Submission for Iodine

Part A
1. International Non-proprietary Name (or British Approved Name or US Adopted Name) of the medicine.

Iodine (including iodides and iodates).

2. Proprietary name(s).

Not applicable.

3. Name of the company / organisation / individual requesting a reclassification.

Not applicable. This request is made on behalf of the natural health products industry.

4. Dose form(s) and strength(s) for which a change is sought.

Not applicable. This request is made on behalf of the natural health products industry.

5. Pack size and other qualifications.

Not applicable. This request is made on behalf of the natural health products industry.

6. Indications for which change is sought.

Not applicable. This request is made on behalf of the natural health products industry.

7. Present classification of the medicine.

At the present time, iodine is:

- Unscheduled when in medicines for external use containing 2.5% or less.
- Unscheduled when in medicines for internal use containing less than 300 micrograms per recommended daily dose.
- A pharmacy medicine when in medicines for external use containing more than 2.5%.
- A pharmacy medicine when in medicines for internal use containing 300 micrograms or more per recommended daily dose.

8. Classification sought.

It is proposed that the classification of iodine is changed to:

- Unscheduled when in medicines for external use containing 2.5% or less.
- Unscheduled when in medicines for internal use containing 800 micrograms or less per recommended daily dose.
- A pharmacy medicine when in medicines for external use containing more than 2.5%.

- A pharmacy medicine when in medicines for internal use containing more than 800 micrograms per recommended daily dose.

9. Classification status in other countries (Australia, UK, USA, Canada).

Australia
Iodine is:

- Unscheduled when in oral preparations for use in prophylaxis and treatment in the event of radioactive iodine exposure under an emergency plan approved by an appropriate authority.
- Schedule 2 (ie pharmacy medicine) when
  a) in preparations for human internal therapeutic use containing 300 micrograms or more of iodine per recommended daily dose; or
  b) in preparations for human external therapeutic use containing more than 2.5 per cent of available iodine (excluding salts, derivatives or iodophors),
- Schedule 4 (ie prescription medicine) except in the above circumstances

Canada
Iodine and its salts and derivatives are:

- Schedule III (ie unscheduled) when in preparations for topical use or in oral doses of 1mg or less per day.
- Schedule II (ie pharmacy medicine) except topical preparations; except in oral doses of 1 mg or less per day.
- Schedule I (ie prescription medicine) for sodium iodine in injectable form for parenteral nutrition.

Povidone-iodine is:

- Schedule III (ie unscheduled) when in topical preparations, except in concentrations of 5% or less.
- Schedule II (ie pharmacy medicine) when in vaginal preparations, except in concentrations of 5% or less.

UK
Iodine is a general sale medicine below 10 mg.

10. Extent of usage in New Zealand and elsewhere (eg sales volumes) and dates of original consent to distribute.

No information was provided by the applicant.

11. Labelling or draft labelling for the proposed new presentation(s).

No labels or package information was provided by the applicant.

12. Proposed warning statements if applicable.

Iodine occurs naturally in high amounts in edible seaweeds, and these are the most common source of iodine found in supplements. The label may need to include a statement to the effect:

RDI from all sources should not exceed x µg/day.

If the proposed change to the recommended daily dose is accepted, the labels of natural health products containing iodine for oral use may be required to state the following dose recommendations (See Part B below):

Children 1-3 years:	*6-133 µg/day*
Children 4-8 years:	*6-200 µg/day*
Adolescents 9-13 years:	*6-400 µg/day*
Adolescents 14+ years and Adults:	*14-800 µg/day*

The recommended daily intake of iodine from all sources should not exceed 800 µg.

13. Other products containing the same active ingredient(s) and which would be affected by the proposed change.

Manufacturers of current dietary supplement-type products may increase the quantity of iodine compounds in their products, or change their dosing instructions to deliver the maximum dose.

It should be noted that all dietary supplement products will be regulated under the Natural Health Products Bill (NHP Bill). When the NHP Bill is passed, natural health products will have to be manufactured according to a Code of Manufacturing Practice.

<u>Approved medicines containing iodine as the active ingredient</u>

The sole approved medicine for internal use containing iodine, iodides, iodates or povidone-iodine is Elevit with Iodine tablets, containing potassium iodide equivalent to 0.25 mg iodine. This is currently a Pharmacy medicine.

If the proposed change is made, it is possible that the sponsor (Bayer New Zealand Ltd) may reformulate this medicine to deliver the maximum permitted dose. However, the proposed change will not affect the Pharmacy medicine classification status of Elevit with Iodine tablets, which is the result of other active ingredients present in the medicine.

Part B Reasons for requesting classification change including benefit-risk analysis.

Multi-ingredient supplements such as trace elements and essential nutrient formulations are usually taken to complement dietary intake of essential vitamins and minerals. Such products are generally regarded as dietary supplements.

At the present time, under the current Dietary Supplements Regulations regime, therapeutic claims are not permitted for dietary supplements. This creates a peculiar situation where, for example, iron supplements are recognised to aid in the treatment of iron deficiency and iron deficiency anaemia, and are taken for these purposes, yet such products cannot provide advice on their labels on how they should be used. The NHP Bill is intended to address this situation.

When the NHP Act comes into effect, certain health benefits will be able to be claimed for allowed health conditions, provided the manufacturer of the natural health product holds evidence to support the claim(s) being made. For example, iron deficiency anaemia is one of the allowed conditions permitted by the NHP Bill. Similarly, a claim for iodine to help with wound healing could be allowed if there was sufficient evidence.

The clear benefit of allowing the requested change is that it will enable easier implementation of the NHP system by allowing the essential vitamin or mineral to be present in effective quantities or in effective doses in natural health products.

Schedule 1 of the Medicines Regulations 1984 restricts the recommended daily dose for iodine to less than 300 µg/day, in order for medicines to remain unscheduled.

Biotrace Ltd has requested an increase to the scheduled limit of iodine for internal use:

Children 1-3 years:	6-133 µg/day
Children 4-8 years:	6-200 µg/day
Adolescents 9-13 years:	6-400 µg/day
Adolescents 14+ years and Adults:	14-800 µg/day

These values for doses are based on the Health Canada monograph for Iodine, which uses the Upper Limit (IUL) values recommended by the Institute of Medicine (IOM, 2006). These UL values are lower than the UL recommended by the Ministry of Health (MOH, 2006):

Age group and gender		Iodine µg / day		
		EAR	RDI	UL
Children	1-3 years	65	90	200
	4-8 years	65	90	300
Boys	9-13 years	75	120	600
	14-18 years	95	150	900
Girls	9-13 years	75	120	600
	14-18 years	95	150	900
Men	19-30 years	100	150	1,100
	31-50 years	100	150	1,100
	51-70 years	100	150	1,100
	> 70 years	100	150	1,100
Women	19-30 years	100	150	1,100
	31-50 years	100	150	1,100

	51-70 years	100	150	1,100
	> 70 years	100	150	1,100
Pregnancy	14-18 years	160	220	900
	19-30 years	160	220	1,100
	31-50 years	160	220	1,100
Lactation	14-18 years	190	270	900
	19-30 years	190	270	1,100
	31-50 years	190	270	1,100

EAR estimated average requirement
RDI recommended daily intake
UL upper level of intake

Health Canada's recommendation for Recommended Daily Allowance for breastfeeding mothers is slightly higher, at 290 µg/day.

1. A statement of the benefits to both the consumer and to the public expected from the proposed change.

Iodine is an essential nutrient for humans. Although only required in very small amounts, it is an important constituent of thyroid hormones. These hormones regulate many important biochemical reactions, including protein synthesis and enzymatic activity, and are critical for maintaining the body's metabolic state and supporting normal growth and development in children. As iodine is essential for normal brain development, it is particularly important that the unborn baby (foetus) and young children have adequate intake

Iodine is a trace element that is naturally present in some foods, added to others, and available as a dietary supplement. As in many other countries around the world, evidence of iodine deficiency has been observed in New Zealand and in the late 1800s and early 1900s goitre was very common. In order to decrease the incidence, table salt was iodised at a low level from 1924. However, this had little effect and the level was increased to 40-80mg of iodine per kilogram of salt in 1938. When iodised table salt was introduced there was a major public education campaign to ensure people understood the benefits of using iodised salt in the home.

Recent evidence from a number of studies has indicated that the iodine status of New Zealanders is now declining to the point where intervention is again required to ensure that iodine deficiency disorders do not once again widely affect the New Zealand population. These studies have provided the evidence for the decision to add iodised salt to commercially prepared bread from September 2009. For example, a study by Skeaff et al (2005) of breast-fed infants showed that iodine levels were less than half of that of formula-fed infants, reflecting the low iodine concentration of breast milk due to the poor iodine status of breast feeding mothers. The 2002 National Children's Nutrition Survey found that New Zealand children (aged 5-14 years) had mild iodine deficiency and that 28 percent of the children studied had low iodine status. During 2005 a nationwide survey of the iodine status of 170 pregnant women was undertaken by the University of Otago (Pettigrew Porter et al 2006). The results showed moderate iodine deficiency and goitre was found in 7 percent of the women. No differences were found across the regions or between the stages of pregnancy (MOH, 2015).

Since October 2009, regulations have required that non-iodised salt be replaced with iodised salt in all bread except organic bread and bread mixes for making bread at home. This

action was taken to address the re-emergence of deficiency in Australia and New Zealand (Food Standards Australia New Zealand, 2014).

Even at a mild level, iodine deficiency can affect hearing, intelligence and mental capability. Cases of severe iodine deficiency can result in goitre (swelling of the thyroid gland in the neck with associated lethargy) and hypothyroidism (caused by insufficient production of the thyroid hormone by the thyroid gland) (NRC, 2005; Santiago et al, 2004; Vermiglio et al, 2004; Dal Maso et al, 2009).

Iodine may have other physiological functions in the body as well. For example, it appears to play a role in immune response and might have a beneficial effect on mammary dysplasia and fibrocystic breast disease (IOM, 2001).

2. Potential risk of harm to the consumer as a result of the proposed change, and factors to mitigate this risk.

Iodine toxicity
The main concern over iodine is inhibition of thyroid hormone production. Minor concerns involve the possibility of interactions with medicines (see Part B 6 below).

Very high intakes (in excess of the established upper level of intake) of iodine may inhibit thyroid hormone production. A sudden increase in iodine intake in those used to very low intakes for prolonged periods of time can produce iodine-induced hyperthyroidism or thyrotoxicosis.

However, this is unlikely to be an issue for the New Zealand consumer as the decline in iodine levels is relatively recent (MOH, 2015). The safety of therapeutic doses above the UL is evident in the lack of toxicity on the Japanese population, where dietary intake is estimated to be as high as 5,280 µg – 13,800 µg, mostly derived from marine sources. Japan's population suffers no demonstrable increased incidence of autoimmune thyroiditis or hypothyroidism (Patrick, 2008). Some Japanese populations have daily iodine intakes of 50 mg-80 mg (Alternative Medicine Review, 2010).

Some studies have used 3mg to 6mg Iodine to treat fibrocystic breast disease for up to five years with no adverse events observed (Ghent et al, 1993; Kessler, 2004).

3. Ease of self-diagnosis or diagnosis by a pharmacist for the condition indicated.

Not applicable.

4. Relevant comparative data for like compounds.

Not applicable.

5. Local data or special considerations relating to New Zealand.

No information was provided or is available.

6. Interactions with other medicines.

Anti-thyroid medicines can interfere with iodine absorption and cause an additive effect, leading to hypothyroidism (NMD, 2015).

Angiotensin-converting enzyme (ACE) inhibitors and potassium-sparing diurectics may interact with potassium iodide and increase the risk of hyperkalaemia (Pennington, 1990; NMD, 2015).

Use with lithium, which may inhibit thyroid function, may also result in hyperthyroidism (UOM, 2007; Sterling and Heymann, 2000).

The risk of potential interaction with prescribed medications may be managed by requiring products containing more than the current permitted level of iodine (less than 300 µg/day), up to the proposed permitted level of iodine (800 µg/day) to carry a label advisory statement to consult a healthcare practitioner if they are using the above types of medicines.

7. Contraindications and precautions.

No information on contraindications to iodine was found.

8. Possible resistance.

Not applicable.

9. Adverse events - nature, frequency, etc.

10. Potential for abuse or misuse.
Iodine is not habit-forming or a drug of abuse. No potential for abuse or misuse is anticipated.

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