kg bw/day (258.3 µg/person/day)
Scenario 2 (all fruit and vegetables unpeeled)	9.8 µg/kg bw/day (150.2 µg/person/day)	18.7 µg/kg bw/day (289.4 µg/person/day)

Estimated mean and 95th percentile dietary intakes of iodine were below the PTDI of 17 µg/kg body weight/day for the baseline scenario and for Scenario 1. For Scenario 2, mean dietary intake of iodine was below the PTDI, with 95th percentile intake exceeding the PTDI (110% PTDI). However, due to the conservative assumptions made in this calculation and that the use of 24 hour dietary survey data tends to over-estimate habitual food consumption amounts for high consumers when not adjusted for intra-individual variation, it is likely that the 95th percentile dietary intake is an over-estimate.

Further details on the estimated dietary intakes of iodine for 'both applications (A493 & A528)' can be found at Attachment 3.

5.3 Nutrition Risk Assessment

The Nutrition Risk Assessment was conducted at Draft Assessment by reviewing several nutritional issues that could inform the identification of nutritional risks for Australian and New Zealand children. These issues were identified as:

- the current iodine status of Australian and New Zealand children;
- the interactions between iodine and other nutrients; and
- the likelihood of adverse health outcomes for young children who consume an excess iodine intake.

5.3.1 Current iodine status of Australian and New Zealand children

To assess the iodine status of Australian and New Zealand children, urinary iodine studies in childhood populations have been reviewed, and current iodine intakes have been compared against the United States Estimated Average Requirement (EAR)[14]. Childhood population studies (Guttikonda *et al* 2003, Li *et al* 2001, McDonnell *et al* 2003, Skeaff *et al* 2002, Ministry of Health 2003) indicate that Australian and New Zealand children have a reduced iodine status. The studies only include 5-18 year old children as subjects, however the results are still seen as an applicable indicator for the iodine status of 1-3 year olds.
Comparisons of dietary iodine intakes against the EAR shows that a substantial proportion of young children have an intake less than the EAR, which reflects the results reported in Australian and New Zealand urinary iodine excretion studies.

5.3.2 Interactions between iodine and other nutrients

There is no available scientific literature that suggests iodine inhibits the bioavailability of any other nutrient. However, the presence of low selenium intakes in a population (such as in New Zealand) may exacerbate any iodine deficiencies that are current prevalent amongst children, because of a relationship between the selenium and iodine status of the human body. This effect magnifies the potential for iodine deficiency in New Zealand 1-3 year olds (as identified in section 5.3.1 above).

5.3.3 Likelihood of adverse health outcomes for young children who consume an excess iodine intake

Children have a similar vulnerability to the adverse health effects that result from excess iodine intakes as for other sections of the population. It can also be established that short-term fluctuations in population iodine intakes are unlikely to adversely affect the health status of
1-3 year olds (COT 2000, SCF 2002).

[14] EAR is a value that represents the medium requirement for the dietary intake of a particular nutrient in a given population group.

However, if the iodine content of FSFYC was consistently up to the maximum limit (i.e. by addition) during times when the natural iodine contribution from milk ingredients decreases, then more chronic exposures to high iodine contents potentially would occur.

5.3.4 Determination of nutritional risk

From the results of FSANZ's dietary intake assessment, Application A528 will have a minor impact on the iodine intakes of 1-3 year olds, and any increase is unlikely to produce adverse health effects due to the already reduced iodine status of Australian and New Zealand young children (assuming the iodine status information for older children applies to 1-3 year olds, and that Australian dietary data is also relevant for New Zealand).

5.4 Characterisation of Risk

The public health and safety risk to Australian and New Zealand populations has been determined from the above findings of the Safety Assessment (Section 5.1), the Dietary Intake Assessment (Section 5.2), and the Nutrition Assessment (Section 5.3).

The risk to Australian and New Zealand children from adopting the proposed amendment is minimal. The findings of the Safety and Dietary Intake Assessments show that iodine intakes of 1-3 year olds will not increase above a safe level when FSFYC contain iodine at 70 µg/serve. The iodine intakes of high FSFYC consumers (the 95th percentile) are also below the safe limit when modelled on the most likely scenario (Scenario 1).

Even when consideration has been given to the combined impact of Application A493 and Application A528, the safe limit is only just exceeded in the 95th percentile, a result that is likely to be an over-estimate.

The safety and dietary intake assessments therefore demonstrate that this Application will affect the 1-3 year old population intake of iodine to a very small degree, and there is evidence indicating that the health risks will be reduced even further given that 1-3 year old children in Australia and New Zealand appear to have a mildly reduced iodine status.

The Safety Assessment also identified those with thyroid disorders or a long history of iodine deficiency as being potentially at risk with intakes below the PTDI. These individuals may respond to excess iodine in the diet by developing thyrotoxicosis (also referred to as iodine-induce hyperthyroidism). However, the most vulnerable are those over 40 years of age who have a long history of iodine deficiency, although individuals with underlying thyroid disorders may also be affected. Although there is evidence of iodine deficiency in the Australian and New Zealand populations, the deficiency is believed to be relatively mild. For these reasons very few young children would be expected to be vulnerable to the occurrence of iodine-induced hyperthyroidism.

Therefore, the proposed amendment accommodates natural iodine fluctuations in milk ingredients only, and with no change to the maximum claim contemplated, it is unlikely that iodine levels would approach the increased maximum quantity through fortification.

6. Risk Management

6.1 Increase in the Maximum Permitted Quantity for Iodine

The rationale for the Applicant requesting an increase in the maximum permitted quantity of iodine is to overcome a problem facing some manufacturers whereby endogenous iodine quantities in milk and milk ingredients occasionally exceed the current upper limits of iodine. The intention of this Application is to accommodate seasonal fluctuations and variations in iodine levels rather then to consistently increase iodine levels to 100% of the RDI per serving. The Risk Assessment concludes that increasing the maximum permitted quantity of iodine in FSFYC from 35 to 70 μg per serving does not pose a significant risk to public health and safety.

The dietary modelling undertaken for this Application (A528) assumed all FSFYC contained the maximum proposed quantity of 70 μg of iodine per serving. This depicts a 'worst case scenario' whereas in reality iodine levels will fluctuate and for the majority of the time will be considerably less than 70 μg of iodine per serving.

Data supplied by the Applicant gives the mean endogenous iodine level for their product as 28.9 μg/serve and the 99.7th percentile as 44.8 μg/serve. This means iodine levels would nearly always be below 45 μg/serve, assuming iodine levels are normally distributed. While dietary modelling results, based on a sustained 70 μg of iodine/serve, show the impact on iodine status is well within safety limits, in reality the increase in iodine status would be less than predicted by this modelling.

Based on the risk assessment, increasing the maximum permitted limit iodine content from 35 (50% RDI) to 70 μg (100% RDI) is safe.

6.1 Issues Raised in Public Submissions

In response to the Initial Assessment Report, seven submissions were received and are summarised at Attachment 5. Five submissions supported increasing the maximum permitted quantity of iodine in FSFYC, one did not and one submitter supported neither option due to the absence of suitable data to assist decision-making.

6.1.1 Variability in Milk Iodine Levels

Not all manufactures of FSFYC have difficulties with endogenous iodine quantities exceeding the maximum permitted quantity in Standard 2.9.3. In their submission Heinz Wattie's have indicated that they source their milk only from New Zealand and due to the naturally low soil levels of iodine in New Zealand, do not have a problem with iodine levels exceeding the upper limits of the Standard. As a result, Heinz Wattie's have recently begun adding additional iodine to their product due to recent data showing iodine deficiency in the Australian and New Zealand population.

Conversely, both Wyeth and Nestlé have indicated that there is potential for their product runs to be outside the maximum permitted quantity of iodine in FSFYC. Nestlé source their milk from the Goulburn Valley in Victoria, Australia and Wyeth from outside Australia.

Given the variability of iodine levels in milk and the difficulty in accessing laboratories for routine iodine testing in food, the Department of Human Services and Health, Tasmania suggested that regulating the level of iodine in milk might be more appropriate rather than in the final product.

6.1.1.1 Assessment

For a significant proportion of the FSFYC market, the endogenous quantity of iodine in the raw materials can at times exceed the maximum permitted iodine quantity in the final product, making it difficult for some manufacturers to comply with the requirements of the Code.

Due to the difficulty and expense of routinely testing iodine quantities in milk, maintaining the regulatory *status quo* has the potential to increase manufacturing costs.

Regulating the level of iodine in milk is beyond the scope of this Application plus any regulation on milk ingredients locally would not have jurisdiction overseas.

6.1.2 Iodine Fortification

The New Zealand Food Safety Authority supported increasing the permitted maximum quantity of iodine in FSFYC but noted that if mandatory iodine fortification is considered, the upper limits of iodine may need to be reassessed.

6.1.2.1 Assessment

As part of the assessment process examining mandatory iodine fortification, FSANZ will consider all potential sources of adventitious and innate iodine in the food supply and if necessary, permissions in the Code will be adjusted to ensure the protection of public health and safety.

6.1.3. Maximum claim limit of 50% RDI/serve.

The Applicant has requested that Standard 2.9.3 be amended to increase the maximum permitted quantity of iodine from 35 μg (50% RDI) to 70 μg (100% RDI) per serving in FSFYC. Heinz Wattie's do not support increasing the maximum permitted quantity and/or the maximum permitted claimable quantity to above 50% of the RDI. They state this would be inconsistent with the nature of the Code where vitamin and mineral permissions for formulated supplementary foods are restricted to a maximum claim limit of 50% RDI/serve.

6.1.3.1 Assessment

FSANZ is proposing to increase the maximum permitted quantity to iodine in FSFYC but **not** to increase the maximum permitted claim applying to the addition of iodine. This will deter manufacturers from adding iodine above the permitted claim limit of 35 μg/serve. The intention of this proposal is to accommodate fluctuating levels of naturally occurring iodine in milk while discouraging the addition of additional iodine to the maximum permitted quantity of 70 μg/serve. This is in keeping with the nature of the Code where vitamin and mineral permissions for formulated supplementary foods are restricted to a maximum claim limit of 35 μg /serve (50%RDI).

Therefore, FSANZ is proposing to retain the maximum permitted claim of 35 µg /serve for iodine. This is consistent with the guiding principles for considering the vitamin and mineral permissions for formulated supplementary foods as outlined in Proposal P199 (See Section 4.3).

6.1.4 Lack of suitable data to assist decision making

The Department of Human Services and Health, Tasmania noted that it is difficult to make informed comment on applications of this type in the absence of:

- up-to-date food intake data;
- comprehensive food composition data;
- data on nutritional status of the population; and
- current nutrient reference values.

They also acknowledged that undertaking iodine analyses in food products is expensive and there are limited numbers of laboratories in Australia that are NATA accredited to perform iodine analysis in food.

FSANZ acknowledges the data provided by the Tasmanian Department of Human Services that highlights the variability of milk iodine levels, included in Table 2 of this report.

6.1.4.1 Assessment

This submission acknowledges the Applicant's concerns as to the difficulty and expense in undertaking frequent iodine analyses. In relation to the lack of accurate and reliable data, FSANZ's assessment of this Application is conservative and thus based on a worst-case scenario.

7. Regulatory Options

There are two possible options to progress this Application:

1. maintain the *status quo* i.e. the permitted maximum quantity for iodine in FSFYC remains unchanged; or

2. amend Standard 2.9.3 to increase the permitted maximum quantity of iodine in FSFYC from 35 to 70 µg/serve.

8. Impact Analysis

8.1 Affected Parties

The parties affected by this Application are: **consumers** who are most likely very young children; **industry** being Australian and New Zealand importers and manufacturers of FSFYC; and the **Governments** of New Zealand and Australia.

8.2 Cost Benefit Analysis

This analysis assesses the immediate and tangible impacts of current food standards under Option 1 and of the proposed amendment under Option 2.

8.2.1 Option 1 – Status quo

It is likely that maintaining the *status quo* will have minimal impact on **consumers**. Some manufacturers may be required to conduct regular batch testing of ingredients to ensure they comply with the maximum permitted quantity of iodine. This may increase costs associated with the manufacture of FSFYC which could be passed on to **consumers** via product price increases.

For **industry** however, maintaining the *status quo* means that potentially, during some periods of the year, some manufacturers will find it difficult to comply with the requirements of the Code due to natural variations in the iodine content of base ingredients. The Applicant claims that under the current requirements in the Code, the maximum limit of iodine is exceeded approximately 30% of the time. Retaining the *status quo* may require some manufacturers to undertake more frequent monitoring of iodine in raw material batches thereby increasing costs and possibly affecting the supply of their products.

With the exception of China, there appears to be no iodine restrictions for FSFYC anywhere else in the world. Maintaining the current iodine maximum limit for FSFYC is likely to necessitate specific formulation for the New Zealand and Australian markets for some producers rather than using one product for the global market. This situation will potentially restrict trade.

With this Application the issue of exceeding the maximum permitted iodine limits in FSFYC manufacture has been highlighted. Consequently there may be increased costs to **government** and enforcement agencies in monitoring the iodine levels in FSFYC.

8.2.2 Option 2 - Amend Standard 2.9.3 to increase the maximum permitted level of iodine in FSFYC from 35 to 70 μg/serve.

An increase in the permitted maximum iodine content of FSFYC may benefit some **consumers** of FSFYC by providing additional iodine in their diet.

An amendment to the Code will have the most benefit for **industry** as there is likely to be fewer manufacturing costs, particularly in the testing of raw ingredients for iodine levels, for FSFYC and a greater opportunity for regulatory compliance. Furthermore by increasing the quantity of iodine permitted in FSFYC industry are less likely to be required to specifically manufacture FSFYC for New Zealand and Australian markets, thereby increasing trade opportunities.

There is likely to be no impact on **government** as a result of an increase in iodine permission for these products.

9. Public Consultation

FSANZ released for public consultation an Initial Assessment for A528 – Maximum Iodine Limits in Formulated Supplementary Foods for Young Children from 17 March 2004 to 28 April 2004. A total of seven submissions were received and are summarised in Attachment 5.

Five submissions supported amending Standard 2.9.3 to increase the permitted maximum level of iodine in FSFYC from 35 to 70 μg/serve and one did not support the proposed amendment. One submitter did not support either option stating it is difficult to make informed comments due to the absence of suitable data to assist decision-making.

FSANZ is now seeking further public comment on this Draft Assessment Report to assist in assessing this Application at Final Assessment.

9.1 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.

Amending the Code to allow an increase in the maximum permitted quantity of iodine in FSFYC, to accommodate levels of naturally occurring iodine in ingredients used to manufacture FSFYC, is unlikely to have a significant negative impact on trade. Therefore, notification will not be made to the WTO as a Technical Barrier to Trade (TBT) in accordance with the WTO agreements.

10. Conclusion and Recommendation

This Draft Assessment Report concludes that amending the Code to accommodate the natural variation of iodine in ingredients used to manufacture FSFYC does not pose a significant risk to public health and safety. Therefore it is recommended that Standard 2.9.3 be amended to increase the maximum permitted level of iodine in FSFYC from 35 to 70 μg per serving (Attachment 1) for the following reasons:

- the resultant increase in iodine status as a consequence of raising the maximum permitted quantity of iodine in FSFYC will not raise any safety concerns or cause any adverse nutritional risks in the target population;

- the proposed draft variation to the Code is consistent with the section 10 objectives of the FSANZ Act. Specifically, FSANZ has addressed the protection of public health and safety by undertaking a risk assessment using the best scientific data available;

- the proposed draft variation to the Code will increase compliance with the Code, reduce manufacturing costs, and prevent unnecessary trade barriers; and

- the regulation impact assessment concludes that the benefits from increasing the maximum permitted quantity of iodine in FSFYC outweigh any potential costs to affected parties.

If approved, the variation to the Code will come into effect on date of gazettal.

11. Implementation

Following the second consultation period for this Application, a Final Assessment Report will be prepared for consideration by the FSANZ Board. If Application A528 is approved by the FSANZ Board, notification will be made to the Ministerial Council and it is anticipated that the proposed draft variations to the Code will come into effect shortly thereafter upon gazettal, subject to any request from the Ministerial Council for a review.

A transition period is not required for the implementation of the proposed draft variations, as manufacturers will be able to continue with existing production and current stock will also be unaffected.

ATTACHMENTS

1. Draft variation to the *Australia New Zealand Food Standards Code*
2. Safety Assessment Report
3 Dietary Intake Assessment Report
4 Nutrition Assessment Report
5 Summary of Submissions

References

COMA, *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report of the Panel on Dietary Reference Values of the Committee on Medical Aspects of Food Policy*. London: The Stationary Office 1999

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) (2000). *Statement on Iodine in Milk.* COT Statement 2000/02, United Kingdom Food Standards Agency, http://www.foodstandards.gov.uk/science/surveillance/maffinfo/2000/maff-2000-198.

Department of Health. Food for Health. *Report of the New Zealand Nutrition Task Force.* Wellington. Department of Health, 1991

Dunn JT. (1998). What's happening to our iodine? *J Clin Endo Metabolism.* **83**: 3398-3400.

Eastman CJ. (1999). Where has all our iodine gone? *Med J Aus.t* **171**: 455-456.

European Scientific Committee on Food (SCF) (2002). *Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine*. European Commission, Brussels. SCF/CS/NUT/UPPLEV/26, http://europa.eu.int/comm/food/fs/sc/scf/out146_en.pdf

FAO/WHO (2002); *'Human Vitamin and Mineral Requirements: Report of a Joint FAO/WHO Expert Consultation Group'*; FAO/WHO, Bangkok; p181-194. www.micronutirent.org/idpas/pdf/846.12-CHAPTER12.pdf - as at January 2004.

Gibson R. (1990) *Assessment of iodine status. Principles of Nutrition Assessment*. New York:Oxford University Press, pages 527-532.

Gunton JE, Hams G, Fiegert M, McElduff A. (1999). Iodine deficiency in ambulatory patients at as Sydney teaching Hospital; Is Australia truly iodine replete? *Med J Aust.* **171**: 467-470.

Guttikonda K, Travers C, Lewis P, Boyages S. (2003). Iodine deficiency in urban primary school children: a cross-sectional analysis. *Med J Aust*. **179**: 346-348.

Li M, Ma G, Guttikonda K, Boyages S, Eastman C (2001). Re-emergence of iodine deficiency in Australia. *Asia Pacific J Clin Nutr.* **10**: 200-203.

McDonnell CM, Harris M, Zacharin MR. (2003). Iodine deficiency and goitre in school children in Melbourne, 2001. Med J Aust. **178**:159-162.

Ministry of Health 2003. *NZ food NZ children: key results of the 2002 National Children's Nutrition Survey*. Wellington: Ministry of Health.

Preiss U, aro Santos C, Spitzer A, Wallnofer PR. (1997). 'Iodine content of Bavarian consumer milk'. *Z Ernahrungswiss*, **36**:220-224 (In German).

Seal J (State Nutrition Officer). (2004). *Personal communication of raw data on the iodine content of milk*; Department of Health and Human Services, Tasmania.

Skeaff SA, Thomson CD, Gibson RS. (2002). Mild iodine deficiency in a sample of New Zealand schoolchildren. *Eur J Clin Nutr*. **56**: 1169-1175.

Stanbury JB. (1996). *Iodine deficiency and the iodine deficiency disorders, present knowledge in nutrition*, Seventh Edition ILSI press, Washington DC.

Thomson CD. (2002). *Australian and New Zealand Nutrient Reference Values for Iodine- Technical report for Ministry of Health*. University of Otago.

Thomson C. (2002). Australian *and New Zealand Nutrient Reference Values for Iodine, prepared for the New Zealand Ministry of Health*.

Truswell AS, Dreosti IE, English RM, Rutishauser IHE, Palmer N. (1990). *Recommended Nutrient Intakes. Australian Papers*. Sydney: Australian Professional Publications.

United Kingdom Food Standards Agency. (2000). *'MAFF UK – Iodine in Milk'*; http://www.foodstandards.gov.uk/science/surveillance/maffinfo/2000/maff-2000-198.

United States Board on Agriculture. (1988). *'Designing Foods: Animal Product Options in the Marketplace'*; National Academy Press, Washington D.C., p236; http://books.nap.edu/books/0309037956/html/236.html

Vannoort R, Cressey P, Silvers K. (2000). '*1997/98 New Zealand Total Diet Survey: Part 2 – Elements'*; New Zealand Ministry for Health, Wellington, http://www.nzfsa.govt.nz/science-technology/research-projects/total-diet-survey/index.htm.

ATTACHMENT 1

Draft Variation to the *Australia New Zealand Food Standards Code*

To commence: On gazettal

[1] ***Standard 2.9.3*** *of the Australia New Zealand Food Standards Code is varied by omitting the entry in* Column 2 *of* Table 3 of the Schedule *for* Iodine*, substituting –*

70 µg (100%)

ATTACHMENT 2

Safety Assessment

Application A528 – Maximum Iodine Limit in Formulated Supplementary Foods for Young Children.

Executive Summary

Iodine is an important trace element that is required for the synthesis of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). These hormones have a key role in influencing cellular metabolism and metabolic rate. The recommended daily intake for iodine for different population groups varies. For adults, the RDI ranges from 100-200 μg/day.

Although iodine is an essential component of the diet, intakes in excess of physiological requirements may produce adverse effects, particularly on the thyroid gland and the regulation of thyroid hormone production and secretion.

Diet is the major source of iodine intake for humans. The major food categories contributing to dietary intake include dairy products, seafood, fruits, vegetables and eggs, with meat and cereals being secondary sources. The iodine content of food is reflective of background levels in the environment as well as the use of iodine and its compounds in food production, processing and manufacturing. In addition to dietary sources, various mineral supplements and medical preparations can further add to iodine intake.

Greater than 97% of ingested iodine is absorbed from the gastrointestinal tract, generally as iodide. Absorbed iodide enters the circulation where it is taken up primarily by the thyroid gland. The uptake of iodide by the thyroid gland is controlled by the thyroid-stimulating hormone (TSH), which is highly sensitive to dietary iodine intake. At low intakes representing iodine deficiency, uptake of iodide into the thyroid gland is increased and at very high intakes, iodine uptake into the thyroid gland decreases. Once the physiological requirements for thyroid hormone synthesis have been met, the thyroid does not accumulate more iodine and any excess is excreted, primarily in the urine.

A large number of human experimental, clinical, and epidemiological studies on the effects of excess iodine on human health have been reported and reviewed in detail by both the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the US Agency for Toxic Substances and Disease Registry (ATSDR). These studies indicate that the primary effect of excess iodine is on the thyroid gland and regulation of thyroid hormone production and secretion, and it is these effects that are the focus of the report.

Excess iodine can produce an enlargement of the gland (goitre) and/or affect the production of the thyroid hormones. A diminished production of the thyroid hormones is referred to as hypothyroidism (and may be accompanied by goitre) and increased thyroid hormone synthesis and secretion by the thyroid gland is referred to as hyperthyroidism.

The effect on the thyroid depends on the current and previous iodine status of the individual and any current or previous thyroid dysfunction. For example, individuals with a history of iodine deficiency may be prone to the development of iodine-induced hyperthyroidism if iodine exposure increases later in life.

The human response to excess iodine can be quite variable. Some individuals can tolerate quite large intakes (up to 50 μg/kg/day) while others may respond adversely to levels close to recommended intakes (3-7 μg/kg/day). Individuals responding adversely to relatively low intake levels typically have an underlying thyroid disorder or have a long history of iodine deficiency.

For the majority of healthy individuals, the most sensitive endpoint for iodine toxicity is sub-clinical hypothyroidism. Sub-clinical hypothyroidism is defined as an elevation in TSH concentration while serum thyroid hormone concentration is maintained within the normal range of values for healthy individuals. While not clinically adverse, such an effect, if persistent, could lead to clinical hypothyroidism. In healthy adults, such an effect has been associated with acute intakes of 1700 μg/day (24 μg/kg body weight/day for a 71 kg person), and for children, has been associated with chronic intakes of 1150 μg/day (29 μg/kg/day for a 40 kg child).

Iodine intakes of approximately 1000 μg/day however appear to be well tolerated by healthy adults. This level has been used by JECFA to establish a provisional maximum tolerable daily intake (PTDI) for iodine of 17 μg/kg bw from all sources. Individuals with thyroid disorders or a long history of iodine deficiency, however, may respond adversely at levels of intake below the PTDI.

1. Introduction

Iodine is an important trace element that is essential for the maintenance of normal thyroid function where it is required for the synthesis of the thyroid hormones, L-triiodothyronine (T_3) and L-thyroxine (T_4) (also called 3,5,3', 5'- tetraiodothyronine). T_3 and T_4 are responsible for regulating cellular oxidation and hence have a key role in influencing cellular metabolism and metabolic rate.

The recommended daily intake (RDI) for iodine varies for individuals. The RDI for adults ranges from 100-150 μg/day, with intakes of 150-290 μg/day recommended for pregnant and lactating women. Intakes of 90 μg/day are recommended for young children.

Although iodine is an essential component of the diet, intakes in excess of physiological requirements may produce adverse effects, particularly on the thyroid gland and the regulation of thyroid hormone production and secretion. This in turn can have downstream impacts on a wide variety of other organ systems, producing an array of debilitating effects in the affected individual.

The purpose of this review is to examine the toxic effects associated with excess iodine and establish a safe level of exposure.

2. PHYSICAL AND CHEMICAL PROPERTIES

Iodine (I) is a non-metallic element belonging to the halogen family and has a molecular mass of 126.9. Iodine is a bluish-black, lustrous solid, which sublimes at room temperature into a blue-violet gas with a sharp characteristic odour. Iodine dissolves readily in alcohol, benzene, chloroform, carbon tetrachloride, ether or carbon disulfide but is only slightly soluble in water (0.03 g/100 ml at 20˚C).

The chemistry of iodine can be quite complex as it can exist in a number of different valence states, is chemically reactive (although less so than other halogens) and forms various organic and inorganic compounds. The most common compounds formed are the iodides (I^-) and iodates (IO_3^-).

Thirty-six isotopes are recognized with fourteen of these yielding significant radiation. The only naturally occurring isotopes are ^{127}I, which is stable, and ^{129}I, which is radioactive. This report will concentrate on toxic effects associated with stable iodine.

3. Sources

The oceans are considered to be the most importance source of natural iodine. Iodine in seawater enters the air via aerosols or as a gas and from there is deposited onto soil, surface water and vegetation.

Diet is regarded as the major source of iodine intake for the population (WHO 1989). Major food categories contributing to dietary intake in Australia and New Zealand include dairy products, seafood (marine fish, shellfish, algae and seaweed), fruits, vegetables and eggs, with meat and cereals being secondary sources.

Additional sources of intake come from the use of iodine and its compounds in a variety of food-related applications including nutrient fortification (e.g., iodised salt), food additives (e.g., dough conditioning and maturing agents), agricultural chemicals (e.g., herbicides and fungicides), animal drugs (e.g., iodine supplements), and sanitisers (e.g., iodophors).

The iodine content of foods is thus both reflective of background levels in the environment as well as processing technology and manufacturing practices. For example, the high iodine content of milk and dairy products has been attributed to the use of iodine-containing supplements in feed for dairy cattle, iodophore-based medications, teat dips and udder washes as well as iodophors used as sanitising agents in dairy processing establishments. The use of iodophors by the dairy industry has however become less commonplace, resulting in milk becoming a less important source of dietary iodine (Eastman 1999).

In addition to dietary sources, various mineral supplements and medical preparations can further increase iodine intake to a significant extent (WHO 1989).

5. TOXICOKINETICS

5.1 Absorption

Inorganic iodine is >97% absorbed from the gastrointestinal tract, generally as iodide. Although some absorption occurs in the stomach, the small intestine appears to be the principal site of absorption in both humans and rats (Riggs 1952, Small et al 1961). The mechanism by which iodide is transported across the intestinal epithelium is not known. Gastrointestinal absorption appears to be similar in children, adolescents and adults, although absorption in infants may be lower than in children and adults (ATSDR 2001).

5.2 Distribution

Once absorbed, iodide enters the circulation and is distributed throughout the extracellular fluid where it is taken up by those tissues with specialized transport mechanisms for iodide (Cavalieri 1980). The human body contains about 10 – 15 g iodine in total, the majority of which (>90 %) is stored by the thyroid gland (Cavalieri 1997). The concentration of iodine in serum is about 50 – 100 µg/L under normal circumstances, with about 5% being in the inorganic form as iodide and the remaining 95% consisting of various organic forms of iodine, principally protein complexes of the thyroid hormones.

Other tissues that accumulate iodide include the salivary glands, gastric mucosa, choroid plexus, mammary glands, placenta, and sweat glands. The tissue distribution of iodide and organic iodine are very different and are interrelated by metabolic pathways that lead to the iodination and de-iodination of proteins and thyroid hormones.

The uptake of iodide by the thyroid gland is controlled by the thyroid-stimulating hormone (TSH), which is secreted from the anterior lobe of the pituitary gland. In addition to stimulating iodide transport from the blood into thyroid cells, TSH is also responsible for stimulating the oxidation of iodide to iodine, and iodine binding to tyrosine.

Iodide taken up by the thyroid gland is used for the production of the thyroid hormones, which are stored in the gland. Approximately 90% of the thyroid iodine content is in the organic form and includes iodinated tyrosine residues comprising the thyroid hormones T_4 and T_3, and their various synthesis intermediates and degradation products. Once requirements for thyroid hormone synthesis have been met, the thyroid does not accumulate more iodine and any excess is excreted in the urine (Bender and Bender 1997).

Iodide uptake into the thyroid gland is highly sensitive to iodide intake. At low intakes representing iodine deficiency, uptake of iodide into the thyroid gland is increased (Delange and Ermans 1996). At very high intakes, iodide uptake into the thyroid gland decreases, primarily as a result of decreased iodothyronine synthesis (the Wolff-Chaikoff effect) and iodide transport into the gland (Nagataki and Yokoyama 1996, Saller 1998).

5.3 Metabolism

Once in the thyroid, iodide is oxidised to elemental iodine by the enzyme thyroid peroxidase (Saller 1998). This reaction is the rate-limiting step for protein iodination and hormone synthesis. Once oxidised, iodine enters the biosynthetic pathway for thyroid hormone synthesis. Initially, iodine is incorporated into monoiodotyrosine and diiodotyrosine, which are then coupled together to form the thyroid hormones T_3 (coupling of a monoiodotyrosine and diiodotyrosine residue) and T_4 (coupling of two diiodotyrosine residues). These reactions occur within a large glycoprotein called thyroglobulin, which is synthesized only in the thyroid gland.

TSH regulates every step in the biosynthesis of the thyroid hormones, from the concentration of iodide to the proteolysis of thyroglobulin (Cavalieri 1980). There is a sensitive feedback mechanism between the thyroid and the pituitary gland to maintain the levels of thyroid hormones. This is influenced by the hypothalamus, with thyrotrophin-releasing hormone mediating the secretion of TSH from the pituitary.

Deiodination reactions are carried out by a family of selenoproteins. Iodotyrosine dehalogenase regenerates iodide from monoiodotyrosine and diiodotyrosine for re-use within the thyroid or release into blood, accounting for the iodide leak in the state of chronic iodine excess or certain thyroid conditions (Cavalieri 1997). The liver contains a considerable amount of T_4, some of which is converted into T_3 and some which is excreted into the bile and ultimately reabsorbed or excreted (Cavalieri 1980).

5.4 Excretion

All absorbed iodine is excreted primarily in the urine and faeces, but is also excreted in breast milk, exhaled air, sweat and tears (Cavalieri 1997). Urinary excretion normally accounts for 97% of the elimination of absorbed iodine, while faecal excretion accounts for about 1-2% (Larsen et al 1998). The fraction of the absorbed iodide dose excreted in breast milk varies with functional status of the thyroid gland. A larger fraction of the absorbed dose is excreted in breast milk in the hypothyroid state compared to the hyperthyroid state. In the hypothyroid state, uptake of absorbed iodide into the thyroid gland is depressed, resulting in greater availability of the absorbed iodide for distribution to the mammary gland and breast milk.

6. TOXICITY OF IODINE

A large number of human experimental, clinical, and epidemiological studies on the effects of excess iodine on human health have been reported. These studies will not be reviewed again in detail as they have already been subject to significant reviews by both the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (WHO 1989) and the Agency for Toxic Substances and Disease Registry (ATSDR 2001).

JECFA concluded there are three potential types of adverse response to excess iodine. The first is disturbance of thyroid activity, which may alter the size of the gland and/or affect the production of thyroid hormones. There is also evidence to indicate that iodine (or the lack of it) may alter the pattern of thyroid malignancy. The second type of response involves sensitivity reactions, and the third type of response results from acute intakes of large quantities of iodine (iodine poisoning).

This review will largely focus on effects on the thyroid gland, which is regarded as the primary and most sensitive indicator of iodine toxicity (ATSDR 2001).

6.1 Disturbance of Thyroid Function

The primary effects of excessive iodine ingestion are on the thyroid gland and regulation of thyroid hormone production and secretion. Adverse effects on the pituitary and adrenal glands are secondary to disorders of the thyroid gland.

Excess iodine can result in goitre, hypothyroidism (with or without goitre), or hyperthyroidism (thyrotoxicosis) (see below). The effect produced depends on the current and previous iodine status of the individual and any current or previous thyroid dysfunction (WHO 1989). For example, individuals exposed to low levels of iodine early in life may be prone to the development of iodine-induced hyperthyroidism if iodine exposure increases later in life. Those with underlying thyroid disease also respond more to increased iodine intake, and it also appears that females are more likely to respond to excess iodine than males.

Definitions

Goitre refers to an enlargement of the thyroid gland that is usually visible as a swelling in the anterior portion of the neck. A number of different types of goitres are known to occur.

Simple or *non-toxic goitre* is an enlargement of the thyroid gland that is not associated with overproduction of thyroid hormone, inflammation or malignancy, whereas *toxic goitre* is one involving excessive production of thyroid hormone. Thyroid enlargement can be uniform (diffuse goitre) or the gland can become enlarged as a result of the occurrence of one or more nodules (nodular goitre).

The two most common causes of simple or non-toxic goitre are iodine deficiency (referred to as endemic goitre) or the ingestion of large quantities of goitrogenic foods or drugs. In these cases, the thyroid gland is unable to meet the demands of the body (i.e., because of an inadequate supply of iodine) and enlarges to compensate. Enlargement of the gland is usually sufficient to overcome the mild impairment to hormone production.

Goitre can also be associated with both hypothyroidism and hyperthyroidism. *Hypothyroidism* refers to the diminished production of thyroid hormone leading to clinical manifestations of thyroid insufficiency and can occur with or without goitre. Typical biomarkers of hypothyroidism are a depression in the circulating levels of T_4 and/or T_3 below their normal ranges. This is usually, but not always, accompanied by an elevation of TSH above the normal range. The most common cause of hypothyroidism is Hashimoto's disease (or lymphocytic thyroiditis). Hashimoto's disease is an autoimmune disease in which abnormal antibodies are produced that impair the ability of the thyroid to produce thyroid hormone. The pituitary gland responds by producing TSH and the additional TSH may cause the thyroid gland to enlarge.

Hyperthyroidism is where accelerated thyroid hormone biosynthesis and secretion by the thyroid gland produce thyrotoxicosis. The term *thyrotoxicosis* refers to the hypermetabolic clinical syndrome resulting from serum elevations in thyroid hormone levels, specifically free thyroxine (T_4), triiodothyronine (T_3), or both. The terms hyperthyroidism and thyrotoxicosis are often used interchangeably but are not synonymous. That is, while many patients have thyrotoxicosis caused by hyperthyroidism, other patients may have thyrotoxicosis caused by inflammation of the thyroid gland, which causes release of stored thyroid hormone but not accelerated synthesis, or thyrotoxicosis, which is caused by ingestion of exogenous thyroid hormone.

The most common cause of hyperthyroidism is Graves' disease (diffuse toxic goitre), an autoimmune disease where the immune system produces antibodies that stimulate the TSH receptors of the thyroid gland resulting in the non-suppressible overproduction of thyroid hormone. This causes the thyroid gland to become enlarged. In the elderly, a condition called toxic nodular goitre may cause hyperthyroidism. Toxic nodular goitre occurs when one or more small benign tumours in the thyroid gland produce excess thyroid hormones.

6.1.1 Iodine-Induced Hypothyroidism

The human body has a number of adaptive mechanisms for dealing with excess iodine. These mechanisms tend to be inhibitory in nature and generally do not significantly affect thyroid function.

The most well known of these is the *Wolff-Chaikoff effect* (Wolff et al 1949), where large dietary or therapeutic intakes of iodine can inhibit organic iodine formation (the binding of iodine to tyrosine in the thyroid), producing a decrease in the circulating thyroid hormone levels, and a subsequent increase in TSH. The effect is typically transient, even if the excess intake continues, with most people being able to escape from the inhibition without a clinically significant change to circulating hormone levels. Most individuals are therefore able to adapt to excess iodine.

Some individuals who fail to escape from the Wolff-Chaikoff effect typically develop goitre and may also become hypothyroid. Susceptible individuals include: foetuses and newborn infants; patients who have autoimmune thyroiditis; patients with Grave's disease previously treated with iodine; women who have post-partum thyroiditis; or those who have subacute thyroiditis. Iodine-induced hypothyroidism is also reported to be more common in women.

Excessive intake of iodine by pregnant women is of particular concern as the foetal thyroid is less able to escape the inhibitory effects of iodine on thyroid hormone formation. Iodine-induced goitres and/or hypothyroidism have occurred in newborn infants of mothers who have taken iodine during pregnancy. Infant goitres may regress spontaneously after several months, but deaths due to compression of the trachea have occurred (WHO 1989).

A number of studies have examined the acute effects of increased intakes of iodine on the thyroid hormone status of adults (Chow et al 1991, Gardner et al 1988, Georgitis et al 1993, Namba et al 1993, Paul et al 1988, Robison et al 1998). These studies suggest that acute (14 days) iodine exposures of 1500 μg/day (21 μg/kg/day) above the pre-existing dietary intake can be tolerated without producing a clinically adverse change in thyroid hormone levels, although such doses may produce a reversible depression in serum T_4 concentration and an elevation in serum TSH concentration, both within the normal range of values for healthy individuals. Changes in thyroid hormone levels within normal ranges are not considered to be clinically adverse; however, they are indicative of a suppressing effect on thyroid hormone production that, if persistent, could result in thyroid gland enlargement and other clinically significant complications. In the case of elderly adults, subclinical hypothyroidism has been induced by an acute increase of 500 μg/day (7 μg/kg/day) (Chow et al 1991), possibly suggesting that the elderly may be less tolerant of excess iodide than younger adults. Based on estimates of the background dietary intakes of the subjects in these studies, in most cases estimated from measurements of urinary iodide excretion, the total iodide intakes producing subclinical hypothyroidism in healthy adults were approximately 1700 μg/day (24 μg/kg/day) (Gardner et al 1988, Paul et al 1988).

Acute intakes of approximately 700 μg/day (10 μg/kg/day) had no detectable effect on thyroid hormone status in healthy individuals. One study also found no evidence of disturbances in thyroid hormone status in 6 healthy euthyroid males who received doses of 20 mg/day (0.3 mg/kg/day) (Robison et al 1998), suggesting that, at least under certain conditions, exposure levels >10-24 μg/kg/day may be tolerated by some individuals.

The level of 1700 μg/day for subclinical hypothyroidism has been used by the Institute of Medicine as a lowest-observable-adverse-effect level (LOAEL) to which an uncertainty factor of 1.5 was applied to derive a Tolerable Upper Intake Level (UL) for iodine in adults of 1100 μg/day (Institute of Medicine 2001). By adjusting this level on the basis of bodyweight, the ULs for other age groups were derived. Thus, a UL of 900 μg/day was established for 14-18 year olds, 600 μg/day for 9-13 year olds, 300 μg/day for 4-8 year olds, and 200 μg/day for 1-3 year olds.

Two studies have been conducted in prison populations exposed to iodine through iodination of the water supply. In a study by Freund et al (1966), the health and thyroid function of representative subjects of a prison population were assessed before and during usage of iodinated water for nine months. Water containing 1000 μg/L iodine induced a marked decrease in the uptake of radioactive iodine but protein bound iodine levels did not increase significantly until the iodine concentration was increased to 5000 μg/L. No information on actual intake is provided but it has been assumed that water consumption would have been about 1-2 litres/day (WHO 1989). In another study, iodination of a prison water supply at a concentration of 500 to 750 μg/L (estimated intake 1000-2000 μg/day) for up to 15 years did not result in any change to serum T_4 levels (Thomas et al 1978). During the same period, 177 women in the prison gave birth to 181 full term infants without any enlargement of the thyroid being noted in the infants (Stockton & Thomas 1978). On the basis of these studies, which indicate that 1000 μg iodine/day is safe for the majority of the population, JECFA set a provisional maximum tolerable daily intake (PTDI) of 17 μg/kg bodyweight for iodine from all sources (WHO 1989).

Results from a number of epidemiological studies (Li et al 1987; Laurberg et al 1998) suggest that chronic exposure to excess iodine can result in or contribute to subclinical hypothyroidism in children (1150 μg/day, 29 μg/kg/day) and elderly adults (160-800 μg/day, 4-12 μg/kg/day). The study in children compared thyroid status in groups of children, aged 7-15 years, who resided in two areas of China with different drinking water iodine concentrations, providing estimated iodine intakes of 29 and 10 μg/kg/day. Both groups were all euthyroid[15] with normal values for serum thyroid hormones and TSH concentrations, although TSH concentrations were significantly higher in the high iodine group. This study was used by the ATSDR to establish a chronic-duration minimal risk level (MRL) for iodine of 10 μg/kg/day based on a no-observed-adverse-effect level (NOAEL) of 10 μg/kg/day and a LOAEL of 29 μg/kg/day for subclinical hypothyroidism in healthy human children (ATSDR 2001).

[15] Where TSH levels are in the normal range and the thyroid is neither hypothyroid nor hyperthyroid and considered "normal".

Populations that are iodine deficient and, in particular, those that include people exhibiting goitre, appear to be particularly sensitive to an increase in their iodine intake. For example, iodine supplementation (200-400 µg/day, 3-6 µg/kg/day) for treatment of endemic goitre has been associated with thyroid dysfunction, including thyroid autoimmunity (Kahaly et al 1997, Kahaly et al 1998).

Very high doses of iodine exceeding 200 mg/day (2.8 mg/kg/day) given during pregnancy have been shown to result in congenital goitre and hypothyroidism in the newborn infant (Iancu et al 1974). Such doses, however, are atypical and clinical experience with lower doses of iodine supplementation given during pregnancy for the purpose of correcting or preventing iodine deficiency and for the management of Grave's disease indicates that oral doses of 4-5 µg/kg/day can be tolerated without any indication of thyroid dysfunction in the newborn (Momotani et al 1992, Pedersen et al 1993, Liesenkötter et al 1996).

6.1.3 Iodine-Induced Hyperthyroidism (Thyrotoxicosis)

Oral exposure to excess iodine can, under certain circumstances, lead to hyperthyroidism. This condition is referred to as "jodbasedow" although it is not thought to be a single aetiological entity (Fradkin and Wolff 1983). The occurrence of iodine-induced hyperthyroidism is most common in iodine deficient populations following the introduction of iodine supplementation programs. The most vulnerable are those over 40 years of age who have been iodine deficient since birth. Other vulnerable groups include those with thyroid diseases such as Graves' disease or postpartum thyroiditis.

The clinical features of iodine-induced hyperthyroidism are said to be similar to that of Graves' disease, however, in contrast to the diffuse goitres associated with Grave's disease, iodine-induced hyperthyroidism is generally associated with nodular goitres. Nodular goitres are fairly common in elderly subjects and are the result of longstanding iodine deficiency. Many of these nodules are autonomous, meaning they are independent of regulation by TSH and produce thyroid hormone in direct response to dietary iodine. Thus excess iodine may precipitate or aggravate hyperthyroidism in these subjects.

Frequently, iodine-induced hyperthyroidism is mild and follows a self-limited course, but in some cases it is more severe and can sometimes be lethal. Iodine-induced hyperthyroidism can be totally prevented in the next and subsequent generations by correction of iodine deficiency.

A number of epidemiological studies have been conducted in Europe and Africa to monitor the incidence of iodine-induced hyperthyroidism in iodine deficient populations following the introduction of iodine supplementation programs (DeLange et al 1999, Mostbeck et al 1998, Lind et al 1998, Stanbury et al 1998). These studies confirm that iodine supplementation of iodine deficient diets does result in a detectable increase in the incidence of hyperthyroidism. A well-documented case also occurred in Tasmania, Australia, following the introduction of iodised bread in 1966 and the addition of iodophors to milk by the dairy industry (Connolly et al 1970). Milk iodine (from the seasonal use of feed supplements) has also been a factor in Europe (Barker and Phillips 1984, Phillips 1983). A review of these studies indicates that iodine intakes in the range of 3-7 µg/kg/day may be sufficient to produce an increase in hyperthyroidism in iodine deficient populations (ATSDR 2001).

In the Tasmanian case, a 2- to 4-fold increase in hyperthyroidism occurred within a few months after diets were supplemented with iodide for the prevention of endemic goitre from iodine deficiency (Connolly et al 1970). The supplemental dose was 80-200 μg/day from the addition of potassium iodate to bread, but mean urinary iodide excretion rates suggested a total post-supplementation iodide intake of about 230 μg/day (range 94-398), equivalent to 3.3 μg/kg/day, some of which came from other sources such as milk (Connolly 1971a, 1971b).

The highest incidence of hyperthyroidism after the iodine supplementation began occurred in people over 40 years of age (Stewart 1975, Stewart and Vidor 1976). Stewart (1975) noted that the small increase in the incidence of hyperthyroidism that occurred in people under 40 years of age was largely due to Graves' disease.

Cases of iodine-induced hyperthyroidism in people who were euthyroid and without apparent thyroid disease have been reported (Rajatanavin et al 1984, Savoie et al 1975, Shilo and Hirsch 1986), however only a few have provided dose information. In these cases, effects were observed following doses in the range 0.05 – 23 mg/kg/day.

6.1.3 Thyroid malignancy

Several large-scale epidemiological studies have examined the relationship between iodine intake and thyroid cancer. The results of these studies suggest that an increased iodine intake may be a risk factor for thyroid cancer in certain populations, namely, populations residing in iodine deficient, endemic goitre regions (Franceschi 1998, Franceschi and Dal Maso 1999). Not all of these studies have found an increased risk of cancer, however, a recurrent observation is an apparent shift in the histopathology towards a higher prevalence of papillary cancers, relative to follicular cancers, after increased iodine intake in otherwise iodine-deficient populations (Bakiri et al 1998, Belfiore et al 1987, Kolonel et al 1990, Petterson et al 1991, 1996). Two studies in particular found a significant excess of thyroid gland cancer in populations from endemic goitre regions whose diets had been supplemented to achieve approximate iodine intakes of 3.5 μg/kg bw/day (Bacher-Stier et al 1997, Harach and Williams 1995).

6.2 Sensitivity Reactions

Oral exposure to excess iodine can produce allergic or sensitivity reactions in certain individuals. The reactions include urticaria (hives), acneiform skin lesions (ioderma), and fevers. Cases of more serious reactions involve angioedema (localised oedema), vasculitis, peritonitis and pneumonitis, and complement activation. Both humoral and cell-mediated immune responses are thought to be involved (Curd et al 1979, Rosenburg et al 1972, Stone 1985). In general, reactions to iodide have occurred in association with repeated oral doses of iodide exceeding 300 mg/day.

Ioderma is thought to be a form of cell-mediated hypersensitivity (Rosenburg et al 1972, Stone 1985) and its occurrence appears to be unrelated to thyroid gland function. Characteristic symptoms include acneiform pustules, which can coalesce to form vegetative nodular lesions on the face, extremities, trunk, and mucous membranes. The lesions regress and heal when the excess iodide intake is discontinued. The literature reports cases of ioderma occurring following oral doses of iodide 300-1000 mg/day.

However, in many of these cases, pre-existing disease and related drug therapy may have contributed to the reaction to iodide; thus the dose-response relationship for ioderma in healthy people remains highly uncertain.

Oral exposures to iodide > 1000 mg/day have been associated with the occurrence of fevers, which cease once exposure to the excessive iodide intake is discontinued (Kurtz and Aber 1982, Horn and Kabins 1972). The fevers are thought to have an immunological basis and do not appear to be related to thyroid gland function. Reported clinical cases have almost always involved a pre-existing disease, usually pneumonia or obstructive lung disease in which potassium iodide was administered along with other drugs, such as antibiotics, barbiturates and methylxanthines.

6.3 Iodine Poisoning

The effects from acute exposure to high iodine concentrations are largely due to the strong oxidising effect of iodine on the gastrointestinal tract and resultant shock. It is these properties of iodine that make it effective as a topical antiseptic and antimicrobial disinfectant.

Cases of iodine poisoning are rare however and are typically associated with intakes of many grams. Symptoms observed in lethal or near-lethal poisonings have included abdominal cramps, bloody diarrhoea and gastrointestinal ulcerations, oedema of the face and neck, pneumonitis, haemolytic anaemia, metabolic acidosis, fatty degeneration of the liver, and renal failure (Clark 1981, Dyck et al 1979, Finkelstein and Jacobi 1937, Tresch et al 1974). Death has occurred from 30 minutes to 52 days after ingestion, although death generally occurs within 48 hours. Where the dose was known, it ranged from 1.1 to 9 g iodine (18-150 mg/kg for a 60 kg adult), although there is a single case report of a 54-year-old male surviving the accidental ingestion of 15 g iodine (Tresch et al 1974).

7. SAFE LIMITS FOR ORAL INTAKE

A number of safe intake levels have been recommended as a result of reviews on the toxicity of excess iodine. The highest level of intake that has been found to be safe for the majority of the population is about 1000 µg iodine/day. This level was used by JECFA to establish a PTDI for iodine of 17 µg/kg bw from all sources (WHO 1989). Individuals with thyroid disorders or a long history of iodine deficiency, however, may respond adversely at levels of intake below the PTDI.

References

ATSDR (2001). Draft toxicological profile for iodine. U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry, Atlanta, GA. http://www.atsdr.cdc.gov/

Bacher-Stier, C., Riccabona, G., Totsch, M. et al (1997). Incidence and clinical characteristics of thyroid carcinoma after iodine prophylaxis in an endemic goiter country. Thyroid 7: 733 – 741.

Bakiri, F., Djemli, F.K., Mokrane, L.A. et al (1998). The relative roles of endemic goiter and socioeconomic developmental status in the prognosis of thyroid carcinoma. *Cancer* **82:** 1146 – 1153.

Barker, D.J.P. and Phillips, D.I.W. (1984). Current incidence of thyrotoxicosis and past prevalence of goitre in 12 British towns. *Lancet* **2:** 567 – 570.

Belfiore, A., La Rosa, G.L., Padova, G. et al (1987). The frequency of cold thyroid nodules and thyroid malignancies in patients from an iodine-deficient area. *Cancer* **60:** 3096 – 3102.

Bender, D.A. & Bender, A.E. (1997). *Nutrition, a Reference Handbook*. Oxford University Press.

Cavalieri, R.R. (1980). Trace elements: iodine. In: *Modern Nutrition in Health and Disease, 6th Edition* (Ed: Goodhardt, R.S). Lea and Febriger. Philadelphia, U.S. pp 395 – 407.

Cavalieri, R.R. (1997). Iodine metabolism and thyroid physiology: current concepts. *Thyroid* **7:** 177 – 181.

Chow, C.C., Phillips, D.I.W. Lazarus, J.H. et al (1991). Effect of low dose iodide supplementation on thyroid function in potentially susceptible subjects: Are dietary iodide levels in Britain acceptable? *Clin. Endocrinol.* **34:** 413 – 416.

Clark, M.N. (1981). A fatal case of iodine poisoning. *Clin. Toxicol*. **18:** 807 – 811.

Connolly, R.J., Vidor, G.I. and Stewart, J.C. (1970). Increase in thyrotoxicosis in endemic goiter area after iodation of bread. *Lancet* **1:** 500 – 502.

Connolly, R.J. (1971a). An increase in thyrotoxicosis in southern Tasmania after an increase in dietary iodine. *Med. J. Aust.* **1:** 1268 – 1271.

Connolly, R.J. (1971b). The changing iodine environment of Tasmania. *Med. J. Aust*. **2:** 1191 – 1193.

Curd, J.G., Milgrom, H., Stevenson, D.D. et al (1979). Potassium iodide sensitivity in four patients with hypocomplementemic vasculitis. *Ann. Intern. Med*. **91:** 853 – 857.

DeLange, F.M. and Ermans, A-M. (1996). Iodine deficiency. In: *Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text* (Eds: Braverman, L.E. & Utiger R.D). Lippincott-Raven, Philadelphia, PA, pp 296 – 316.

DeLange, F., de Benoist, B. and Alnwick, D., (1999). Risks of iodine-induced hyperthyroidism after correction of iodine deficiency by iodized salt. *Thyroid* **9:** 545 – 556.

Dyck, R.F., Bear, R.A., Goldstein, M.B. et al (1979). Iodine/iodide toxic reaction: Case report with emphasis on the nature of metabolic acidosis. *Can. Med. Assoc. J*. **120:** 704 – 706.

Eastman, C.J. (1999). Where has all our iodine gone? *Med. J. Aust*. **171:** 455-456.

Finkelstein, J. and Jacobi, M. (1937). Fatal iodine poisoning: A clinico-pathologic and experimental study. *Adv. Intern. Med*. **60:** 1283 – 1296.

Fradkin, J.E. and Wolff, J. (1983). Iodide-induced thyrotoxicosis. *Medicine* **62:** 1 – 20.

Franceschi, S (1998). Iodine intake and thyroid carcinoma – a potential risk factor. *Exp. Clin. Endocrinol. Diabetes* **106 (Suppl):** S38- S44.

Franceschi, S. and Dal Maso, L. (1999). Hormonal imbalances and thyroid cancers in humans. In: Species Differences in Thyroid, Kidney and Urinary Bladder Carcinogenesis (Eds: Capen, C.C., Dybing, E., Rice, J.M. et al). Lyon, France, International Agency for Research on Cancer, pp 33 – 43.

Freund, G., Thomas Jr, W.C., Bird, E.D., Kinman, R.N. and Black, A.P. (1966). Effect of iodinated water supplies on thyroid function. *J. Clin. Endocr*. **26:** 619 – 624.

Gardner, D.F., Centor, R.M. and Utiger, R.D. (1988). Effects of low dose oral iodide supplementation on thyroid function in normal men. *Clin. Endocrinol.* **28:** 283 – 288.

Georgitis, W.J., McDermott, M.T. and Kidd, G.S. (1993). An iodine load from water purification tablets alters thyroid function in humans. *Mil. Med*. **158:** 794 – 797.

Harach, H.R. and Williams, E.D. (1995). Thyroid cancer and thyroiditis in the goitrous region of Salta, Argentina before and after iodine prophylaxis. *Clin. Endocrinol*. **43:** 701 – 706.

Horn, B and Kabins, S.A. (1972). Iodide fever. *Am. J. Med. Sci*. **264:** 467 – 471.

Iancu, T., Boyanower, Y. and Laurian, N. (1974). Congenital goiter due to maternal ingestion of iodide. *Am. J. Dis. Child* **128:** 528 – 530.

Institute of Medicine (2001). *Dietary reference intakes: vitamin A, K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc*. A Report of the Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and of Interpretation and Use of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. National Academy Press, Washington DC.

Kahaly, G., Dienes, H.P., Beyer, J. et al (1997). Randomized, double blind, placebo-controlled trial of low dose iodide in endemic goiter. *J. Clin. Endocr. Metab*. **82:** 4049 – 4053.

Kahaly, G., Dienes, H.P., Beyer, J. et al (1998). Iodide induced thyroid autoimmunity in patients with endemic goiter: A randomized, double blind, placebo-controlled trial. *Eur. J. Endocrinol*. **139:** 290 – 297.

Larsen, P.R., Davies, T.F. and Hay, I.D. (1998). The thyroid gland. In: *William's Textbook of Endocrinology* (Eds: Wilson, J.D., Foster, D.W. and Kronenberg, H.M), Philadelphia, PA, W.B. Saunders Company, pp 390-515.

Kolonel, L.N., Hankin, J.H., Wilkins, L.R. et al (1990). An epidemiologic study of thyroid cancer in Hawaii. *Cancer Causes Control* **1:** 223 – 234.

Kurtz, S.C. and Aber, R.C. (1982). Potassium iodide as a cause of prolonged fever. *Arch. Intern. Med*. **142:** 1543 – 1544.

Laurberg, P., Pedersen, K.M., Hreidarsson, A. et al (1998). Iodine intake and the pattern of thyroid disorders: A comparative epidemiological study of thyroid abnormalities in the elderly in Iceland and in Jutland, Denmark. *J. Clin. Endocr. Metab.* **83:** 765 – 769.

Li, W., Qu, C, Jia, G. et al (1987). Endemic goiter in Central China caused by excessive iodine intake. *Lancet* **1:** 257 – 258.

Liesenkötter, K.P., Gopel, W., Bogner, U. et al (1996). Earliest prevention of endemic goitre by iodine supplementation during pregnancy. *Eur. J. Endocrinol.* **134:** 443 – 448.

Lind, P., Langsteger, W., Molnar, M., Gallowitsch, H.J., Mikosch, P. and Gomez, I. (1998). Epidemiology of thyroid diseases in iodine sufficiency. *Thyroid* **8:** 1179 – 1183.

Momotani, N., Hisaoka, T., Noh, J. et al (1992). Effects of iodine on thyroid status of foetus versus mother in treatment of Graves' disease complicated by pregnancy. *J. Clin. Endocrinol. Metab*. **75:** 738 – 744.

Mostbeck, A., Galvan, G., Bauer, P et al (1998). The incidence of hyperthyroidism in Austria from 1987 to 1995 before and after an increase in salt iodization in 1990. *Eur. J. Nucl. Med*. **25:** 367 – 374.

Nagataki, S. and Yokoyama, N. (1996). Other factors regulating thyroid function: autoregulation: effects of iodide. In: *Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text* (Eds: Braverman, L.E. & Utiger R.D). Lippincott-Raven, Philadelphia, PA, pp 241-247.

Namba, H., Yamashita, S., Kimura, H. et al (1993). Evidence of thyroid volume increase in normal subjects receiving excess iodide. *J. Clin. Endocrinol. Metab.* **76:** 605 – 608.

Paul, T., Meyers, B., Witorsch, R.J., Pino, S., Chipkin, S., Ingbar, S.H. and Braverman, L.E. (1988). The effect of small increases in dietary iodine on thyroid function in euthyroid subjects. *Metabolism* **37:** 121 – 124.

Pedersen, K.M., Laurberg, P., Iverson, E. et al (1993). Amelioration of some pregnancy-associated variations in thyroid function by iodine supplementation. *J. Clin. Endocrinol. Metab.* **77:** 1078 – 1083.

Petterson, B, Adami H-O., Wilander, E. et al (1991). Trends in thyroid cancer incidence in Sweden, 1958-1981, by histopathologic type. *Indian J Cancer* 48**:** 28 – 33.

Petterson, B., Coleman, M.P., Ron, E. et al (1996). Iodine supplementation in Sweden and regional trends in thyroid cancer incidence by histopathologic type. Indian J Cancer **65:** 13 – 19.

Phillips, D.I.W., Barker, D.J.P., Winter, P.D. and Osmond, C. (1983). Mortality from thyrotoxicosis in England and Wales and its association with the previous prevalence of endemic goitre. *J. Epidemiol. Community Health* **37:** 305 – 309.

Rajatanavin, R., Safran, M., Stoller, W.A., Mordes, J.P. and Braverman, L.E. (1984). Five patients with iodine-induced hyperthyroidism. *Am. J. Med*. **77:** 378 – 384.

Riggs, D.S. (1952). Quantitative aspects of iodine metabolism in man. *Pharmacol. Rev*. **4:** 284 – 370.

Robison, L.M., Sylvester, P.W., Birkenfeld, P. et al (1998). Comparison of the effects of iodine and iodide on thyroid function in humans. J. Toxicol. Environ. Health 55: 93 – 106.

Rosenburg, F.R., Einbinder, J., Walzer, R.A. et al (1972). Vegetating iododerma. *Arch. Dermatol*. **105:** 900 – 905.

Saller, B. (1998). Kinetics of acute and chronic iodine excess. *Exp. Clin. Endocrinol. Diabetes* **106 (Suppl):** S34 – S38.

Savoie, J.C., Massin, J.P., Thomopoulos, P. et al (1975). Iodine-induced thyrotoxicosis in apparently normal thyroid glands. *J. Clin. Endocr. Metab*. **41:** 685 – 691.

Shilo, S and Hirsch, H.J. (1986). Iodine-induced thyrotoxicosis in a patient with a normal thyroid gland. *Postgrad. Med. J*. **62:** 661 – 662.

Small, M.D., Bezman, A., Longarni, A.E., et al (1961). Absorption of potassium iodide from gastro-intestinal tract. *Proc. Soc. Exp. Biol. Med*. **106:** 450 – 452.

Stanbury, J.B., Ermans, A.B., Bourdoux, P. et al (1998). Iodine-induced hyperthyroidism: Occurrence and epidemiology. *Thyroid* **8:** 83 – 100.

Stewart, J.C. (1975). Epidemiology and pathogenesis of iodine-induced thyrotoxicosis in Northern Tasmania. *N.Z. Med. J*. **81:** 25 – 26.

Stewart, J.C. and Vidor, G.I. (1976). Thyrotoxicosis induced by iodine contamination of food: a common unrecognized condition? *Br. Med. J.* **1:** 372 – 375.

Stockton, L.K. and Thomas Jr, W.C. (1978). Absence of neonatal goiter during maternal use of iodinated water. *Clin. Res*. **26:** 586A.

Stone, O.J. (1985). Proliferative iododerma: A possible mechanism. *Int. J. Dermatol*. **24:** 565 – 566.

Thomas Jr, W.C., Malagodi, M.H., Oates, T.W. and McCourt, J.P. (1978). Effects of an iodinated water supply. *Trans. Am. Clin. Climatological Assoc*. **90:** 153 – 162.

Tresch, D.D., Sweet, D.L., Keelan, M.H.J. et al (1974). Acute iodide intoxication with cardiac irritability. *Arch. Intern. Med*. **134:** 760 – 762.

WHO (1989). Evaluation of Certain Food Additives and Contaminants (Thirty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series. No. 776.

Wolff, J., Chaikoff, I.L., Goldberg, R.C. et al (1949). The temporary nature of the inhibitory action of excess iodide on organic iodine synthesis in the normal thyroid. *Endocrinol*. **45:** 504 – 513.

ATTACHMENT 3

Dietary Intake Assessment

Application A528 – Maximum Iodine Limit in Formulated Supplementary Foods for Young Children.

A dietary intake assessment was deemed necessary in order to determine the potential impact of granting permission to increase the maximum permitted quantity of iodine in FSFYC from 35 µg/serve to 70 µg/serve on the iodine intake of the target population. One serve of a FSFYC is equivalent to 200 ml. Iodine intakes, based on naturally occurring concentrations of iodine in foods and the requested permissions for iodine in FSFYC, were assessed to determine if iodine intakes exceeded health standards.

Summary

There are no Australian food consumption data for children aged below 2 years of age and there are no New Zealand food consumption data for children aged 1-3 years. Consequently, dietary iodine intake was only calculated for the population group of Australian children aged 2-3 years.

No FSFYC were consumed in the 1995 Australian National Nutrition Survey (NNS) and, as a consequence, assumptions were made about the consumption of FSFYC. The baseline dietary intake of iodine assumed that 2-3 year old children would replace 20% of full fat and unspecified fat content fluid cow's milk, including that used in cooking, with FSFYC. The dietary model used to estimate iodine intake converted all milk and milk products consumed to 'full fat milk equivalents', calculated on the basis of the fat content of the milk. 'Full fat milk equivalents' intake therefore includes fluid milks, cheese, cream, yoghurt etc.

Approximately 65% of 'full fat milk equivalents' intake for 2-3 year old children in the NNS was consumed as full fat or unspecified fat content fluid cow's milk. The Applicant indicated that approximately 70% of consumers make up the product using milk with customers probably using fewer scoops per serve than those who use water to make up the product (more likely using the full 5 scoops per serve). The iodine concentration of 'full fat milk equivalents' was adjusted to take into account the differences in iodine concentration for the different preparation methods for FSFYC.

Baseline intakes of iodine were calculated using naturally occurring concentrations of iodine in food in addition to the consumption of FSFYC with a maximum permitted iodine quantity of 35 µg/serve (if prepared according to directions). One other scenario was examined in the dietary intake assessment; Scenario 1 applied a maximum permitted iodine quantity in FSFYC of 70 µg/serve (if prepared according to directions), with iodine concentration adjustments for different preparation methods, in addition to intakes from naturally occurring iodine from all other food sources. Iodine from added salt or supplements was not included in the calculation as no data were available on consumption levels.

For children aged 2-3 years, the estimated mean dietary intake of iodine was 5.4 µg/kg bw/day (83 µg/person/day) at baseline and 6.0 µg/kg bw/day (92 µg/person/day) for Scenario 1.

The estimated 95th percentile dietary intake of iodine was 9.9 µg/kg bw/day (165 µg/person/day) at baseline and 11.0 µg/kg bw/day (179 µg/person/day) for Scenario 1. Mean and 95th percentile estimated dietary intakes of iodine were below the Provisional Tolerable Daily Intake (PTDI) for iodine of 17 µg/kg bw/day (WHO 1989) in all of the scenarios examined.

The major contributors to dietary iodine intake were dairy products (70% for baseline and 73% for Scenario 1) and fruits (15% for baseline and 13% for Scenario 1).

While an upper intake level (PTDI) has been set for iodine, iodine is also an essential micronutrient. Consequently, dietary intakes were also assessed for the purpose of comparison with the Estimated Average Requirements (EARs) for iodine. Further details regarding the results of the comparison of dietary intake with the EAR for iodine can be found in the Nutrition Report at Attachment 5.

Background

The vast majority of FSFYC available in Australia and New Zealand are milk-based supplementary drinks known as 'toddler formula'. FSANZ is not aware of other products that are currently manufactured to the FSFYC provisions. Toddler formula is generally promoted as a supplementary milk drink for children aged over 12 months of age. According to the label directions on the product, toddler formula is made up by mixing the powdered formula with water. The Applicant has indicated that, in most cases (approximately 70%), the product is made up by consumers using milk. In addition, toddler formulas are sometimes promoted as being suitable as a replacement for milk in other foods e.g. custards.

The Applicant has indicated that the average number of scoops of the powdered product used to make up the beverage is 2.5 per serve, based on those customers who make up the product using either milk or water. The Applicant indicated that customers who use milk to make up the product would probably use fewer scoops per serve than those who use water to make up the product (more likely using the full 5 scoops per serve). The recommended number of serves per day is two, with market research by the Applicant showing that children usually have 1 serve per day.

Dietary intake assessment provided by the Applicant

The Applicant submitted iodine dietary intake assessment data for British children aged 1½ - 4½ years indicating that estimated iodine dietary intakes may vary between 87-309 µg/day, with almost all iodine being derived from the consumption of milk.

The dietary intake assessment submitted by the applicant was not detailed enough to allow FSANZ to determine a conclusion since the dietary intake data submitted relate to dietary intake for British children. No Australian or New Zealand dietary intake assessment data were provided therefore FSANZ conducted a dietary intake assessment.

FSANZ Dietary modelling

The dietary intake assessment was conducted using dietary modelling techniques that combine food consumption data with food chemical concentration data to estimate the intake of the food chemical from the diet. The dietary intake assessment was conducted using FSANZ's dietary modelling computer program, DIAMOND.

Dietary intake = food chemical concentration x food consumption

The dietary intake was estimated by combining usual patterns of food consumption, as derived from national nutrition survey (NNS) data, with proposed levels of use and naturally occurring concentrations of iodine in foods.

Dietary survey data

DIAMOND contains dietary survey data for both Australia and New Zealand; the 1995 NNS from Australia that surveyed 13 858 people aged 2 years and above, and the 1997 New Zealand NNS that surveyed 4 636 people aged 15 years and above. Both of the NNSs used a 24-hour food recall methodology.

These data were sufficient to estimate baseline intakes of iodine from naturally occurring sources. The New Zealand data were not used for this assessment as they did not including children in the target age group.

Additional food consumption data or other relevant data

In the 1995 NNS, no consumption of FSFYC was recorded. Data derived from the 1995 NNS indicate that approximately 65% of 'full fat milk equivalents' consumption of 2-3 year olds is in the form of either full fat or unspecified fat content fluid cow's milk. In this case, 'full fat milk equivalents' was assumed to refer to consumption of all foods derived from milk, including liquid milks, cheese, yoghurt, cream sauces etc. It was assumed that only full fat or unspecified fat content fluid cow's milks would be replaced by FSFYC.

The A528 Applicant reported that between 7-10% of parents who have children aged 13-36 months are 'regular' users of toddler drinks. The market share of FSFYC in 2-3 year age group was assumed to be 20% to allow for the consumption of FSFYC by more than one child (1-3 years) per household, for market growth and to allow for the use of FSFYC by children who are not 'regular' consumers of the product.

Each of the factors listed above were used to adjust the iodine concentration of 'full fat milk equivalents' used in the models to account for the consumption of FSFYC (see Figure 1 below for details of the adjustment of the iodine concentration of 'full fat milk equivalents').

Population groups assessed

The dietary intake assessment was conducted for Australian children aged 2-3 years since these were the only data available to cover the 1-3 year old target group for FSFYC. No NNS data are available for Australian children below 2 years of age or for New Zealand children aged 1-3 years.

Iodine concentration levels

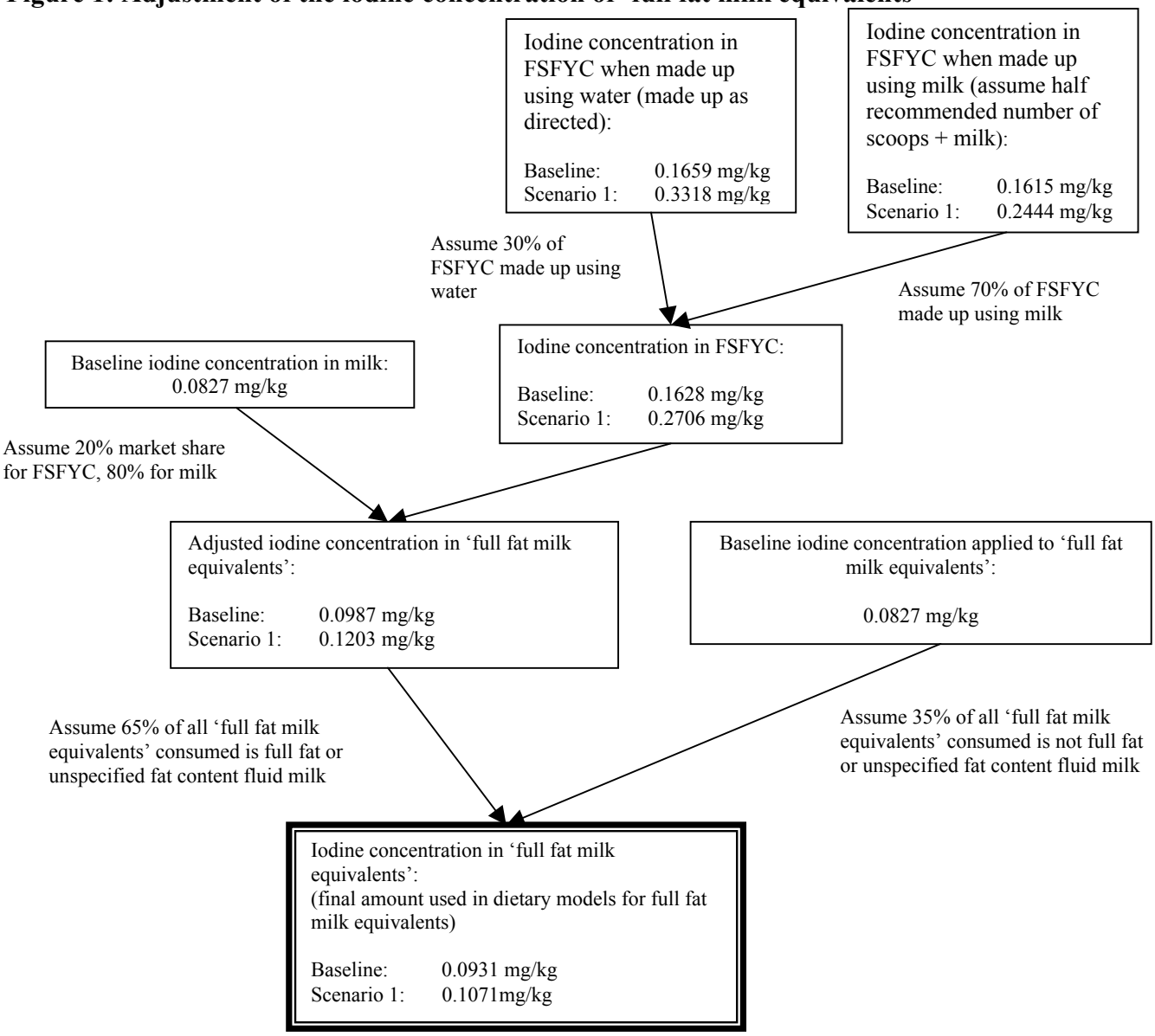
The levels of iodine in foods that were used in the dietary intake assessment were derived from the application for FSFYC, Australian and New Zealand food composition and Total Diet Survey data, overseas food composition data, the Australian Dairy Corporation, and the Applicant for A493 – Iodine as a Processing Aid for naturally occurring levels. The foods and levels of iodine used in the intake assessment are shown below in Table 1.

Concentrations of iodine were assigned to food groups using DIAMOND food classification codes based on raw agricultural commodities. The foods proposed by the Applicant to contain iodine were matched to the most appropriate DIAMOND code for dietary modelling purposes.

Scenarios for dietary modelling

Baseline
A baseline iodine dietary intake assessment was conducted to estimate dietary iodine intake before permission to increase the maximum permitted iodine quantity in FSFYC from 35 µg/serve to 70 µg/serve was considered. The baseline assessment incorporated naturally occurring levels of iodine in addition to currently permitted maximum quantities of iodine in FSFYC.

Figure 1: Adjustment of the iodine concentration of 'full fat milk equivalents'



Scenario 1

The scenario intake assessment (Scenario 1) takes into account the increase in the maximum permitted iodine quantity in FSFYC from 35 µg/serve to 70 µg/serve, with iodine concentration adjustments for different preparation methods, in addition to the naturally occurring levels in food.

In both the baseline and Scenario 1 dietary intake assessments, the milk iodine concentration data was weighted to take into account the consumption of FSFYC as discussed under "Additional Food Consumption Data or Other Relevant Data".

Table 1: Concentrations of iodine in foods used in the intake assessment

Food Code	Food Name	Concentration Level (µg/kg)		Source of Baseline Data
		Baseline	Scenario 1	
AP0001	Honey	3.4	3.4	2,3
DM, GS	Sugars	6.7	6.7	2,3
CF, GC	Cereal foods	16.8	16.8	2,3,4
CF0600	Bran, processed and unprocessed	10.0	10.0	2,3
CF1210	Germ	20.0	20.0	2
CM	Bran, unprocessed	8.9	8.9	2,3
CM1205	Rice	5.1	5.1	2,3
DF	Dried fruits	8.4	8.4	2
DF0295	Dried dates	14.8	14.8	2,3
DT	Teas	15.0	15.0	2,3
DV	Dried vegetables	236.3	236.3	8
FB	Berries and other small fruits	1.8	1.8	4
FB0269	Grapes	2.0	2.0	4
FB02691	Wine	23.3	23.3	2
FB0275	Strawberries	1.5	1.5	4
FC	Citrus fruits	73.4	73.4	7
FC0004	Oranges	73.4	73.4	7
FI	Tropical fruits – inedible peel (smooth skinned)	0.1	0.1	2
FI0326	Avocado	1.0	1.0	4
FI0327	Banana	0.1	0.1	2
FI0341	Kiwifruit	5.5	5.5	2,4
FI0353	Pineapple	10.0	10.0	2
FI0331, FI0332, FI0334, FI0338, FI0342, FI0343, FI0356, FI0358	Tropical fruits – inedible peel (rough skinned)	5.5	5.5	2,4
FP	Pome fruits	9.6	9.6	2,4
FP0226	Apples	6.3	6.3	2,4
FP0230	Pears	13.0	13.0	2,4
FS	Stone fruits (smooth skinned)	29.9	29.9	7
FS0240	Apricots	50.5	50.5	7
FS0245	Nectarines	29.9	29.9	7
FS0247	Peaches	50.5	50.5	7

Food Code	Food Name	Concentration Level (µg/kg)		Source of Baseline Data
		Baseline	Scenario 1	
FT, DM0305	Tropical fruit – edible peel	15.0	15.0	5
HH	Herbs	75.8	75.8	8
HS	Spices	75.8	75.8	8
IM	Molluscs	1050.0	1050.0	1
MF	Other mammalian fats (not cattle, pig or sheep)	27.7	27.7	1,2
MF0812	Cattle fat	50.0	50.0	1
MF0818	Pig fat	22.9	22.9	2
MF0822	Sheep fat	0.2	0.2	2
ML	Milk ('full fat milk equivalents')	93.1	107.1	6,8,10
MM	Other mammalian meats (not cattle, pig or sheep)	19.8	19.8	2,3,4
MM0812	Cattle meat	17.8	17.8	2,3,4
MM0818	Pig meat	25.3	25.3	2,3,4
MM0822	Sheep meat	13.9	13.9	2,3,4
MO	Mammalian offal	65.6	65.6	2,3,4
OC, OR	Fats and oils	1.6	1.6	2,3
PE	Eggs	501.0	501.0	1,7
PF, PM, PO	Chicken meat and offal	53.0	53.0	2,3
SB	Coffee, cocoa, cola	5.3	5.3	2,4
SO, CO0691, TN	Oilseeds and nuts	42.1	42.1	1
SO0697	Peanuts	32.5	32.5	1
TN0663	Cashews	100.0	100.0	1
VA	Bulb vegetables	12.5	12.5	2,4
VA0384	Leeks	12.5	12.5	2,4
VA0386	Onions	12.5	12.5	2,4
VB	Brassica vegetables	9.5	9.5	2,4
VB0041	Cabbage	13.0	13.0	2,4
VB0400	Broccoli	1.5	1.5	4
VB0404	Cauliflower	5.8	5.8	2,4
VC	Cucurbit vegetables	9.7	9.7	2,4,7
VC0046	Melons, except watermelon	27.0	27.0	7
VC0424	Cucumber	1.0	1.0	4
VC0429	Pumpkin	5.5	5.5	2,4
VC0431	Zucchini	1.3	1.3	4
VC0432	Watermelon	1.0	1.0	4
VD	Pulses	69.3	69.3	2,3
VL	Leafy vegetables	75.8	75.8	7
VL0482	Lettuce	75.8	75.8	7
VO	Other fruiting vegetables (smooth skinned)	24.8	24.8	2,4,7
VO0051	Capsicum	1.0	1.0	4
VO0448	Tomatoes	36.0	36.0	7
VO0442, VO0446	Other fruiting vegetables (rough skinned)	21.4	21.4	2,4
VO0447	Sweetcorn	40.0	40.0	2

Food Code	Food Name	Concentration Level (µg/kg)		Source of Baseline Data
		Baseline	Scenario 1	
VO449, VO0450	Mushrooms	2.8	2.8	4
VP	Legume vegetables	125.0	125.0	1
VP00611	Beans, green	200.0	200.0	1
VP0529	Peas, garden	50.0	50.0	1
VR	Root and tuber vegetables	20.2	20.2	1,2,4,7
VR0508	Sweet potatoes	2.0	2.0	4
VR0574	Beetroot	50.0	50.0	1
VR0577	Carrots	8.3	8.3	2,4
VR0589	Potatoes	32.7	32.7	7
VS	Stalk and stem vegetables	5.0	5.0	4
VS0621	Asparagus	5.0	5.0	4
VS0624	Celery	5.0	5.0	4
WC	Crustacea	300.0	300.0	1
WD	Diadromous fish	600.0	600.0	1
WF	Other freshwater fish	625.0	625.0	1
WF0864, WF0866, WF0870, WF0897	Morwong	950.0	950.0	1
WR, WS	Other marine fish	254.2	254.2	1
WS0003	Fish portions	31.2	31.2	2,3
WS0004	Gemfish	250.0	250.0	1
WS0008	Flathead	75.0	75.0	1
WS0010	Snapper	400.0	400.0	1
WS0130	Sardine	100.0	100.0	1
WS0131	Flake	100.0	100.0	1
WS0858, WF0858	Bream	300.0	300.0	1
WS0927	Cod	250.0	250.0	1
WS0943	Mullet	100.0	100.0	1
WS0952	Tuna	150.0	150.0	1
WS0953	Whiting	50.0	50.0	1
WW	Water	0.8	0.8	2,4
XX0001	Seaweed	14,700.0	14,700.0	9
XX0002	Dry soup mixes	120.0	120.0	1

(1) unpublished Australian food composition data; (2) unpublished New Zealand food composition data; (3) 1997/8 New Zealand Total Diet Survey (Ministry of Health 2000); (4) 2003/4 New Zealand Total Diet Survey (Vannoort 2003); (5) German Food Composition tables (Souci et al 1994); (6) Australian Dairy Corporation (Australian Dairy Corporation 1999); (7) A493 applicant; (8) derived data; (9) British food composition data (Holland et al 1991), (10) A528 applicant.

How were the estimated dietary intakes calculated?

The DIAMOND program allows iodine concentrations to be assigned to food groups. Each individual's intake of iodine was calculated using their individual food records from the dietary survey. The DIAMOND program multiplies the specified concentration of iodine by the amount of food that an individual consumed from that group in order to estimate the iodine intake from each food. Once this has been completed for all of the foods specified to contain iodine, the total amount of iodine consumed from all foods is summed for each individual. Population statistics (mean and high percentile intakes) are then derived from the individuals' ranked intakes.

Where estimated dietary intakes are expressed per kilogram of body weight, each individuals' total dietary intake is divided by their own body weight, the results ranked, and population statistics derived. A small number of NNS respondents did not provide a body weight.

These respondents are not included in calculations of estimated dietary intakes that are expressed per kilogram of body weight.

Where estimated intakes are expressed as a percentage of the reference health standard, each individual's total intake is calculated as a percentage of the reference health standard (in units per kilogram of body weight per day), the results are then ranked, and population statistics derived.

Food consumption amounts for each individual take into account where each food in a classification code is consumed alone and as an ingredient in mixed foods. For example, raw tomato eaten as a part of a salad, tomato in pasta sauce, and tomato paste are all included in the consumption of tomatoes. Where a higher level food classification code (e.g. FI Tropical fruits – inedible peel) is given an iodine concentration, as well as a sub-category (e.g. FI0326 Avocado), the consumption of the foods in the sub-classification is not included in the higher level classification code.

In DIAMOND, all mixed foods have a recipe. Recipes are used to break down mixed foods into their raw commodity components (e.g. bread will be broken down to wheat flour, yeast, water etc). The data for consumption of the raw commodities are then used in models that assign iodine permissions to raw commodity classifications.

When a food is classified in two food groups (for example, mixed fruit juice may be entered in the apple and pear groups), and these food groups are assigned different iodine permissions, DIAMOND will assume the food is in the food group with the highest assigned iodine level to assume a worst case scenario. If the food groups have the same permitted iodine level, DIAMOND will assume the food is in the food group that appears first, based alpha-numerically on the DIAMOND food code.

In DIAMOND, hydration and raw equivalence factors are applied to some foods to convert the amount of food consumed in the dietary survey to the equivalent amount of the food in the form to which a food chemical permission is given. Factors are only applied to individual foods, and not major food group codes. For example, consumption figures for instant coffee powder are converted into the equivalent quantities of coffee beans; consumption figures for tomato paste are converted into the equivalent quantities of raw tomatoes.

Percentage contributions of each food group to total estimated intakes are calculated by summing the intakes for a food group from each individual in the population group who consumed a food from that group and dividing this by the sum of the intakes of all individuals from all food groups containing iodine, and multiplying this by 100.

Assumptions in the dietary modelling

The aim of the dietary intake assessment was to make as realistic an estimate of dietary intake as possible. However, where significant uncertainties in the data existed, conservative assumptions were generally used to ensure that the dietary intake assessment did not underestimate intake.

Assumptions made in the dietary modelling include:

- where a permission for an iodine is given to a food classification, all foods in that group contain iodine;
- all the foods within the group contain iodine at the levels specified in Table 1;
- consumption of foods as recorded in the NNS represent current food consumption patterns;
- 20% of all full fat and non-specified fat content fluid cow's milks, as recorded in the NNS, are substituted with FSFYC;
- only full fat or unspecified fat content fluid cow's milk is replaced by FSFYC (65% of 'full fat milk equivalents' consumed);
- 70% of all FSFYC are made up using milk and 30% using water (as per the Applicant's market research data);
- when the consumer uses milk to make up FSFYC, half of the recommended number of scoops are used;
- when the consumer uses water to make up FSFYC, the recommended number of scoops are used;
- the mean iodine concentration values determined from the listed data sources are representative of the levels found in foods throughout Australia with no regional, seasonal or natural variation;
- all iodine present in foods is 100% bioavailable, therefore there are no inhibitors to iodine absorption (such as goitrogens) present in the diet;
- where the concentration of iodine in a food was reported as being less than the Limit of Detection (LOD), then the iodine concentration of the food was equal to half of the LOD value. The LOD is the lowest concentration of a chemical that can be qualitatively detected using a specified laboratory method and/or item of laboratory equipment (i.e. its presence can be detected but not quantified);
- where there were no Australian iodine data for specific food groups, it was assumed that New Zealand data were representative of these food groups, and vice versa for New Zealand;
- where there were no Australian or New Zealand data on iodine concentrations of food groups, it was assumed that overseas data (British and German) were representative of these food groups;
- where a food or food group has a zero concentration of iodine, it was not included in the intake assessment;
- where a food has a specified iodine concentration, this concentration is carried over to mixed foods where the food has been used as an ingredient e.g. milk in custard;
- there is no consumption of iodine through salt (since NNS did not measure discretionary salt use) or supplements;
- there are no reductions in iodine concentrations on cooking; and
- food manufacturers do not use iodised salt in their products. In a study by Gunton et al (1999), three major Australian food manufacturers of processed food were contacted and reported using only non-iodised salt.

These assumptions are likely to lead to a conservative estimate for iodine dietary intake.

Limitations of the dietary modelling

A limitation of estimating dietary intake over a period of time associated with the dietary modelling is that only 24-hour dietary survey data were available, and these tend to over-estimate habitual food consumption amounts for high consumers. A second 24-hour recall dietary survey was conducted on a subset of the respondents from the NNSs. These data were not used in this Application to calculate a 2-day adjusted nutrient intake, which gives a better indication of longer-term nutrient intakes. Therefore, predicted high percentile intakes are likely to be higher than actual high percentile intakes over a lifetime.

Daily food consumption amounts for occasionally consumed foods based on 24 hour food consumption data would be higher than daily food consumption amounts for those foods based on a longer period of time.

Over time, there may be changes to the ways in which manufacturers and retailers make and present foods for sale. Since the data were collected for the Australian and New Zealand NNSs, there have been significant changes to the Code to allow more innovation in the food industry. As a consequence, another limitation of the dietary modelling is that some of the foods that are currently available in the food supply were either not available or were not as commonly available in 1995/1997.

The NNSs did not collect data on the use of complementary medicines (Australia) or dietary supplements (New Zealand). Consequently, these could not be included in the dietary intake assessment.

While the results of NNSs can be used to describe the usual intake of groups of people, they cannot be used to describe the usual intake of an individual (Rutishauser 2000). In particular, they cannot be used to predict how consumers will change their eating patterns as a result of an external influence such as the availability of a new type of food.

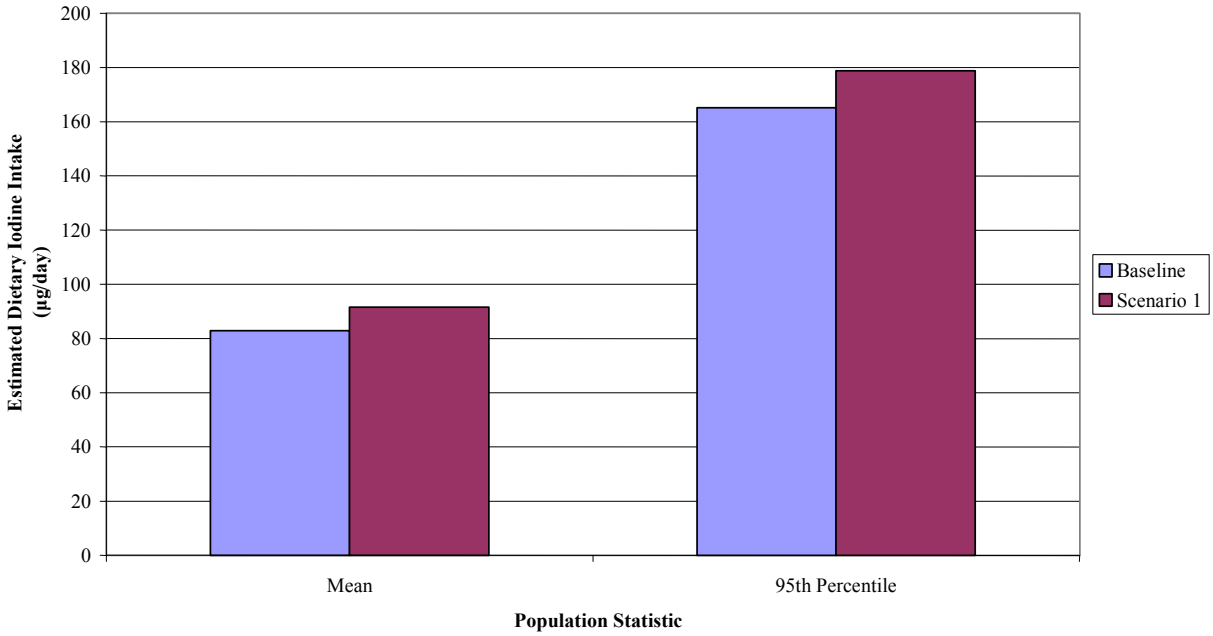
FSANZ does not apply statistical population weights to each individual in the NNSs in order to make the data representative of the population. This prevents distortion of actual food consumption amounts that may result in an unrealistic intake estimate.

Results

Estimated dietary intakes of iodine

The estimated dietary intakes for iodine are shown in Figure 2 (full results in Table A1.1 in Appendix 1). The results are presented for all survey respondents in the 2-3 year age group (n=383) because all respondents had an iodine intake due to the nutrient being ubiquitous in the food supply. For children aged 2-3 years, the estimated mean dietary intake of iodine was 5.4 µg/kg bw/day (83 µg/person/day) at baseline and 6.0 µg/kg bw/day (92 µg/person/day) for Scenario 1. The estimated 95th percentile dietary intake of iodine was 9.9 µg/kg bw/day (165 µg/person/day) at baseline and 11.0 µg/kg bw/day (179 µg/person/day) for Scenario 1.

Figure 2: Estimated dietary intakes of iodine for Australian children aged 2-3 years



Major contributing foods to total estimated dietary intakes

The major contributors (>5%) to total iodine dietary intakes for Australian children aged 2-3 years were dairy products (70% at baseline and 73% for Scenario 1) and fruits (15% at baseline and 13% for Scenario 1). A full list of all the food groups and their contributions can be found in Table A1.2 in Appendix 1.

Risk characterisation

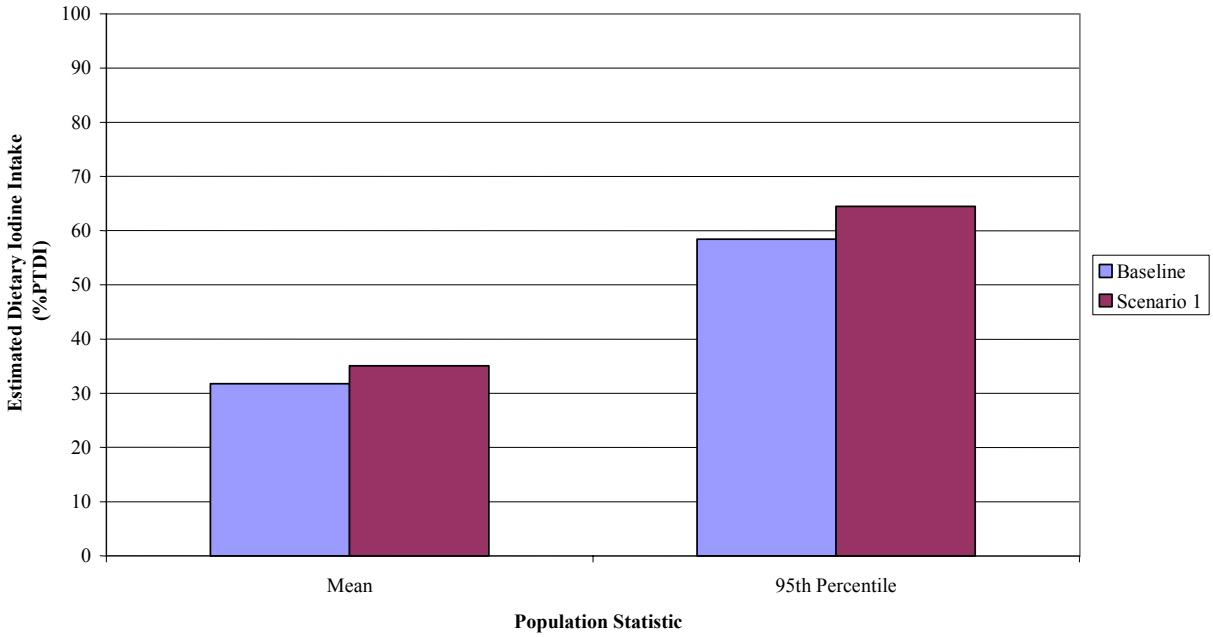
In order to determine if the level of dietary iodine intake are likely to be of public health and safety concern, the estimated dietary intakes were compared to a Provisional Tolerable Daily Intake (PTDI) for iodine of 17 µg/kg bw/day. Provisional Tolerable Daily Intakes (PTDI) are upper limits that are set for substances that do not accumulate in animals and humans (WHO 2001) and are estimates of the amount of a chemical that can be ingested daily over a lifetime without appreciable risk to health.

Comparison of the estimated dietary intakes with the PTDI

The estimated dietary intakes of iodine, as compared to the PTDI are shown in Figure 3 (full results in Table A2.1 in Appendix 2).

For children aged 2-3 years, the estimated mean dietary intake of iodine was 32% PTDI at baseline and 35% PTDI for Scenario 1. The estimated 95th percentile dietary intake of iodine was 58% PTDI at baseline and 65% PTDI for Scenario 1. Mean and 95th percentile estimated dietary intakes of iodine were below the PTDI in all of the scenarios examined.

Figure 3: Estimated dietary intakes of iodine for Australian children aged 2-3 years, as a percentage of the PTDI



REFERENCES

Food Standards Agency (UK FSA), 2002, *Revised Review of Iodine: Prepared for the Expert Group on Vitamins and Minerals (EVM/00/06.REVISEDAUG2002)*, www.foodstandards.gov.uk/multimedia/pdfs/evm0006p.pdf

Institute of Medicine, National Academy of Sciences, 2000, *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*, National Academy Press, Washington, DC.

National Health and Medical Research Council, 2001,*National Health and Medical Research Council Website (www.health.gov.au/nhmrc/publications/diet)*

Rutishauser I. 2000. *Getting it right:- how to use the data from the 1995 National Nutrition Survey*. Commonwealth of Australia: Canberra

World Health Organisation, 1989, Toxicological evaluation of certain food additives and contaminants (Thirty-third Report of the Joint FAO/WHO Expert Committee on Food Additives), WHO Food Additive Series No. 24, WHO, Geneva.

World Health Organization, 2001, *Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA 1956-2001) (First through fifty-seventh meetings) Internet Edition*, ILSI Press International Life Sciences Institute, Washington DC.

Appendix 1

Complete information on dietary intake assessment results

Table A1.1: Estimated dietary intakes of iodine for Australian children aged 2-3 years

Number of consumers of iodine	Consumers♦ as a % of total respondents#	Average body weight (kg)	Mean consumers µg/day (µg/kg bw/day)		95th percentile consumers µg/day (µg/kg bw/day)	
			Baseline	Scenario 1	Baseline	Scenario 1
383	100	16	83.0 (5.4)	91.7 (6.0)	165.1 (9.9)	178.9 (11.0)

Total number of respondents for Australia: 2-3 years = 383. Respondents include all members of the survey population whether or not they consumed a food that contains iodine.
♦ Consumers only – This only includes the people who have consumed a food that contain iodine.

Table A1.2: Contribution of each food group to total iodine dietary intakes for Australian children aged 2-3 years

Food Name	% Contribution to iodine dietary intake	
	Baseline	Scenario 1
Dairy products	69.6	72.5
Fruits:	14.8	13.4
citrus fruits	11.7	10.6
Eggs	4.7	4.3
Vegetables (including herbs):	4.7	4.2
Meat & poultry	2.2	2.0
Cereals	1.8	1.6
Seafood (including seaweed)	1.0	0.9
Water	0.6	0.6
Other foods	0.6	0.6

Complete information on risk characterisation

Table A2.1: Estimated dietary intakes of iodine for Australian children aged 2-3 years, as a percentage of the PTDI

Number of consumers of iodine	Consumers♦ as a % of total respondents#	Average body weight (kg)	Mean consumers %PTDI		95th percentile consumers %PTDI	
			Baseline	Scenario 1	Baseline	Scenario 1
383	100	16	31.8	35.1	58.4	64.5

Total number of respondents for Australia: 2-3 years = 383. Respondents include all members of the survey population whether or not they consumed a food that contains iodine.
♦ Consumers only – This only includes the people who have consumed a food that contains iodine.
* PTDI = 17 µg/kg bw/day

Combined Dietary Intake Assessment

A dietary intake assessment was undertaken to determine the impact on dietary iodine intake if the requested changes to the Code from both applications A493 and A528 were approved. The assessment of the combination of requested permissions from A493 and A528 is referred to as 'both applications (A493 & A528)' hereafter. The assessment for 'both applications (A493 & A528)' was only conducted for Australian children 2-3 years of age.

Results for each separate Application can be found as an attachment to the relevant Draft Assessment report for each Application.

For the purpose of the 'both applications (A493 & A528)' dietary intake assessment, three different scenarios were examined:

- Baseline: naturally occurring levels of iodine in addition to currently permitted maximum quantities of iodine, with adjustments for variations in preparation method, in FSFYC were considered;

- Scenario 1: this scenario applies a peeling factor to the iodine concentrations of those fruits and vegetables that may be consumed either peeled or unpeeled (e.g. apples) and that may be washed with an elemental iodine wash. This scenario reflects a more accurate estimate of the likely extent to which an elemental iodine wash (A493) will impact on the iodine dietary intakes for Australian and New Zealand population groups. Scenario 1 also takes into account the increase in the maximum iodine level in FSFYC from 35 µg/serve to 70 µg/serve, with adjustments for variations in preparation method, by using an adjusted 'full fat milk equivalents' iodine concentration (A528);

- Scenario 2: this scenario assumes that fruits and vegetables that may be consumed either peeled or unpeeled (e.g. apples) are always eaten unpeeled after being treated with an elemental iodine wash (A493). Scenario 2 also takes into account the increase in the maximum iodine level in FSFYC from 35 µg/serve to 70 µg/serve, with adjustments for variations in preparation method, by using an adjusted 'full fat milk equivalents' iodine concentration (A528). Scenario 2 is a worst-case scenario.

At baseline, the estimated mean dietary intake of iodine for children aged 2-3 years for 'both applications (A493 & A528)' was 5.4 µg/kg bw/day (83 µg/person/day), with the 95th percentile intake being 9.9 µg/kg bw/day (165 µg/person/day). The baseline for 'both applications (A493 & A528)' is the same as that for the A528 baseline. For Scenario 1 for 'both applications (A493 & A528)', the estimated dietary intake of iodine was 8.7 µg/kg bw/day (133.9 µg/person/day) at the mean and 16.1 µg/kg bw/day (258.3 µg/person/day) at the 95th percentile. For Scenario 2 for 'both applications (A493 & A528)', the estimated dietary intake of iodine was 9.8 µg/kg bw/day (150.2 µg/person/day) at the mean and 18.7 µg/kg bw/day (289.4 µg/person/day) at the 95th percentile.

Estimated mean and 95th percentile dietary intakes of iodine were below the PTDI of 17 µg/kg body weight/day (WHO 1989) for the baseline scenario and for Scenario 1. Provisional Tolerable Daily Intakes (PTDI) are upper limits that are set for substances that do not accumulate in animals and humans (WHO 2001) and are estimates of the amount of a chemical that can be ingested daily over a lifetime without appreciable risk to health.

For Scenario 2, mean dietary intake of iodine was below the PTDI, with 95th percentile intake exceeding the PTDI (110% PTDI). However, due to the conservative assumptions made in this calculation and that the use of 24-hour dietary survey data tends to over-estimate habitual food consumption amounts for high consumers, it is likely that the 95th percentile dietary intake is an over-estimate.

At baseline, the major contributors to iodine dietary intake were dairy products (70%) and fruits (15%). For Scenario 1, the major contributors to iodine dietary intake were dairy products (50%), fruits (28%) and vegetables (including herbs) (16%). For Scenario 2, the major contributors to iodine dietary intake were dairy products (44%), fruits (28%) and vegetables (including herbs) (22%).

Background

For the detailed background to each separate application for A493 and A528, please refer to the reports for each individual application, as only a summary from each is provided below.

Two separate applications were received by FSANZ requesting amendment of the Food Standards Code (the Code) in relation to iodine: (1) to Standard 1.3.3 'Processing Aids' – Clause 12 'Permitted bleaching agents, washing and peeling agents' to allow the use of iodine as a processing aid for fruits, vegetables, nuts and eggs (A493); and (2) to Standard 2.9.3 – Formulated Meal Replacements and Formulated Supplementary Foods to increase the maximum iodine limit in formulated supplementary foods for young children (FSFYC) from 35 µg /serve to 70 µg/serve (A528). One serve of a FSFYC is equivalent to 200 ml.

Formulated supplementary foods for young children (FSFYC) are for children aged 1-3 years. Since there are no Australian food consumption data for children aged below 2 years of age and there are no New Zealand food consumption data for children aged 1-3 years, dietary iodine intakes were only calculated for the population group of Australian children aged 2-3 years for 'both applications (A493 & A528)'.

In A493, baseline intakes of iodine were calculated using naturally occurring iodine concentrations. For children aged 2-3 years, estimated mean dietary intake of iodine was 5.0 µg/kg bw/day (76.7 µg/person/day) and 95th percentile dietary intake was estimated as 9.2 µg/kg bw/day (153.7 µg/person/day).

The baseline intakes of iodine for A528 differ from those in A493. This is because no FSFYC were consumed in the 1995 Australian National Nutrition Survey and, as a consequence, assumptions were made about the consumption of FSFYC. The baseline dietary intake of iodine for A528 assumed that 2-3 year old children in the NNS would replace 20% of full fat and unspecified fat content fluid cow's milk, including that used in cooking, with FSFYC. The dietary model used to estimate iodine intake converted all milk and milk products consumed to 'full fat milk equivalents', calculated on the basis of the fat content of the milk. 'Full fat milk equivalents' intake therefore includes fluid milks, cheese, cream, yoghurt etc.

Approximately 65% of 'full fat milk equivalents' intake for 2-3 year old children in the NNS was consumed as full fat or unspecified fat content fluid cow's milk. The A528 Applicant indicated that approximately 70% of consumers make up the product using milk with customers probably using less scoops per serve than those who use water to make up the product (more likely using the full 5 scoops per serve).

The iodine concentration of 'full fat milk equivalents' was adjusted to take into account the differences in iodine concentration for the different preparation methods for FSFYC.

The A528 application baseline dietary iodine intake has been used as the baseline for the dietary intake assessment for 'both applications (A493 & A528)'. Details on how the iodine concentration of 'full fat milk equivalents' was adjusted to take into account the consumption of FSFYC can be found in Figure 1 at Attachment 3A.

Dietary Modelling

Refer to the reports for the individual applications for details regarding the dietary modelling techniques, dietary survey data, population groups, additional food consumption data used and assumptions made in dietary modelling.

Iodine concentration levels

The levels of iodine in foods that were used to establish the baseline level of estimated dietary intake of iodine were derived from a number of sources including Australian, New Zealand, British, and German food composition data, the 1997/8 and 2003/4 New Zealand Total Diet Surveys, the Australian Dairy Corporation, the A493 Applicant, and the A528 Applicant. The foods and proposed levels of use for 'both applications (A493 & A528)' are shown below in Table 1.

Table 1: Iodine levels in foods available in Australia at baseline and with the proposed levels of use for 'both applications (A493 & A528)'

Food Code	Food Name	Concentration Level (µg/kg)			Source of Baseline Data
		Baseline	Scenario 1	Scenario 2	
AP0001	Honey	3.4	3.4	3.4	2,3
DM, GS	Sugars	6.7	6.7	6.7	2,3
CF, GC	Cereal foods	16.8	16.8	16.8	2,3,4
CF0600	Bran, processed and unprocessed	10.0	10.0	10.0	2,3
CF1210	Germ	20.0	20.0	20.0	2
CM	Bran, unprocessed	8.9	8.9	8.9	2,3
CM1205	Rice	5.1	5.1	5.1	2,3
DF	Dried fruits	8.4	8.4	8.4	2
DF0295	Dried dates	14.8	14.8	14.8	2,3
DT	Teas	15.0	15.0	15.0	2,3
DV	Dried vegetables	236.3	236.3	236.3	8
FB	Berries and other small fruits	1.8	151.8	151.8	4
FB0269	Grapes	2.0	2.0	2.0	4
FB02691	Wine	23.3	23.3	23.3	2
FB0275	Strawberries	1.5	301.5	301.5	4
FC	Citrus fruits	73.4	73.4	73.4	7
FC0004	Oranges	73.4	73.4	73.4	7
FI	Tropical fruits – inedible peel (smooth skinned)	0.1	0.1	0.1	2
FI0326	Avocado	1.0	1.0	1.0	4
FI0327	Banana	0.1	0.1	0.1	2

Food Code	Food Name	Concentration Level (µg/kg)			Source of Baseline Data
		Baseline	Scenario 1	Scenario 2	
FI0341	Kiwifruit	5.5	5.5	5.5	2,4
FI0353	Pineapple	10.0	10.0	10.0	2
FI0331, FI0332, FI0334, FI0338, FI0342, FI0343, FI0356, FI0358	Tropical fruits – inedible peel (rough skinned)	5.5	5.5	5.5	2,4
FP	Pome fruits	9.6	159.6	159.6	2,4
FP0226	Apples	6.3	97.8	156.3	2,4
FP0230	Pears	13.0	112.0	163.0	2,4
FS	Stone fruits (smooth skinned)	29.9	179.9	179.9	7
FS0240	Apricots	50.5	335.5	350.5	7
FS0245	Nectarines	29.9	166.4	179.9	7
FS0247	Peaches	50.5	182.5	350.5	7
FT, DM0305	Tropical fruit – edible peel	15.0	165.0	165.0	5
HH	Herbs	75.8	3075.8	3075.8	8
HS	Spices	75.8	75.8	75.8	8
IM	Molluscs	1050.0	1050.0	1050.0	1
MF	Other mammalian fats (not cattle, pig or sheep)	27.7	27.7	27.7	1,2
MF0812	Cattle fat	50.0	50.0	50.0	1
MF0818	Pig fat	22.9	22.9	22.9	2
MF0822	Sheep fat	0.2	0.2	0.2	2
ML	Milk ('full fat milk equivalents')	93.1	107.1	107.1	6,8,10
MM	Other mammalian meats (not cattle, pig or sheep)	19.8	19.8	19.8	2,3,4
MM0812	Cattle meat	17.8	17.8	17.8	2,3,4
MM0818	Pig meat	25.3	25.3	25.3	2,3,4
MM0822	Sheep meat	13.9	13.9	13.9	2,3,4
MO	Mammalian offal	65.6	65.6	65.6	2,3,4
OC, OR	Fats and oils	1.6	1.6	1.6	2,3
PE	Eggs	501.0	575.0	575.0	1,7
PF, PM, PO	Chicken meat and offal	53.0	53.0	53.0	2,3
SB	Coffee, cocoa, cola	5.3	5.3	5.3	2,4
SO, CO0691, TN	Oilseeds and nuts	42.1	42.1	42.1	1
SO0697	Peanuts	32.5	32.5	32.5	1
TN0663	Cashews	100.0	100.0	100.0	1
VA	Bulb vegetables	12.5	162.5	162.5	2,4
VA0384	Leeks	12.5	162.5	162.5	2,4
VA0386	Onions	12.5	63.5	63.5	2,4
VB	Brassica vegetables	9.5	407.5	407.5	2,4
VB0041	Cabbage	13.0	13.0	13.0	2,4
VB0400	Broccoli	1.5	540.0	540.0	4
VB0404	Cauliflower	5.8	403.8	403.8	2,4
VC	Cucurbit vegetables	9.7	159.7	159.7	2,4,7
VC0046	Melons, except watermelon	27.0	27.0	27.0	7
VC0424	Cucumber	1.0	151.0	151.0	4
VC0429	Pumpkin	5.5	5.5	5.5	2,4
VC0431	Zucchini	1.3	151.3	151.3	4

Food Code	Food Name	Concentration Level (µg/kg)			Source of Baseline Data
		Baseline	Scenario 1	Scenario 2	
VC0432	Watermelon	1.0	1.0	1.0	4
VD	Pulses	69.3	69.3	69.3	2,3
VL	Leafy vegetables	75.8	744.8	744.8	7
VL0482	Lettuce	75.8	735.8	735.8	7
VO	Other fruiting vegetables (smooth skinned)	24.8	174.8	174.8	2,4,7
VO0051	Capsicum	1.0	151.0	151.0	4
VO0448	Tomatoes	36.0	157.5	186.0	7
VO0442, VO0446	Other fruiting vegetables (rough skinned)	21.4	321.4	321.4	2,4
VO0447	Sweetcorn	40.0	340.0	340.0	2
VO449, VO0450	Mushrooms	2.8	214.8	214.8	4
VP	Legume vegetables	125.0	595.0	595.0	1
VP00611	Beans, green	200.0	670.0	670.0	1
VP0529	Peas, garden	50.0	67.8	304.0	1
VR	Root and tuber vegetables	20.2	20.2	20.2	1,2,4,7
VR0508	Sweet potatoes	2.0	2.0	2.0	4
VR0574	Beetroot	50.0	50.0	50.0	1
VR0577	Carrots	8.3	293.5	293.5	2,4
VR0589	Potatoes	32.7	98.7	332.7	7
VS	Stalk and stem vegetables	5.0	426.0	426.0	4
VS0621	Asparagus	5.0	513.0	513.0	4
VS0624	Celery	5.0	338.0	338.0	4
WC	Crustacea	300.0	300.0	300.0	1
WD	Diadromous fish	600.0	600.0	600.0	1
WF	Other freshwater fish	625.0	625.0	625.0	1
WF0864, WF0866, WF0870, WF0897	Morwong	950.0	950.0	950.0	1
WR, WS	Other marine fish	254.2	254.2	254.2	1
WS0003	Fish portions	31.2	31.2	31.2	2,3
WS0004	Gemfish	250.0	250.0	250.0	1
WS0008	Flathead	75.0	75.0	75.0	1
WS0010	Snapper	400.0	400.0	400.0	1
WS0130	Sardine	100.0	100.0	100.0	1
WS0131	Flake	100.0	100.0	100.0	1
WS0858, WF0858	Bream	300.0	300.0	300.0	1
WS0927	Cod	250.0	250.0	250.0	1
WS0943	Mullet	100.0	100.0	100.0	1
WS0952	Tuna	150.0	150.0	150.0	1
WS0953	Whiting	50.0	50.0	50.0	1
WW	Water	0.8	0.8	0.8	2,4
XX0001	Seaweed	14,700.0	14,700.0	14,700.0	9
XX0002	Dry soup mixes	120.0	120.0	120.0	1

(1) unpublished Australian food composition data; (2) unpublished New Zealand food composition data; (3) 1997/8 New Zealand Total Diet Survey (Ministry of Health 2000); (4) 2003/4 New Zealand Total Diet Survey (Vannoort 2003); (5) German Food Composition tables (Souci et al 1994); (6) Australian Dairy Corporation (Australian Dairy Corporation 1999); (7) A493 applicant; (8) derived data; (9) British food composition data (Holland et al 1991); (10) A528 Applicant.

Concentrations of iodine were assigned to food groups using DIAMOND food classification codes. Where the A493 Applicant provided a range of possible concentrations, the highest level in the range was used for calculating the estimated intakes in order to assume a worst-case scenario.

Scenarios for dietary modelling

Baseline

A baseline iodine dietary intake assessment was conducted for 'both applications' to estimate iodine dietary intake before permission to use iodine as a washing agent was considered and before permission to increase the maximum permitted iodine level in FSFYC from 35 µg/serve to 70 µg/serve, with adjustments for variations in preparation method, was considered. The baseline assessment incorporated naturally occurring levels of iodine in addition to currently permitted maximum quantities of iodine in FSFYC. This was done by using an adjusted 'full fat milk equivalents' iodine concentration level to account for the consumption of FSFYC replacing 20% of full fat and unspecified milk consumption of 2-3 year olds.

Scenario 1

The first scenario (Scenario 1) applies a peeling factor to the iodine concentrations of those fruits and vegetables that may be consumed either peeled or unpeeled (e.g. apples). This scenario reflects a more accurate estimate of the likely extent to which an elemental iodine wash (A493) will impact on the iodine dietary intakes for Australian and New Zealand population groups. Scenario 1 also takes into account the increase in the maximum iodine level in FSFYC from 35 µg/serve to 70 µg/serve, with adjustments for variations in preparation method, by using an adjusted 'full fat milk equivalents' iodine concentration (A528).

Scenario 2

The second scenario (Scenario 2) assumes that fruits and vegetables that may be consumed either peeled or unpeeled (e.g. apples) are always eaten unpeeled after being treated with an elemental iodine wash (A493). Scenario 2 also takes into account the increase in the maximum iodine level in FSFYC from 35 µg/serve to 70 µg/serve, with adjustments for variations in preparation method, by using an adjusted 'full fat milk equivalents' iodine concentration (A528). Scenario 2 is a worst-case scenario.

How were the estimated dietary intakes calculated?

Please refer to the reports for A493 and for A528 for further details on the calculation of dietary intakes.

Assumptions in the dietary modelling

Please refer to the reports for A493 and for A528 for details on the assumptions used in the estimation of dietary intakes of iodine.

Other information used in the dietary modelling

The other information used in conducting the dietary intake assessment includes:

- grapes are never washed prior to use for technological reasons;
- an iodine wash system will never be used on fruits and vegetables that are dried; and
- all of the iodine stays on the surface of the produce, essentially remaining on the surface or within a few millimetres of the surface. Therefore, removal of the peel from fruits and vegetables and the shell from nuts results in the removal of additional iodine residues from the elemental iodine wash system.

Limitations of the dietary modelling

Please refer to the reports for A493 and for A528 for further details on the limitations of the dietary modelling.

Results

Estimated dietary intakes of iodine

The estimated dietary intakes of iodine are shown in Figure 1 (full results in Table A1.1 in Appendix 1). The results are presented for all survey respondents in the 2-3 year age group (n=383) because all respondents had an iodine intake due to the nutrient being ubiquitous in the food supply.

The estimated mean dietary intake of iodine for consumers was estimated at 5.4 µg/kg bw/day (83 µg/day) at baseline, 8.7 µg/kg bw/day (134 µg/day) for Scenario 1, and 9.8 µg/kg bw/day (150 µg/day) for Scenario 2. The estimated 95th percentile dietary intake of iodine was estimated at 9.9 µg/kg bw/day (165 µg/day) at baseline, 16.1 µg/kg bw/day (258 µg/day) for Scenario 1, and 18.7 µg/kg bw/day (289 µg/day) for Scenario 2.

Major contributing food groups to total estimated dietary intakes

The food group contributors to total iodine dietary intakes are shown in Figure 2. At baseline, the major contributors (<5%) to iodine dietary intake were dairy products (70%) and fruits (15%). For Scenario 1, the major contributors to iodine dietary intake were dairy products (50%), fruits (28%) and vegetables (including herbs) (16%). For Scenario 2, the major contributors to iodine dietary intake were dairy products (44%), fruits (28%) and vegetables (including herbs) (22%). A full list of all the food groups and their contributions can be found in Table A1.2 in Appendix 1.

Figure 1: Estimated dietary intakes of iodine from 'both applications' (A493 & A528) for Australian children aged 2-3 years

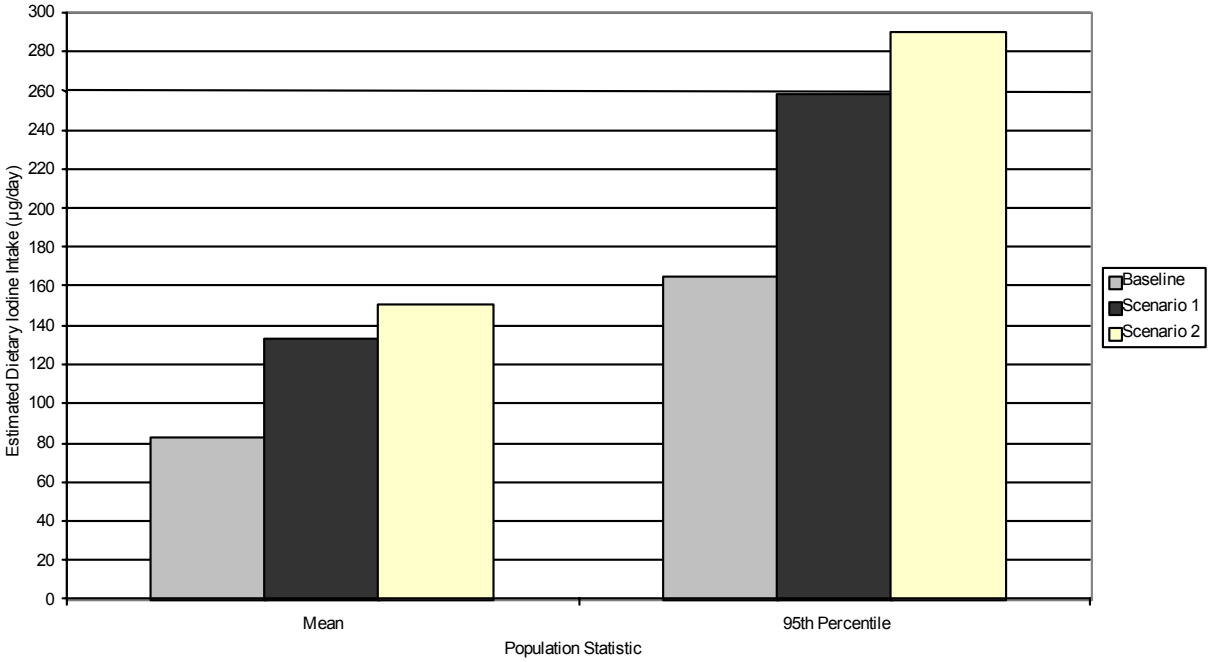
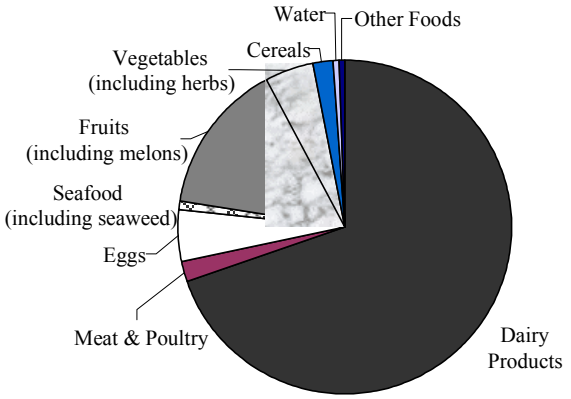
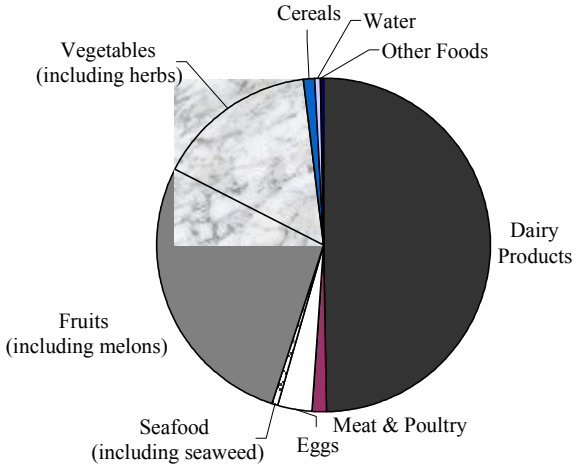


Figure 2: Contributors to total iodine intakes for the Australian population aged 2-3 years



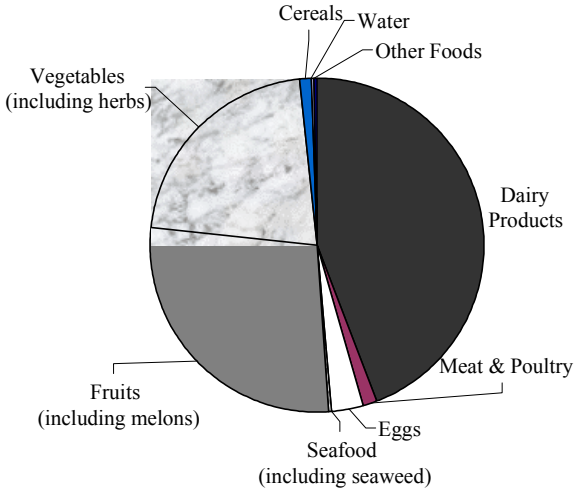
Baseline

(83 µg/day)



Scenario 1

(134 µg/day)



Scenario 2

(150 µg/day)

Risk Characterisation

Comparison of the estimated dietary intakes with the reference health standard

In order to determine if the level of dietary intake of iodine will be a public health and safety concern if an iodine wash is applied to fruits, vegetables (including herbs), eggs and nuts and if the maximum iodine limit in FSFYC is increased from 35 µg/serve to 70 µg/serve, the estimated dietary intakes were compared to a Provisional Tolerable Daily Intake (PTDI) of 17 µg/kg body weight/day. The PTDI was set by the FAO/WHO Joint Expert Committee on Food Additives (JECFA) (WHO 1989).

The estimated dietary intakes of iodine, as compared to the PTDI are shown in Figure 3 (full results in Table A2.1 in Appendix 2).

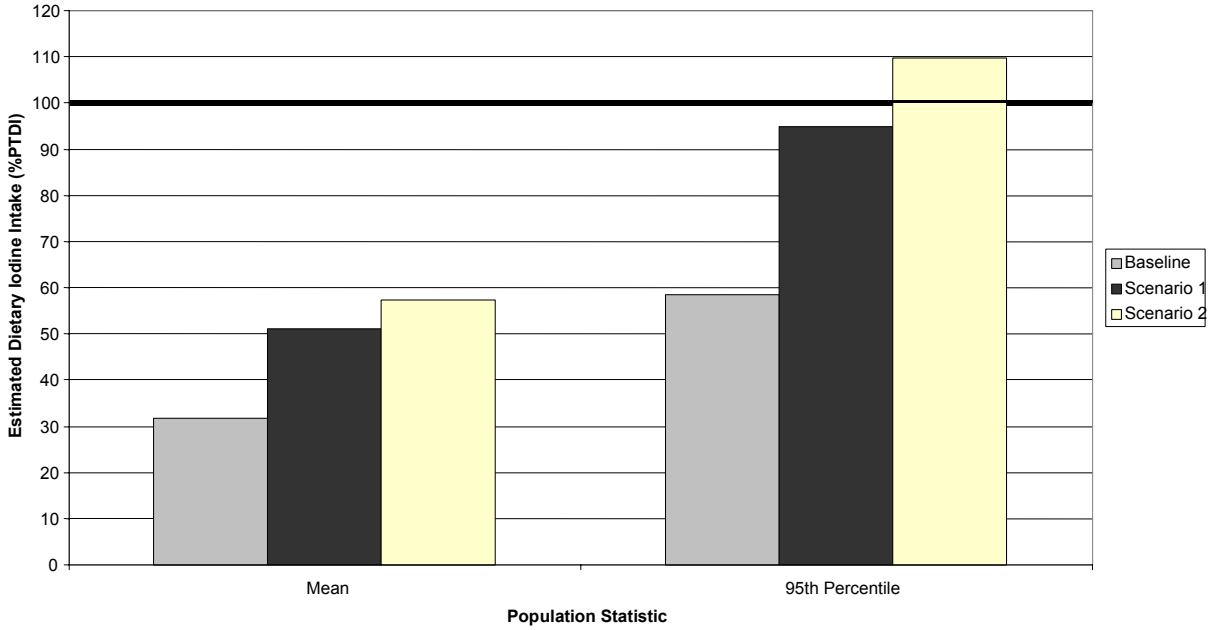
For 'both applications (A493 & A528)', estimated mean and 95th percentile dietary intakes of iodine were below the PTDI for the baseline scenario and for Scenario 1. For Scenario 2, the mean dietary intake of iodine was below the PTDI, with 95th percentile intake exceeding the PTDI (110% PTDI). Scenario 2 assumes that fruits and vegetables that may be consumed with the peel on or off were consumed unpeeled and that all FSFYC contain the proposed maximum iodine level of 70 µg/serve. However, due to the conservative assumptions made in this calculation and that the use of 24-hour dietary survey data tends to over-estimate habitual nutrient intakes for high consumers, it is likely that the 95th percentile dietary intake is an over-estimate of what this age group would be consuming on a daily basis over a lifetime.

For A493, estimated mean dietary intakes of iodine were below the PTDI for Australian children aged 2-3 years for all scenarios examined. Baseline and Scenario 1 estimated 95th percentile dietary intakes of iodine were also below the PTDI, with Scenario 2 estimated 95th percentile dietary iodine intakes exceeding the PTDI (101% PTDI).

For A528, mean and 95th percentile estimated dietary intakes of iodine were below the PTDI in all of the scenarios examined.

The estimated dietary intakes of iodine, as compared to the PTDI, for A493, A528, and 'both applications (A493 & A528)' are shown in Table A2.2 in Appendix 2. From these data, it would appear that the requested permissions from A493 have a greater impact on iodine dietary intakes for Australian children aged 2-3 years than do the requested permissions from A528.

Figure 3: Estimated dietary intakes of iodine, as a percentage of the PTDI



REFERENCES

Food Standards Agency (UK FSA), 2002, *Revised Review of Iodine: Prepared for the Expert Group on Vitamins and Minerals (EVM/00/06.REVISEDAUG2002)*, www.foodstandards.gov.uk/multimedia/pdfs/evm0006p.pdf

Institute of Medicine, National Academy of Sciences, 2000, *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*, National Academy Press, Washington, DC.

National Health and Medical Research Council, 2001, *National Health and Medical Research Council Website (www.health.gov.au/nhmrc/publications/diet)*

Rutishauser I. 2000. *Getting it right:- how to use the data from the 1995 National Nutrition Survey*. Commonwealth of Australia: Canberra

World Health Organisation, 1989, Toxicological evaluation of certain food additives and contaminants (Thirty-third Report of the Joint FAO/WHO Expert Committee on Food Additives), WHO Food Additive Series No. 24, WHO, Geneva.

World Health Organization, 2001, *Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA 1956-2001) (First through fifty-seventh meetings) Internet Edition*, ILSI Press International Life Sciences Institute, Washington DC.

Complete Information on Dietary Intake Assessment Results for 'both applications A493 & A528)'

Table A1.1: Estimated dietary intakes of iodine for Australian children aged 2-3 years

Number of consumers of iodine	Consumers♦ as a % of total respondents#	Mean consumers µg/day (µg/kg bw/day)			95th percentile consumers µg/day (µg/kg bw/day)		
		Baseline	Scenario 1	Scenario 2	Baseline	Scenario 1	Scenario 2
383	100	83.0 (5.4)	133.9 (8.7)	150.2 (9.8)	165.1 (9.9)	258.3 (16.1)	289.4 (18.7)

Total number of respondents for Australia: 2-3 years = 383. Respondents include all members of the survey population whether or not they consumed a food that contains iodine.
♦ Consumers only – This only includes the people who have consumed a food that contain iodine.

Table A1.2: Contribution of each food group to total iodine dietary intake for Australian children aged 2-3 years

Food Name	% Contribution to iodine dietary intake		
	Baseline	Scenario 1	Scenario 2
Dairy products	69.6	49.7	44.3
Fruits:	14.8	27.5	1.2
citrus fruits	11.7	7.3	6.5
pome fruits	1.7	15.9	16.5
Eggs	4.7	3.4	3.0
Vegetables (including herbs):	4.7	15.6	21.6
root & tuber vegetables	1.8	5.1	11.1
Meat & poultry	2.2	1.4	1.2
Cereals	1.8	1.1	1.0
Seafood (including seaweed)	1.0	0.6	0.5
Water	0.6	0.4	0.3
Other foods	0.6	0.4	0.4

Complete Information on Risk Characterisation for 'both applications (A493 & A528)'

Table A2.1: Estimated dietary intakes of iodine for Australian children aged 2-3 years, as a percentage of the PTDI

Number of consumers of iodine	Consumers♦ as a % of total respondents#	Mean consumers (%PTDI)			95th percentile consumers (%PTDI)		
		Baseline	Scenario 1	Scenario 2	Baseline	Scenario 1	Scenario 2
383	100	31.8	51.2	57.5	58.4	94.8	109.7

Total number of respondents for Australia: 2-3 years = 383. Respondents include all members of the survey population whether or not they consumed a food that contains iodine.
♦ Consumers only – This only includes the people who have consumed a food that contains iodine.
* PTDI = 17 µg/kg bw/day

Table A2.2: Estimated dietary intakes of iodine for Australian children aged 2-3 years for consumers, as a percentage of the PTDI for A493, A528, and 'both applications (A493 & A528)'

Application No. –Scenario	Mean dietary intake of iodine for consumers (% PTDI)	95th percentile dietary intake of iodine for consumers (% PTDI)
A493 – Baseline	29.4	54.3
A493 – Scenario 1	45.5	87.9
A493 – Scenario 2	51.7	101.2
A528 – Baseline	31.8	58.4
A528 – Scenario 1	35.1	64.5
'Both applications (A493 & A528)' –- Baseline	31.8	58.4
'Both applications (A493 & A528)' – Scenario 1	51.2	94.8
'Both applications (A493 & A528)' – Scenario 2	57.5	109.7

Total number of respondents for Australia: 2-3 years = 383. In this case, all respondents are consumers. Respondents include all members of the survey population whether or not they consumed a food that contains iodine. Consumers only include the people who have consumed a food that contains iodine.
* PTDI = 17 µg/kg bw/day

ATTACHMENT 4

Nutrition Assessment

Application A528 – Maximum Iodine Limit in Formulated Supplementary Foods for Young Children

The aim of this nutrition risk assessment is to consider the nutritional risks to Australian and New Zealand children from increasing the maximum permitted iodine content of formulated supplementary foods for young children (FSFYC). This assessment will be conducted by reviewing the following nutritional issues:

- the current iodine status of Australian and New Zealand young children;
- the interactions between iodine and other nutrients; and
- the likelihood of adverse health outcomes for young children who consume high iodine intakes.

These issues will inform a determination of the nutritional risks from the proposed amendments to the Code.

1. CURRENT IODINE STATUS OF AUSTRALIAN AND NEW ZEALAND CHILDREN

The International Council for the Control of Iodine Deficiency Disorders (ICCIDD) and the World Health Organization (WHO) have established median urinary iodine concentration criteria for determining a population's iodine status (see Table 1) (ICCIDD 2001). A median of 100 μg/L or greater is recommended by the WHO as being indicative of iodine sufficiency.

Table 1: Epidemiological Criteria for Assessing Iodine Nutrition Based on Median Urinary Iodine Concentrations in School-Aged Children (Iccidd 2001)

Median urinary iodine (μg/L)	Iodine intake	Iodine nutrition
< 20	Insufficient	Severe iodine deficiency
20 – 49	Insufficient	Moderate iodine deficiency
50 – 99	Insufficient	Mild iodine deficiency
100 – 199	Adequate	Optimal
200 – 299	More than adequate	Risk of iodine-induced hyperthyroidism (populations with long-standing iodine deficiency only)
≥300	Excessive	Risk of thyroiditis, goiter, hypothyroidism, autoimmune thyroid diseases, and iodine sensitivity reactions; and in iodine deficient populations, the additional risk of iodine-induced hyperthyroidism.

1.1 Population Iodine Data

In the early 1990s it was reported that there was no evidence of iodine deficiency in Australia (Stanbury 1996). A downward trend in iodine status has been noted in more recent years (Thomson 2002), and has been identified in several Australian and New Zealand urinary iodine studies that specifically focus on children (see Table 2).

While this information is significant, it should be noted that none of the study populations include the FSFYC target group of 1-3 year olds, and can be used only as an indicator rather than as a definitive measurement of iodine status.

Table 2: Results from Australian and New Zealand Urinary Iodine Studies on Children

Author	Study Design	Subject Type and Numbers		Urinary Iodine Results		
				% Subjects with < 50 μg/L	% Subjects with < 100 μg/L	Median concentration (μg/L)
Australian Studies						
Guttikonda *et al* (2003)	Prospective cross-sectional study, conducted at NSW Central Coast primary school. Urine collected as 1st morning spot samples.	301 children 5 -13 years (133 females, 168 males)		14	69	82
Li *et al* (2001)	Randomised cross-sectional study within Sydney. Urine collected as spot samples.	School children 6 - 13 years		13.8	-	84
McDonnell *et al* (2003)	Prospective cross-sectional study within Melbourne. Urine collected as 1st morning spot samples.	577 school children aged 11-18 years.	Male (n=167)	17	68	82
			Female (n=410)	31	79	64
			Total	27	76	70
New Zealand Studies						
Skeaff *et al* (2002)	Randomised cross-sectional study, undertaken across two New Zealand cities.	300 Children aged 8 - 10 years.		31.4	79.7	66
Ministry of Health (2003)	Randomised sampling from representative schools. Urine collected as spot samples.	3275 Children 5 -14 years	Male	25	-	68
			Female	31	-	62
			Total	28	-	66

- = not assessed as part of the study.

Both the WHO and the ICCIDD have established that more than 50% of a population must have a urinary iodine concentration above 100 μg/L before it can be considered iodine replete, and that no more than 20 percent of a population should have urinary iodine levels less than 50 μg/L (ICCIDD 2001). However, as Table 2 demonstrates, a number of the childhood populations studied had more than 20 percent with levels less than 50 μg/L, with only Guttikonda *et al* (2003) and by Li *et al* (2001) as exceptions.

This information indicates that a proportion of Australian and New Zealand 5-18 year old children may not be consuming iodine at sufficient levels to meet their requirements, and suggests that 1-3 year old children may also have inadequate iodine intakes.

As detailed in Table 1, the WHO and ICCIDD have established that a population is at risk of hyperthyroidism if median urinary iodine concentrations are between 200-299 μg/L, and that median concentrations above 300 μg/L represent an excessive population intake of iodine. None of the above studies have produced results that approach these values.

1.2 Iodine Intake Compared to Estimated Average Requirements

An EAR is a value representative of a population's median requirement for the dietary intake of a particular nutrient (in this case iodine). The adequacy of nutrient intakes can therefore be assessed according to the percentage of the population with an intake below the EAR. Where a proportion of the population has an intake less than the EAR, it can be concluded that their distribution of intakes has shifted below the distribution of requirements (IOM 2001).

FSANZ has assessed the dietary iodine status of children by comparing dietary iodine intake data for 2-3 year olds against the EAR. This assessment was undertaken using 1995 Australian National Nutrition Survey information only, as New Zealand dietary information on young children is unavailable. Furthermore, Australia and New Zealand have not established an EAR for iodine, and therefore the US EAR (IOM 2001) has been used as a substitute. Full details of the methodology used by FSANZ for dietary modelling is detailed in the Dietary Exposure Assessment (Attachment 3). The results of this assessment are provided in Table 3 below, and show that 37% of 2-3 year olds consumed iodine below the EAR and thus are likely to have an inadequate iodine intake.

Table 3: Comparison of Australian 2-3 Year-Old Children's Iodine Intakes against the Ear

Scenario	Median Dietary Iodine Intake μg/day (% of EAR)	% of Consumers with Dietary Iodine Intakes < EAR
Baseline dietary pattern*	71.2 (109.5)	43
Baseline dietary pattern, including modelled use of FSFYC#	76.0 (116.9)	37

* This scenario is based on the Australian National Nutrition Survey 1995 (NNS), which does not include data on FSFYC use by 1-3 year olds.

\# This scenario has modified NNS data by applying assumption on the use of FSFYC by 1-3 year olds. A full detail of these assumptions is located in Attachment 3.

1.3 Conclusion

Published urinary iodine studies for 5-18 year old children, and dietary intake data for 1-3 year old children, indicate that there is a level of iodine inadequacy within the population of young children. Although this information is limited to the population groups that were assessed, the results are considered to be generally applicable to young children within Australia and New Zealand.

2. Nutrient Interactions

2.1 Bioavailability

Some nutrients are known to compete with each other for absorption and bioavailability when they are consumed together in the same meal. There is no literature to suggest that iodine inhibits the bioavailability of any other nutrient, however the absorption of dietary iodine can be reduced by the calcium, magnesium and iron content in food and water (SCF 2002). Goitrogens (found in the vegetables of the *Brassica* genus, *Cruciferae* family: cabbage, broccoli, turnips, and Brussels sprouts) can affect the utilisation of dietary iodine in the body by interfering with the biosynthesis of the hormones T3 and T4. Heat from cooking will inactivate most of the goitrogens present in these vegetables.

Of particular importance for Application A528 is that iodine bioavailability can also be compromised by the consumption of soy flour. The digestive by-products of soy flour block the enterohepatic circulation of thyroxine (T_4) (ESCF 2002), and therefore soy-based FSFYC may inadvertently have the potential to affect iodine status. However, this effect is expected to be negligible as it is only the exclusive use of soy products (e.g. feeding of soy-based formulas to infants, who cannot receive nutrition from other sources) that has been known to adversely impact on iodine status, and not supplementary feeding as occurs with FSFYC.

2.2 Selenium and Iodine Interactions

Iodine status is also influenced by selenium intakes. Although iodine is essential for the synthesis of thyroid hormones, selenium-dependent enzymes (iodothyronine deiodinases) are also required for the conversion of T_4 to the biologically active thyroid hormone triiodothyronine (T_3) (Goyens 1987, Vanderpas 1990). Selenium deficiency can thus exacerbate the thyroid complications of iodine toxicity, as the uptake of iodide by the thyroid gland increases in compensation to a reduced T_3 production (ATDSR 2001). The selenium/iodine interaction is particularly important for New Zealand children, as the New Zealand population has a reduced selenium status compared to other countries, and may even border on insufficiency (Thompson 2004).

2.3 Conclusion

The bioavailability of iodine or other nutrients is not likely to be affected as a result of this Application. However, the potential for selenium deficiency to exacerbate iodine deficiency is of importance, as it could impact on the iodine status of young children especially in New Zealand.

3. The Health Consequences for Young Children Who Consume High Levels of Iodine

3.1 Susceptibility of Children to a High Dietary Iodine Intake

Prenatal and newborn infants are susceptible to the effects of a high iodine intake because of an immature thyroid gland. Children in the 1-3 year group, however, have a more mature thyroid gland and are instead vulnerable to iodine toxicity primarily as a result of their lower body weight compared to adults (IOM 2001).

For the majority of healthy individuals, including children, the most sensitive endpoint for iodine toxicity is sub-clinical hypothyroidism. Sub-clinical hypothyroidism is defined as an elevation in thyroid stimulating hormone (TSH) concentration while serum thyroid hormone concentration is maintained within the normal range of values. While not clinically adverse, such an effect could lead to full clinical hypothyroidism over a prolonged period of time.

In children, sub-clinical hypothyroidism has only been associated with very high chronic iodine intakes (1150 μg/day, or 29 μg/kg/day for a 40 kg child). This level was derived from a study by Mu *et al* (1987), which is the only study identified by FSANZ that specifically assesses the susceptibility of a childhood population to high iodine intake levels. The results of the study (see Table 4 below) show that although both groups showed no clinical signs of hypothyroidism or hyperthyroidism, the TSH levels, thyroid size and goitre results demonstrate that sub-clinical hypothyroidism was significantly more prevalent in the group exposed to high intakes of iodine.

Table 4: Details of the Study by Mu *Et Al* (1987)

Study Design	Subject Type and Numbers		Iodine in Drinking Water (μg/L)	Mean Serum Thyroid Hormone Results			% Group with Goitre	Thyroid gland volume (mL)
				TSH (mIU/L)	T_3 (nmol/L)	T_4 (nmol/L)		
Prospective controlled parallel group study, conducted in Central Chinese schools. Thyroid volumes assessed by ultrasonography	School children aged 7-15 years	Huanglou village, control (n=51)	54	3.9+1.0	1.9+0.2#	101+14	15.4*	5.9
		Gaojiabu village, test (n=120)	462.5	7.8+11.0#	1.6+0.3	101+19	65*	13.3#

* = the statistical significance of these results was not documented

\# = this value is significantly higher than the value obtained for the other group ($p<0.05$)

3.2 Health Risks from Iodine Variability

The levels of iodine in the diet can vary significantly over a given period of time due to the natural fluctuations of iodine content across the food supply. The variability of iodine in the food supply, and particularly within milk, has lead United Kingdom and European agencies to conduct assessments on the potential safety risks of dietary iodine fluctuations (ESCF 2002, COT 2000). These assessments recognise that established safety limits for iodine intake do not represent an absolute threshold for toxicity, and that children can tolerate natural iodine fluctuations for a short period of time without any appreciable health risk. As the iodine contents in some FSFYC currently vary in response to the natural iodine fluctuations in their milk ingredients, it is expected that FSFYC consumption will also create low-risk short-term exposures to high iodine intakes.

An assessment of the available information has not revealed whether a similarly low health risk occurs with chronically elevated iodine intakes. Were manufacturers to add permitted forms of iodine as a means of bringing levels up to the maximum limit during times when the iodine contribution from milk ingredients decreases. As a result, FSFYC average iodine levels would be sustained continuously at the maximum permission, making chronic exposures to high iodine intakes more likely. Therefore, without information to suggest a low risk from chronically high iodine intakes, this scenario could pose a higher public health and safety risk than a scenario where dietary intakes are derived purely from natural iodine fluctuations.

The majority of FSFYC manufacturers do not add iodine to compensate for low milk iodine levels. However, if the maximum claimable iodine limit for FSFYC were to also increase to a high level in concert with the maximum content limit, then sections of the industry may see a marketing advantage in adding iodine up to the maximum claimable limit. This would result in the maintenance of iodine contents at a constantly high level.

3.3 Conclusion

Young children are no more susceptible to high iodine intakes than adults (relative to body weights), and the most sensitive health problem – subclinical hypothyroidism – occurs only with very high iodine intakes. Short-term high iodine intakes also represent a low health risk for young children, although the effects from chronically elevated intakes of iodine is unknown. This could represent a potential nutritional risk for Application A528, should the proposed amendments encourage the maintenance of FSFYC iodine contents at constantly higher levels.

4. ASSESSMENT OF NUTRITIONAL RISKS FOR APPLICATION A528

Overall, the risk to the nutrition and health status of 1-3 year olds from Application A528 is minor. An increased dietary iodine intake is unlikely to adversely affect the nutritional status of 1-3 year olds – provided the increase is of a small to moderate degree – due to the presumed reduced iodine status of Australian and New Zealand young children.

This risk assessment has been conducted on the basis of the following findings:

- For the current iodine status of Australian and New Zealand children:
- Although studies are underway to further quantify the current iodine status of the Australian and New Zealand populations, there is sufficient information to determine that a proportion of Australian and New Zealand children currently have a reduced iodine status.

- For the interactions between iodine and other nutrients:

    - an increased supply of iodine from FSFYC is unlikely to adversely affect the bioavailability of other nutrients;
    - the presence of low selenium intakes in New Zealand may, however, exacerbate any iodine deficiencies that are current prevalent amongst children.

- For the likelihood of adverse health outcomes for young children who consume a high iodine intake:

    - children have a similar vulnerability to the adverse health effects that result from high iodine intakes as for other sections of the population (relative to body weight);
    - short-term fluctuations in the iodine content of FSFYC are unlikely to adversely affect the health status of 1-3 year olds;
    - however, a constant supply of iodine from FSFYC at a high level may increase the health risks for 1-3 year olds.

5. OVERALL CONCLUSION

The potential for Application A528 to produce sustained, high iodine contents across the range of FSFYC represents a potential nutritional risk, although this risk is not expected to have a major impact on childhood nutrition. All other nutritional aspects of this Application have been assessed as posing no risk to the nutritional status of 1-3 year old children.

Reference List

Agency for Toxic Substances and Disease Registry (ATSDR) (2001). *Draft toxicological profile for iodine.* U.S. Department of Health and Human Services, Atlanta, GA. http://www.atsdr.cdc.gov/

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) (2000). *Statement on Iodine in Milk.* COT Statement 2000/02, United Kingdom Food Standards Agency, http://www.foodstandards.gov.uk/science/surveillance/maffinfo/2000/maff-2000-198.

European Scientific Committee on Food (ESCF) (2002). *Opinion of the Scientific Committee on Food on the Tolerable Upper Intake of Iodine.* SCF/CS/NUT/UPPLEV/26, European Commission, Brussels.

Goyens P, Golstein J, Nsombola B, Vis H, Dumont JE (1987). Selenium deficiency as a possible factor in the pathogenesis of myxoedematous endemic cretinism. *Acta Endocrinol,* **114**(4): 497-502.

Guttikonda K, Travers C, Lewis P, Boyages S (2003). Iodine deficiency in urban primary school children: a cross-sectional analysis. *Med J Aust.* **179**: 346-348.

Institute of Medicine (IOM) (2001). *Dietary reference intakes*: *Vitamin A, Vitamin K, Arsenic , Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* National Academy Press, Washington DC; p73-105.

International Council for Control of Iodine Deficiency Disorders (ICCIDD) (2001). *Assessment of Iodine Deficiency Disorders and Monitoring their Elimination: A guide for programme managers.* WHO/NHD/01.1. United Nations Children's Fund and World Health Organisation, Geneva.

Li M, Ma G, Guttikonda K, Boyages S, Eastman C (2001). Re-emergence of iodine deficiency in Australia. *Asia Pacific J Clin Nutr.* **10**: 200-203.

McDonnell C, Harris M, Zacharin M (2003). Iodine Deficiency and Goitre in School Children in Melbourne, 2001. *Med J Aust.* **178**: 159-162.

Ministry of Health (2003). *NZ food NZ children: key results of the 2002 National Children's Nutrition Survey*. Ministry of Health, Wellington.

Mu L, Chengyi Q, Quidong Q, Qingzhen J, Eastman CJ, Collins JK, Derun L, Peiying Z, Chunde Z, Huaixing W, Boyages SC, Jupp J (1987). Endemic goiter in Central China caused by excessive iodine intake. *Lancet* **1:** 257 – 258.

Skeaff S, Thomson C, Gibson R (2002). Mild Iodine Deficiency in a Sample of New Zealand Schoolchildren. *Eur J Clin Nutr*. **56**: 1169-1175.

Stanbury J (1996). *Iodine Deficiency and the Iodine Deficiency Disorders*, Present Knowledge in Nutrition, Seventh Edition ILSI press, Washington DC.

Thomson CD (2002). *Australian and New Zealand Nutrient Reference Values for Iodine*, prepared for the New Zealand Ministry of Health.

Thompson CD (2004). Selenium and iodine intakes and status in New Zealand and Australia. *Br J Nutr,* 91(5): 661-672.

Vanderpas JB, Contempre B, Duale NL, Goossens W, Bebe N, Thorpe R, Ntambue K, Dumont J, Thilly CH, Diplock AT (1990). Iodine and selenium deficiency associated with cretinism in northern Zaire. *Am J Clin Nutr,* **52**(6): 1087-93.

ATTACHMENT 5

SUMMARY OF SUBMISSIONS

FSANZ received 7 submissions in response to public consultation on Application A528 – Maximum Iodine Limit in Formulated Supplementary Foods for Young Children (FSFYC), during the 6 week public consultation period of 17 March to 28 April 2004. A summary of submitter comments is provided in the table below.

Two regulatory options were presented in the Initial Assessment Report. These were:

Option 1 – Maintaining the *status quo* by not increasing the permitted maximum iodine limit in FSFYC; or

Option 2 – Amending Standard 2.9.3 to increase the permitted maximum level of iodine in FSFYC from 35µg to 70 µg/serve.

No.	Submitter	Submission Comments
1	Nestlé Robyn Banks	**Supports Option 2** Supports the application for an increase in the permitted iodine level in formulated supplementary foods for young children (FSFYC) at a level where there is no safety concern. <u>Current Market</u> Nestlé does not intentional add iodine to FSFYC. Iodine levels are inherent to the raw materials used. They are aware that some consumers make up their product in milk. However, the amount of iodine permitted to be in a product is based on a serving when prepared according to the manufacturers directions i.e. in water. Therefore this must be used when determining compliance. <u>Iodine variability</u> Iodine levels in milk from northern Victoria range from 3 to 35 µg/100g with an average of 15 µg/100g. Therefore, there is potential for products to be outside the maximum permitted level of iodine. The testing of milk occurs well after the milk is used therefore not possible for fresh milk to be tested for iodine prior to use. It is not easy to modify the production of FSFYC. <u>Impact Analysis</u> In retaining the current permitted maximum level there is potential for batches of product to be rejected creating costs for manufacturers.
2	New Zealand Food Safety Authority (NZFSA) Carole Inkster	**Supports Option 2** Notes that if mandatory iodine fortification is considered for any staple food product, all other sources of iodine in the diet will need to be considered. Upper limits in other food products (such as Formulated Supplementary Foods for Young Children) may need to be reassessed.

No.	Submitter	Submission Comments
3	Heinz Wattie's NZ & Heinz Australia Julie Dick	**Supports Option 1** Believe that Option 2 would be inconsistent with the nature of the Code where maximum permitted levels and/or maximum permitted claimable levels for vitamins and minerals do not go above 50% of the RDI or ESADDI. <u>Iodine Variability</u> Heinz Wattie's manufacture their product using New Zealand milk and advise that they do not have any problems with iodine levels. Recently have commenced adding iodine to meet the 50%RDI level due to the evidence of increasing iodine deficiency in Australian and New Zealand populations. <u>Impact Analysis</u> Disagree with the suggestion that consumer may be adversely affected by possible supply difficulties under Option 1 as Heinz can continue to supply FSFYC under current regulatory permissions. Heinz claim the identified problem exists for the Applicant only. Therefore the cost benefit analysis should identify the issue as particular to the Applicant and not extrapolate across all industry.
4	Dept of Health & Human Services (Tasmania) Judy Seal	Did not support either option noting that it is difficult to make informed comment on applications of this type in the absence of: • up-to-date food intake data; • comprehensive food composition data; • data on nutritional status of the population; and • current nutrient reference values. <u>Iodine Variability</u> Confirms that the Tasmanian data on iodine levels in milk is accurate. Notes that iodine analysis is expensive and that there are limited labs in Australia that are accredited to do iodine analysis. Therefore manufacturers would find it difficult to regulate the iodine level in final products given the iodine variability in milk and limited access to laboratories for testing. Believes that regulating the iodine levels in the raw product i.e. milk may make more sense. Provided information on data available on daily requirements and iodine deficiency in Australian & NZ.
5	Dietitians Association of Australia (DAA) Ruth Kharis	**Supports Option 2** Notes that there have been: • no adverse reports of iodine toxicity in children consuming FSFYC; • reports of iodine deficiency; and that • other countries have higher RDIs for iodine than Australia & NZ, which indicate that levels as high as 100µg per day are quite safe.
6	Fonterra Joan Wright	**Supports Option 2** No additional comments.
7	Food Technology Association of Victoria Inc (FTAV) David Gill	**Supports Option 2** No additional comments