

EuSalt Comments on the Consultation on EFSA Scientific Opinion on Dietary Reference Values for Iodine

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Background document: [EFSA Draft Scientific Opinion on Special Dietary Reference Values for Iodine](#).

I. Introduction

Iodine is an essential nutrient for mammals, being required as a mandatory structural and functional element of thyroid hormones. Through these hormones, iodine has an important role in energy yielding metabolism and on the expression of genes that impact many physiological functions, from embryogenesis to growth and development, neurological and cognitive functions. Iodine deficiency remains a major public health concern in many countries, including some European countries (WHO/UNICEF, 2007b; Zimmermann and Andersson, 2011).

Comment:

Nutrition is still a major concern in both developed and developing countries and the problems related to it tend to differ according to the financial situation on the respective state. This is especially a topic of concern in states, where there is a nutrition transition. Iodine deficiency has been recognised as a worldwide problem for the last century¹. The International Council for Iodine Deficiency Disorders Global Network (ICCIDD GN) has underpinned remarkable progress in ameliorating this problem during the last nearly 30 years and especially during the last decade². The number of iodine deficient countries in the world has decreased from 54 in 2003 to 47 in 2007 and 32 in 2011.³This a remarkable rate of progress has been largely due to intensive work by ICCIDD GN ,UNICEF and WHO. Nevertheless, of these 32 countries 11 (34%) are in Europe, the largest number from any continent.⁴

EuSalt supports UNICEF and WHO's policy for the addition of nutrients such as iodine, fluoride or folic acid to salt in order to counter this problem. As stated by the WHO, iodine deficiency is in fact the most common, yet preventable, cause of brain damage worldwide. It has been established that there is a definite relationship between the dietary intake of iodine and contribution to normal cognitive and neurological function. We further support the EFSA Panel's considerations regarding food as a source of iodine, as per Annex to Regulation (EC) No 1924/2006. Such amounts can indeed be easily consumed as part of a balanced diet. The iodisation of salt is still considered to be the easiest and most efficient way to counter iodine deficiency and even though many low- and middle-income countries may not

¹ Hetzel BS: The development of a global program for the elimination of brain damage due to iodine deficiency. *Asia Pac J Clin Nutr* 2012;21:164-170.

² Andersson, M. Karumbunathan, V. Zimmermann, M.B.: Global iodine status in 2011 and trends over the past decade. *J Nutr* 2012; 142: 744–750.

³ Zimmermann, MB Andersson, M: Update of iodine status worldwide. *Curr Opin Endocrinol Diabetes Obes* 2012;19: 382-387.

⁴ Ibid.

have the resources necessary for monitoring, an integrated and proactive approach could help overcome this barrier.

[2.2.2.] Health consequences of deficiency and excess

According to their thyroid status, individuals are classified as euthyroid (i.e. having normal thyroid function), hypothyroid or hyperthyroid. Various mechanisms can lead to thyroid disorders, and hypo- and hyperthyroid status can be observed in cases of both insufficient and excessive iodine intakes.

Comment:

Iodine deficiency is now known to have multiple adverse effects on health. Disorders, caused by this deficiency, also known as IDD, all result from inadequate thyroid hormone. Even though some IDDs are more common than others, those related to cognitive impairment should be the focal point of concern. The clinical effects are seen at all stages of development and are particularly noticeable in the fetus, the neonate and the infant as goitre, this being the commonest cause of human thyroid disease. Furthermore, according to a study, reviewed by Prof. Zimmermann, iodine-deficient thyroid takes up more radioactive iodine, which increases the risk of more severe health impairment.

Currently, iodine deficient soils are common in industrialized countries across Europe, the Midwest in North America, southern Australia. And it is the commonality of the issue that calls for comprehensive counter- strategy that is to be implemented at a global level.

At the other side of the spectrum stands another issue related to health consequences. There is currently a great risk of iodine overdose if inappropriate actions are taken, hence a safe approach and controlled approach is required. It is crucial to be noted that if the introduction of iodised salt to combat IDD is accompanied by poor monitoring of the quality of the iodised salt and of the iodine intake of the affected population cases of iodine-induced hyperthyroidism will occur. This was noted in Zimbabwe and the Democratic Republic of Congo⁵ (Intake of water containing 1 mg I-/L caused impaired iodotyrosine formation in 13% of individuals. In asthmatics and bronchitics treated with KI some 0.5% developed myxoedema and 0.2% showed slight thyroid enlargement. In cystic fibrosis patients treated with saturated KI solution some 15% developed goitre, 5%hypothyroidism and 5% goitre plus hypothyroidism'.⁶ Furthermore, the aforementioned statement, supported by Prof. Gerasimov, a consultant at UNICEF, should be leading for the conclusions of this consultation. It should be closely considered that a transitory increase of hyperthyroidism may occur with a rapid increase of iodine intake, particularly in the elderly population, hence a rather progressive increase would allow for effective control and would prevent such an overdose. Several strategies regarding the control and monitoring of iodine intake have been launched by Member States with different degrees of success. Now a common approach is required, so as to ensure the health of the future generations.

⁵ Delange et al., 1999

⁶ Opinion of the Scientific Committee on Food on Tolerable Upper Intake Level of Iodine, 2002

[3.1.] Dietary sources

Iodine occurs in food and water mainly as iodide. Iodine can also enter the food chain via sanitising solutions and iodophores, which may provide significant amounts of iodine but are difficult to control (Phillips, 1997). Iodine readily binds to double bonds in fatty acids, allowing the preparation of iodised oils that are used for supplementation outside the EU (EFSA ANS Panel, 2013. The iodine content of foods is highly variable between food categories as well as within each category. The richest sources are marine products (such as fish, shellfish and molluscs), eggs and milk, as well as their derivatives and iodised salt.

Comment:

As discussed in the Dietary sources section of this Consultation, there are many sources of iodine, number of which differs at state to state basis. Milk for instance remains the major source of dietary iodine in the UK. 'Milk and dairy products contain relatively high amounts derived from iodinated cattle feed supplements, from iodophor medication, iodine-containing sterilizers of milking equipment, teat dips and udder washes. Some of the iodide in cereal products derives from iodate-containing dough conditioners. Other sources of iodide in food are iodised salt (Germany: 15- 25 mg I/kg as KIO₃; Austria 20 mg I/kg as KI; Switzerland 25 mg I/kg as KI), bread and sugar supplemented with iodide in some countries, and iodine-containing herbicides/fungicides. Cooking reduces the iodine content of food, frying by 20%, grilling by 23% and boiling by 58%.'⁷

However, iodised salt or IS is considered to be the universal method for ID prevention. From 1991 to 2011 global consumption of iodised salt on household level increased from 10 to 70 per cent. However, this percentage is not equally distributed among countries. For instance, in the UK and Ireland, iodised salt makes up less than 5% of all salt consumed. That is why alternative vehicles to carry iodine are being investigated.

However, what is needed is in fact salt iodization- or iodine fortification of salt for domestic, public and agricultural uses. This is to be implemented so as to have dual effect- decreasing iodine deficiency levels without impeding the implementation of salt reduction strategies. Even though these may seem contradictory, there are no sufficient barriers apart from the need for inclusion of states' differentiating consumer patterns and existing programs, agreement on a European/global level regarding recommended quantities of iodine and monitoring and control.

[3.2.] Dietary intake

Dietary assessment methods do not accurately quantify habitual iodine intakes. The lack of accuracy in measuring iodine intake from iodised salt is a major limitation of dietary assessment. In addition, the quality of iodine data in food composition tables is often poor, and depends on whether the food iodine analysis is up-to-date and to what extent natural variability in iodine content is taken into account. Food composition databases generally contain information on the salt content of foods, but they rarely specify if the salt used in processed foods is iodised or not. Because

⁷ Ibid.

of these limitations, UI excretion as a valuable marker of iodine intake (see Section 2.4.1) is listed for various European countries in Appendix B.

Comment:

EuSalt supports a legislative market approach for iodine intake, that is to be very selective, progressive and closely monitored allowing the free marketing of iodized salt.

During the WHO Expert Consultation, 21–22 March 2007, Luxembourg USI was recommended as the strategy to control iodine deficiency and urged for the continuation of currently established successful programs. Furthermore, there has been a recommendation that multinational food industries should harmonize the salt content of their products according to lowest threshold possible to avoid variations in products in different countries. The meeting concluded that the policies for salt iodization and reduction of salt to less than 5 g/day are compatible, cost-effective and of great public health benefit.

Another recommendation circulating amongst interested parties has been that increasing the content of iodine fortified salt for instance in baked goods will be an easy and effective option. The target group being the general population and as bread is one of the most commonly consumed foods, it has been concluded in previous surveys and research that it would prove easier and more efficient to implement, as well as regulate the iodine content in one food item instead of many. Moreover, this would decrease the risk of over dosage, referred to previously. Such a selective approach is particularly relevant in countries affected by MID, like Belgium for instance. Barriers of course may occur due to lack of normative base, and arising economic issues such as effects on price and labelling. Furthermore, concerns arise due to difference of dietary preferences of the population in different countries, a point raised in previous comments to this consultation. Hence additional vehicles for iodine intake are not to be disregarded.

[4.3] Pregnancy

Comment:

In general the iodine deficiency is mild, but nevertheless this may impact on childhood development. For example, mild-moderate iodine deficiency in the first trimester of pregnancy was associated with increased odds of offspring intelligence quotient (IQ) being in the lowest quartile (OR 1.43 95%CI 1.04, 1.98, $p=0.03$) with the greatest negative impact observed with verbal IQ (OR 1.66, 95%CI 1.20, 2.31, $p=0.002$).⁸ Review of the current evidence indicates that correction of mild-to-moderate iodine deficiency improves cognitive performance in school age children but there is insufficient data on developmental outcomes in early life⁹. There are 2 randomised studies of iodine supplementation in children with mild iodine deficiency in Albania¹⁰ and New Zealand showing improved cognition. However, large scale controlled trials are now needed to clarify whether gestational iodine

⁸ Bath SC, Steer CD, Golding J, Emmett P & Rayman MP: Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). *Lancet* 2013;382:331-337.

⁹ Taylor PN, Okosieme OE, Dayan CM, Lazarus JH: Impact of iodine supplementation in mild-to-moderate iodine deficiency: systematic review and meta-analysis. *Eur J Endocrinol* 2013 Nov 22;170(1):R1-R15. doi: 10.1530/EJE-13-0651.

¹⁰ Zimmermann MB, Connolly K, Bozo M, Bridson J, Rohner F, Grimci L: Iodine supplementation improves cognition in iodine-deficient schoolchildren in Albania: a randomized, controlled, double-blind study. *Am J Clin Nutr* 2006;83:108-114

supplementation will benefit infant and childhood neurodevelopment in more European countries with marginal iodine deficiency.

As a conclusion from a study¹¹, successful iodine supplementation must target reproductive-age and pregnant women and be substantiated by ongoing monitoring during pregnancy and lactation. A mandatory salt iodisation has international endorsement, and should be considered the preferred strategy for eliminating iodine deficiency.

While diet-induced hypothyroidism can occur at any stage of life, the vast consequences of ID take place during fetal development and early childhood. Iodine deficiency during pregnancy can cause miscarriage, stillbirth and congenital abnormalities such as cretinism. The WHO, United Nations Children's Fund (UNICEF) and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) Global Network recommend an intake of 220–290 µg/day for pregnant and lactating women and salt has continued to be the most common food vehicle for iodine fortification.

A few country examples will illustrate the situation further. In The Netherlands iodine intake in pregnant women is sufficient as determined by a single urinary iodine measurement in >1000 pregnant women in Rotterdam with a median UI of 225µg/L¹². This is in contrast to Norway where the median UI was <100µg/L in an admittedly smaller sample¹³. In Poland there has been an improvement in median UI in pregnancy from 2010 (105µg/L) to 121µg/L in 2011 but this figure is still suboptimal¹⁴. A comprehensive evaluation of iodine status in pregnancy in Belgium has shown that median UI values are suboptimal¹⁵. This is despite the fact that 60% of women reported taking iodine supplements during gestation¹⁶. Interestingly the frequency of elevated neonatal TSH was still low (3%) in this population¹⁷. In Denmark, while the majority of pregnant women took iodine-containing supplements,

¹¹ John R Burgess, Judy A Seal, Georgina M Stilwell, Peter J Reynolds, E Roscoe Taylor and Venkat Parameswaran, A case for universal salt iodisation to correct iodine deficiency in pregnancy: another salutary lesson from Tasmania; 2007

¹² Medici M, Ghassabian A, Visser W, de Muinck Keizer-Schrama SM, Jaddoe VW, Visser WE, Hooijkaas H, Hofman A, Steegers EA, Bongers-Schokking JJ, Ross HA, Tiemeier H, Visser TJ, de Rijke YB, Peeters RP. Women with high early pregnancy urinary iodine levels have an increased risk of hyperthyroid newborns: the population-based Generation R Study. *Clin Endocrinol (Oxf)*. 2013 Aug 31. doi: 10.1111/cen.12321. [Epub ahead of print]

¹³ Brantsæter AL, Abel MH, Haugen M, Meltzer HM: Risk of Suboptimal Iodine Intake in Pregnant Norwegian Women. *Nutrients* 2013; 5: 424-440

¹⁴ Szybiński Z: Work of the Polish Council for Control of Iodine Deficiency Disorders, and the model of iodine prophylaxis in Poland. *Pol J Endocrinol* 2012; 63: 85–89

¹⁵ Moreno-Reyes R, Glinoe D, Van Oyen H, Vandevijvere S: High prevalence of thyroid disorders in pregnant women in a mildly iodine-deficient country: a population-based study. *J Clin Endocrinol Metab* 2013;98:3694-3701.

¹⁶ Vandevijvere S, Amsalkhir S, Mourri AB, Van Oyen H, Moreno-Reyes R: Iodine deficiency among Belgian pregnant women not fully corrected by iodine-containing multivitamins: a national cross-sectional survey. *Br J Nutr*. 2013;109:2276-2284.

¹⁷ Vandevijvere S, Coucke W, Vanderpas J, Trumpff C, Fauvart M, Meulemans A, Marie S, Vincent MF, Schoos R, Boemer F, Vanwynsberghe T, Philips E, Eyskens F, Wuyts B, Selimaj V, Van Overmeire B, Kirkpatrick C, Van Oyen H, Moreno-Reyes R: Neonatal thyroid-stimulating hormone concentrations in Belgium: a useful indicator for detecting mild iodine deficiency? *PLoS One*. 2012;7(10):e47770. doi: 10.1371/journal.pone.0047770.

the subgroup of non-users was still iodine-deficient after the introduction of iodine fortification of salt¹⁸.

Conclusions and Recommendations related to salt

There is re-emerging iodine deficiency in industrialized countries of Europe although the iodine status of some countries is satisfactory. Of particular concern is the fact that many countries have inadequate iodine nutrition in their pregnant women. It also appears that about 400m people from 20 countries have no or limited access to iodised salt. The demonstration of adequate iodine intake in some sections of the population (eg. schoolchildren) should not be a barrier to recommending a national salt iodization program.

The endorsement of SI whereby salt for human and animal consumption is iodised (including salt for processing), would lead to health improvement on a global scale- through the setting of health goals, increasing customer awareness and coherence between policies of reducing salt consumption to prevent NCDs and the policy of salt iodization to eliminate iodine deficiency disorders. The fact that many countries have adopted USI in response to the resolution passed in the 43rd World Health Assembly that addressed the elimination of iodine deficiency disorders can serve as an initiation of a global process in this direction. However authorities should remain cautious and incorporate the differences among countries' consumption preferences and consider adjustment in national strategies.

Currently, in the WHO European Region (EURO), 26 of the 53 EURO Member States have operational salt reduction policies. However, few countries have adopted salt iodization, as this requires appropriate legislation, regulation and surveillance. A strategy, that only addresses mandatory fortification of table salt or its use in one or a range of products, as previously suggested may have limitations. By contrast, salt iodization mandated by law and successfully implemented can be a more equitable strategy, having larger outreach, readily monitored and flexible due to the possibility for adjustment of fortification levels. ICCIDD GN has an admirable record in advocacy during the past nearly 30 years in relation to promotion of salt iodisation and increasing awareness of iodine deficiency and its adverse consequences particularly in children. A significant population in Europe is mildly deficient in iodine; an increase in dietary iodine consumption by 50-100 mcg/day would be beneficial with minimal or no adverse consequences.

¹⁸ Andersen SL, Sørensen LK, Krejbjerg A, Møller M Laurberg P: Iodine deficiency in Danish pregnant women, Dan Med J 2013;60:A4657.