TOX/2020/61

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

First draft statement on the potential effects that excess iodine intake may have during preconception, pregnancy and lactation.

Background

1. The Scientific Advisory Committee on Nutrition (SACN) last considered maternal diet and nutrition in relation to offspring health in its reports on 'The influence of maternal, fetal and child nutrition on the development of chronic disease in later life' (SACN, 2011) and on 'Feeding in the first year of life' (SACN, 2018). In the latter report, the impact of breastfeeding on maternal health was also considered. In 2019, SACN agreed to conduct a risk assessment on nutrition and maternal health focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery; this would include the effects of chemical contaminants and excess nutrients in the diet.

2. SACN agreed that, where appropriate, other expert Committees would be consulted and asked to complete risk assessments e.g. in the area of safety advice. A provisional list of chemicals was proposed by SACN and updated and amended following discussions by COT who will be guiding the toxicological risk assessment process.

3. Iodine is an essential micronutrient in the human diet, required for the production of thyroid hormones including thyroxine. These hormones are necessary for cell metabolism, growth and development at all stages of life. The most visible manifestation of iodine deficiency is goitre - an enlargement of the thyroid gland in the neck but there is concern, that in the fetus, infant, and young child, more modest changes may impair psychomotor development in the absence of overt thyroid enlargement in the mother (SACN, 2014). Excess iodine may lead to compensatory thyroid hypertrophy.

4. The National Diet and Nutrition Survey (NDNS) suggests that children aged ten years and younger and adults aged 19 years and older in the UK generally have adequate iodine intakes. Pregnant and lactating women are not included in the NDNS, however, data from women of childbearing age

indicate that iodine intake is not sufficient in pregnant and lactating women. The NDNS Rolling Programme data for years 7 to 8 of the survey, published in 2018, showed that the median urinary iodine for women of childbearing age (16 to 49 years) was 102 µg/L with 17% of the population below 50 µg/L. While these values met the WHO criterion for adequate intake for the general population, they did not meet the criterion for iodine sufficiency in pregnant and lactating women (i.e. median urinary iodine concentration within 150-249 µg/L) (Bates et al, 2018).

5. The COT was asked to consider whether exposure to excess intake of iodine would pose a risk to maternal health in a discussion paper (TOX/2020/54)[1]. The Committee considered iodine intake in the population but also considered smaller groups who may be exposed to higher levels of dietary iodine.

6. The Committee are asked to consider the draft statement presented at Annex A.

Questions for the Committee

Members are asked to consider the following questions:

a) Do members have any comments on the structure and content of the statement?

b) Does the Committee have any further comments?

Secretariat

November 2020

[1] TOX/2020/54 is available on the COT website

TOX/2020/61 ANNEX A

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

First draft statement on the potential effects that excess iodine intake may have during preconception, pregnancy and lactation.

Background

1. In the environment, iodine is usually found in the form of iodate salts or organo-iodide compounds synthesised by algae and bacteria. Iodate is reduced in the gastrointestinal tract to iodide which is the biologically active from of iodine (SACN, 2014).

Iodine function

2. Iodine is essential in the human diet primarily because it is required for the synthesis of the thyroid hormones tri-iodo- and tetra-iodothyronine (T3 and T4 or thyroxine). The thyroid hormones exert effects on a wide range of bodily functions such as basal metabolism, brain development and bone growth, especially in the fetus, which is exposed to iodine via the placenta, so maternal underexposure by iodine deficiency can have profound effects on both mother and offspring. Both chronic iodine deficiency and excess may lead to compensatory thyroid hypertrophy, known as goitre, in adults and children. Iodine deficiency in pregnancy is also associated with an increased risk of miscarriage, stillbirth and congenital abnormality. Iodine deficiency in the developing fetus can lead to congenital hypothyroidism (previously known as cretinism), which can have serious effects on both physical and mental development. Clinical features of acute iodine toxicity include vomiting and diarrhoea, seizure, delirium and collapsing. Sensitivity reactions such as iodide mumps following treatment with iodine-containing medication may also occur (EVM, 2003).

Iodine function and status in pregnancy

3. Thyroid function and iodine levels are altered during pregnancy. In early gestation, maternal thyroid hormone production increases in response to the Thyroid Stimulating Hormone (TSH) (Glinoer, 2001). It is possible that the increase in glomerular filtration rate (GFR) results in a decrease to the

circulating pool of plasma iodine (Glinoer, 2007; Gaberscek and Zaletel, 2011); it is unclear if this might be mitigated by increased renal retention of iodine. Additionally, any fall in plasma iodine concentrations would also be attributable, in part of least, to expansion of the plasma volume. A proportion of maternal thyroid hormone is transferred to the fetus, as in iodine via the placental NIS (Sodium Iodide symporter) (Glinoer, 2001; Zimmermann, 2009).

4. Urinary iodine concentration (UIC) is a good indicator of short-term iodine status as >90% of dietary iodine eventually appears in urine (Rohner, 2014). A median UIC of ≤100 µg/L specifies insufficient iodine intake, a median UIC of ≥100 µg/L indicates adequate iodine intake for women who are breastfeeding their infants and children under two years of age (Harding, 2017). UIC levels of >500 µg/kg are considered excessive in pregnant women (WHO, UNICEF and ICCIDD, 2007).

5. As an alternative to UIC, Katko et al (2018) used plasma thyroglobulin (Tg) as a measure of iodine status in 164 pregnant Hungarian women in week 16 of pregnancy, the period corresponding to major brain development. They found that UIC corresponded with daily iodine intake whereas Tg corresponded with long-term storage levels of iodine.

6. Sixteen healthy lactating American women with no known history of thyroid disease were administered 600 µg oral potassium iodide (KI) (456 µg iodine) after an overnight fast. Iodide measurements were taken from breastmilk and urine at baseline and hourly for 8 hours following iodine intake. All dietary iodine ingested during the study period was also measured. Baseline breastmilk and urine iodine levels were 45.5 µg/L and 67.5 µg/L, respectively. Following 600 µg KI administration, median increase in breastmilk iodine levels above baseline was 280.5 µg/L and median peak breastmilk iodine concentration was 354 µg/L. Median time to peak breastmilk iodine levels following KI administration was 6 hours (IQR 5– 7). Dietary iodine sources provided an additional 36–685 µg iodine intake during the 8-hour study. It was concluded that breastmilk iodine concentrations can be interpreted in relation to recent iodine intake (Leung et al, 2012).

7. Although, iodine-deficiency is a known issue in maternal health, excess iodine intake may also occur and may potentially affect maternal health. Sources of excess iodine intake may occur via the consumption of naturally occurring iodine in water supplies, seaweed, iodine supplements, medication and milk which contains iodine resulting from feed supplements and iodophor disinfectants. Most healthy individuals are unaffected by excess iodine, however susceptible individuals such as those who have other thyroid disorders (e.g. Hashimoto's Disease, Grave' Disease) and those who are sensitive to iodine are more likely to respond adversely to excess iodine. The

excessive intake of iodine during pregnancy may have an adverse effect on the fetus without affecting the mother's health. (JECFA, 1989).

8. Excessive iodine dietary intake and/or iodine supplementation during pregnancy may cause adverse effects on maternal and fetal thyroid function, birth outcomes, and offspring growth and development (Le et al, 2018). Excess iodine briefly inhibits thyroid hormone synthesis through decreasing organification[2] by an autoregulatory mechanism known as the acute Wolff-Chaikoff effect (Wolff et al, 1949); The Wolff-Chaikov effects thus prevents the production of excess thyroid hormones in response to the intake of high levels of iodine. Healthy individuals can escape the Wolff-Chaikoff effect via downregulation of the sodium/iodide symporter in the thyrocytes, after which normal thyroid hormone synthesis restarts (Eng et al, 1999; Markou et al, 2001). Although the mechanism is not completely understood, susceptible individuals fail to escape the Wolff-Chaikoff effect. Under 36 weeks of gestational age, the immature fetal thyroid gland is unable to escape from the acute Wolff-Chaikoff effect, making the fetus and infant more susceptible to iodine-induced hypothyroidism (Markou et al, 2001). Neonates are also more susceptible to suffer possible tracheal compression. However, it was reported that the condition may regress spontaneously postnatally after several months (SCF, 2006).

Excess iodine – human health studies

9. In some countries, including Denmark, iodine deficiency in the population has been addressed through the mandatory iodization of all salt, including table salt and salt in bread. Monitoring instigated prior to mandatory fortification in Denmark found an increase in thyroid autoantibodies and higher levels of thyroid autoimmune disease in the 15 years following fortification (Laurberg et al, 2008; Rasmussen et al, 2008; Pedersen et al, 2011; Bliddal et al, 2015). The UK has no such fortification scheme for iodine.

10. The association of thyroid nodules (TNs)[3] and iodine intake in pregnant women was investigated in a study by (Gao et al, 2019). Serum and spot urine samples from 2353 pregnant women were collected. Urine iodine concentration (UIC) and creatinine (Cr) level were determined in spot urine samples, serum thyroid hormones and thyroid autoantibodies. The UIC and

[2] Organification: A biochemical process that takes place in thyroid gland. Iodine is incorporated into thyroglobulin for the production of thyroid hormone (Comprehensive Pharmacy Review)
[3] Thyroid nodule (TNs): TNs are solid or fluid-filled lumps that form within the thyroid (Mayoclinic, 2020).

UIC to creatinine ratio (I/Cr ratio) was found to be significantly higher in pregnant women with TNs. Thyroglobulin, age, pre-pregnancy body mass index and iodine-excessive region were associated with TNs. The I/Cr ratio was not a significant risk factor for TNs in pregnant women in their second trimester.

11. The effects of high iodine intake on thyroid function in pregnant and lactating women was investigated in China. An epidemiological study was conducted among 130 pregnant women and 220 lactating women aged 19 – 40 years in areas that had a drinking water iodine content of >300 and 50-100 µg/L in Shanxi in 2014. Urinary iodine levels and blood thyroid stimulating hormone levels were examined. It was concluded that excess iodine intake might increase the risk of subclinical hypothyroidism in pregnant women and lactating women. It was suggested that iodine nutrition and thyroid function should be monitored in women, pregnant women and lactating women who live in areas with high environmental iodine. (Ren et al, 2018).

12. A cross-sectional study was performed amongst 111 lactating women in a refugee camp in Algeria who lived in areas with high and very high iodine concentrations in drinking water. Breast milk iodine concentration (BMIC), UIC and the iodine concentration in the most commonly consumed foods/drinks were measured. A 24-h dietary recall was used to estimate iodine intake. Thyroid hormones and antibodies were measured in serum. Median UIC, BMIC and iodine intake across both areas were 350 µg/L, 479 µg/L and 407 µg/day, respectively. Thyroid dysfunction and/or positive thyroid antibodies were found in 33.3% of the women, of which 18.9% had hypothyroidism and 8.1% had hyperthyroidism and 6.3% had positive antibodies with normal thyroid function. Elevated thyroid antibodies were in total found in 17.1% of the women. There was no difference in the distribution of thyroid dysfunction or positive antibodies between high iodine and very high iodine drink water areas. It was found that BMIC could be considered as a good indication for iodine status among lactating women. There was an association found between BMIC and thyroid dysfunction and positive antibodies, which indicated that thyroid dysfunction may be caused by an excessive iodine intake. The high prevalence of thyroid dysfunction and the chronically high intake of iodine might have adverse health consequences for the women and their children. (Akare et al, 2015).

13. Three years after the baseline study described above (Akare et al, 2015) a follow-up study was conducted. This included seventy-six children from the original study with a new sample of randomly selected children being included to increase the sample size to 289. At follow-up, urinary iodine, and blood levels of thyroid hormones and serum thyroglobulin were measured. Excessive iodine intake (defined as urinary iodine levels of ≥300 µg/L) was

identified in 88% of the group at baseline (children aged 0 – 6 months) and 72% at follow-up (3 years later). At follow-up, 24% of the study group had thyroid hormone disturbance and 9% had subclinical hypothyroidism. Children with subclinical hypothyroidism showed poorer growth and were more likely to be underweight than those without (Aakre et al, 2016).

14. Case reports were collected following the recall of a prenatal supplement containing excessive iodine levels in Brazil. In all cases, the infant was born with goitre. In the first case, a pregnant woman at 22 weeks' gestation was diagnosed with fetal goitre via a prenatal ultrasound. It was reported that she had taken 2 prenatal vitamin pills/day which was requested for at a local pharmacy. The maternal UIC on the 24th week of gestation was 902 µg/24 h (normal 100 – 460 µg/24 h). The prenatal vitamin was analysed and found to contain 40 mg of potassium iodide per pill. It was found that the pregnant woman was exceeding the recommended dose of 200 µg. The prenatal vitamins were discontinued. No iodine doses were reported in the remaining case reports.(de Vasconcellos Thomas and Collett-Solberg, 2009).

15. There is also evidence that excessive iodine supplementation during pregnancy can increase serum TSH concentrations and thus have a negative impact on maternal thyroid function. In one observational study, pregnant women who ingested supplements containing >200 µg /d were found to be at an increased risk of hyperthyrotropinemia and a TSH above 3 muU/ml (Rebagliato et al, 2010).

16. Human epidemiological studies have shown variations in the incidence of thyroid cancer. In the past, Iceland has been known for its population's excess iodine intake from seafood and milk. Between 1944 to 1964, surgical specimens from Iceland and northern Scotland were compared. The PTC (Papillary thyroid cancer):FTC (Follicular thyroid cancer) ratio was 6.5 in Iceland and 3.6 in Scotland. The age-specific incidence rates for papillary carcinoma were approximately five times higher in Iceland than in Scotland in adults older than 35 years of age. It was hypothesised that high iodine intakes contributed to the high incidence of thyroid cancer in cancer. However, it was argued the high rates are due to the volcanic nature of the island (Williams et al, 1977; Feldt-Rasmussen, 2001). Between 2003 and 2008 the German population had sufficient iodine intakes from voluntary iodization of salt. The incidence rate of thyroid cancer rose from 2.7 to 3.4 (men) and from 6.5 to 8.9 (women) per 100,000 per year and was mainly PTC (Radespiel-Troger et al, 2014).

Excess iodine – animal studies

17. Rats were fed a diet containing excess iodine (~120 mg of iodine per day) or a control diet for 9 months. There was a 40% increase in thyroid weight, and histologic changed included enlarged follicles with increased colloid lined by flattened epithelia, but no thyroid tumours were found (Correa et al, 1960).

Health based guidance values

18. The Expert Group on Vitamins and Minerals (EVM) looked in detail at the metabolism of iodine and the effect of excess iodine in 2003. EVM examined iodine but were unable to set a safe upper limit (SUL) due to lack of data. It was noted that supplemental doses of 0.5 to 1.5 mg iodine/day showed a decrease in the thyroid hormone levels (Paul et al, 1988; Chow et al, 1991; Gardner et al, 1988). The Saxena et al, 1962; Freund et al, 1966 studies indicated that the supplemental doses of 2 mg/day in addition to the dietary iodine resulted in the blockage of further iodine uptake. For guidance purposes, the EVM indicated that a level of 0.5 mg/day of supplemental iodine in addition to the background intake of 0.43 mg/day (equivalent to 0.015 mg/kg bw/day in 60 kg adult) would be unlikely to cause adverse effects in adults based on slight decreases in serum thyroid hormone levels at supplemental doses of 0-2 mg/day in a range of human studies.

19. In 2002, the European Scientific Committee on Food published an opinion on the tolerable upper intake levels of vitamins and minerals. For iodine, they set a tolerable upper level (TUL) for total iodine intake of 600 µg/day, based on the finding that biochemical changes in TSH levels and the TSH response to TRH administration were marginal and not associated with any clinical adverse effects at estimated intakes of 1700 and 1800 µg/day. The studies on which these UL estimates were based were all only of short duration, with a small number of individuals but the results were supported by a 5- year study of exposure with an iodide intake of 30 µg/kg bw/day (equivalent to1800 µg iodide/day for a 60 kg adult), where there was no clinical thyroid pathology. An uncertainty factor (UF) of 3 was considered adequate and provided the UL for adults The UL of 600 µg was also considered to be acceptable for pregnant and lactating women based on of lack of adverse effects at significantly higher exposures (SCF, 2006).

20. JECFA established a provisional Maximum Tolerable Daily Intake (PMTDI) of 17 µg/kg bw/day (equivalent to 1020 µg/day for a 60 kg adult) for iodine from all sources, based on an epidemiological study in which 750 men and women were exposed to iodinated water in prison and consumed 1-2 mg of iodine per day for various time periods. Adverse effects were observed in four women who had previous thyroid issues before entering prison and

became more symptomatic receiving the iodinated water supply. Out of 15 tested inmates, two had impaired organification of thyroidal iodine (JECFA, 1989).

Iodine exposures in maternal health

Sources of iodine exposure

Food

21. Iodine levels have been measured in the composite food samples of The 2014 Total Diet Study (TDS) (FSA, 2016). The richest dietary sources of iodine are fish and seafood, seaweed, eggs and dairy products.

22. Seaweed has been used for centuries as a staple food in Asian countries. In some Asian countries, it is customary to serve seaweed soup to new mothers (Moon et al, 2009). Seaweed consumption is also popular in people who are on a plant-based diet (EFSA, 2019). A study found that iodine in seaweed contributed significantly to diets of vegans with excessive iodine intake (Eveleigh et al, 2020). EFSA conducted an analysis and risk assessment on seaweed. Estimated mean exposures to iodine ranged from 94.9 – 11, 512.3 µg/day. Estimated 95th percentile exposures to iodine ranged from 86.0 – 18,677.2 µg/day (EFSA, 2019).

Human breast milk

23. An iodine concentration of 70 µg/kg is reported for mature breast milk by the Committee on Medical Aspects of Food Policy (COMA) (DHSS,1977). This value was obtained using the pooled samples of breast milk donated by 96 mothers from different parts of Great Britain. Up to 15% of the mothers in this study took vitamin and/or iron supplements during lactation but the iodine content of the supplements, if any, was not reported. No data specifically focussing on the influence of regular use of iodine supplements on levels of iodine in breast milk of UK mothers were identified.

Cows' milk and milk products

24. Iodine-based compounds are used to clean the udders of cows during milk collection and these leach into the milk, adding to the natural levels of iodine present. Cows' milk is therefore considered to be one of the richest sources of iodine in the diet. A survey of cows' milk carried out in 1998-9 found that the overall mean iodine concentration in cows' milk was 311 µg/kg. Mean iodine concentrations were found to be lower in summer (200 µg/kg)

compared to winter (430 µg/kg). The higher concentrations in winter may reflect greater use of supplemented compound feedstuffs during this period. At these levels, the COT concluded that the concentrations of iodine in cows' milk were unlikely to pose a risk to health, even in those children who are high level consumers (COT, 2000).

Drinking water

25. Iodine was detected at low levels (8 µg/L) in tap water in the 2014 TDS (FSA, 2016).

Supplements

26. A range of supplements that contain iodine are available to women who are trying to conceive as well as pregnant women and breastfeeding mothers. These supplements contain multiple components and can contain up to 150 µg of iodine per dose. Women are usually advised to consult their doctor before taking these supplements. The NHS states that adults need to have a daily iodine intake of 140 µg However, most people should be able to obtain the required amount of iodine by eating a varied and balanced diet. People who follow a strict vegan diet and do not consume any fish are advised to take an iodine supplement (NHS, 2020). The UK Dietary Reference Values (DRVs) do not include an increment in iodine for pregnant or lactating women. COMA advised on the premise that women of reproductive age should have customary intakes that would enable them to manage pregnancies without any need for supplements. In its statement on iodine and health, SACN considered there was insufficient evidence to substantiate revisions to the UK DRVs for iodine for pregnant and lactating women (SACN, 2014). No data specifically focusing on the influence of regular use of iodine supplements on levels of iodine in breast milk of UK mothers were identified.

Environmental – Dust and soil

27. Iodine levels in soil are highly variable. A median value of 5.9 mg/kg and a 90th percentile value of 14.2 mg/kg have been reported for UK soil by the British Geological Survey (BGS 2016). No specific value for dust was identified from the literature.

Air

28. According to the expert panel on Air Quality Standards, concentrations

of particle bound iodine in UK air between 1996 and 2001 ranged from 0.8 x10-6 - 2.0 x 10-6 mg/m^3 (DEFRA, 2006).

Medication

29. Iodine is used as a topical antiseptic, which can result in absorption through the skin. Excessive iodine intakes can occur following the ingestion of iodide-containing pharmaceuticals for the treatment of asthma, bronchitis, cystic fibrosis, chronic obstructive pulmonary disease, goitre. Iodine is also found in tropical antiseptics, mouthwashes, vaginal solutions and burn and wound treatments (SCF, 2006). Absorption in infants appears to be greater than in adults (Leung and Braverman, 2014). There are other medications that also contain iodine, which may be released metabolically into the systemic circulation.

Exposure assessment

Exposure estimates based on the TDS

30. A Total Diet Study (TDS) is described as a complementary approach to traditional monitoring and surveillance programs (EFSA, 2011). The TDS is used to calculate population dietary exposure to a range of chemicals in food and to assess the safety and/or nutritional quality of food. TDSs involve selecting, collecting and analysing commonly consumed food purchased at retail level, processing the food as for consumption, pooling the prepared food items into food groups that are representative, homogenising the pooled samples and analysing them for harmful and/or beneficial chemical substances (FSA, 2019).

31. Table 2 summarises total dietary exposures to iodine calculated using the iodine concentrations determined from food groups in 2014 Total Diet Study (TDS). The exposure assessment was carried out for women of childbearing age (16 – 49 years old) using food groups and consumption data from years 1 – 8 of the NDNS survey (Bates et al., 2014; 2016; 2018). The NDNS (Bates et al., 2014; 2016; 2018) does not provide data for pregnant or lactating women so while data is based on women of childbearing age, this data may not necessarily be representative of the maternal diet. Mean chronic iodine exposures from the total diet of women aged 16- 49 years old was 1.7 µg/kg bw/day and the 97.5th percentile chronic exposure was 3.7 µg/kg bw/day.

32. This TDS comprises of 27 food groups. The food groups making the highest contribution to iodine exposure in the TDS were milk, followed by fish

and seafood. It should be noted that it is advised that pregnant women should avoid particular types of cheese, dairy products, meat, eggs, fish and avoid drinking alcohol (NHS, 2020b). Therefore, pregnant or breastfeeding women may have a different diet compared to non-pregnant or breastfeeding women in the same age range as they may choose to increase or decrease consumption of certain foods or drinks due to this advice.

Consumer- based and population-based exposures estimates based on foods in the Total Diet Study (TDS)

Table 2. Estimated chronic exposure for iodine from the total diet in women aged 16 – 49 years old (TDS 27 groups) (Bates et al., 2014; 2016; 2018)

Consumers (n)	Chronic exposure		
	Mean (µg/kg bw/day)	P97.5th (µg/kg bw/day)	*Respondents in population group (n)*
1874	*1.7*	*3.7*	*1874*

Exposure estimates for seaweed

33. As noted in paragraph 22, seaweed has been noted as a high source of iodine, particularly in people on a plant-based diet or from a culture where dietary seaweed consumption is high. For this reason, iodine levels in seaweed have been used to give exposure estimates.

34. A search within the recipes database of the NDNS (Bates et al., 2014; 2016; 2018) was conducted to retrieve seaweed and seaweed products which had been recorded in the survey. These can be seen in column one of table 3. Column three is the assumption made for the type of seaweed in each food, where it has not been specified. These assumptions were based on common uses of seaweed.

Table 3. Seaweed or seaweed-containing foods recorded in the NDNS (Bates et al., 2014; 2016; 2018)

Food as recorded in NDNS	**Description of food**	***Assumed type of seaweed***
Higher nature energy breakfast shake dry powder	Meal replacement shake	*Kelp/ kombu*
Laverbread	Welsh seaweed dish	*Laver seaweed aka Nori*

Sushi, tuna based	NA	*Nori*
Sushi, vegetarian	NA	*Nori*
Sushi, salmon based	NA	*Nori*
Soup with tofu and seaweed	NA	*Wakame*
Vecon	Vegetable stock	*Kelp/ kombu*
Seaweed wakame dried raw	*NA*	*Wakame*

35. It should be noted that levels of iodine vary between types of seaweed; this can be seen in the EFSA ‘Analysis and Risk Assessment of Seaweed’ where kelp (Saccharina latissima) had a higher iodine concentration in comparison to other seaweed species (EFSA, 2019). In this case, iodine concentration in kelp ranged from 333.0 – 4,782.2 μg/g freeze dried weight. Three other species had lower ranges of 137.8-451.2 μg/g, 105.2-961.4 μg/g and 17.2-20.8 μg/g of freeze-dried weight (fdw).

36. The levels of iodine vary in different types seaweeds (Yeh et al, 2014) where kelp/ kombu can be compared to wakame and nori, which is more specific to the data available from the NDNS. In this case, the range for nori was 29.3 – 45.8 μg/g, for wakame 93.9 – 185.1 μg/g and for kombu 241- 4921 μg/g in dried seaweed weight.

37. Seaweed harvested from different countries may also have differing levels of iodine, this is also illustrated by Yeh et al, 2014. 10 samples each of nori, wakame and kombu harvested from China, Japan, Korea and Taiwan were analysed with varied results (Yeh et al, 2014).

38. Another uncertainty was that seaweed consumption based on the foods in table 3 and NDNS survey data for women of childbearing age (16 – 49 years) yielded consumption data based on very few consumers (Bates et al., 2014; 2016; 2018). Exposure or consumption estimates based on very few consumers should be treated with caution, particularly 97.5th percentile estimates based on less than 60 consumers. Furthermore, as mentioned previously, the NDNS does not consider pregnant or lactating women so these estimates may not be representative of the target population. The chronic consumption estimates can be seen in table 4.

Table 4. Chronic consumption estimates of seaweed in women aged 16 – 49 years old (Bates et al., 2014; 2016; 2018)

Consumers (n)	g/ person/day*		g/kg bw/day*		
	Mean	P97.5th	Mean	P97.5th	*Respondents in population*

					group (n)
36	*1.1*	*3.8*	*0.017*	*0.060*	*1874*

*rounded to 2.s.f

39. Further to the data considered from literature in paragraphs 33 – 35, real time data was consulted. The Rapid Alert for Food and Feed (RASFF Portal) is a tool that provides information on public health warnings issued by food safety authorities and food companies. It also provides the latest information on food recall notices. Between March 2019 to August 2020, there were 37 reported incidences whereby levels of iodine were detected in seaweed samples at above the alert, recall or 'information for follow-up' level according to the RASFF Portal. The concentrations of iodine in these seaweed samples ranged from 25 µg/g to 20,620 µg/g. Countries of origin in order of contribution were: South Korea, China, Germany, Spain, Japan, Belgium and Austria. These are similar to countries from which samples were derived by Yeh et al, 2014. This range is much greater than that seen by the EFSA analysis of kelp (EFSA, 2019) and is considered to be a worst-case scenario.

40. After reviewing all of the information in paragraphs 35– 36 and tables 3 and 4, exposure estimates were calculated using NDNS seaweed consumption data and the iodine concentration range measured in 16 kelp samples by EFSA, 333.0 – 4,782.2 µg/g fdw (EFSA, 2019). Due to the various uncertainties discussed such as the varying levels of iodine in different types of seaweed and the limited consumption data available in the NDNS this was considered the most realistic scenario.

Table 5: Chronic exposure estimates using chronic consumption data from table 4 and the iodine concentration range measured in kelp by EFSA, 2019 (minimum: 333.0 µg/g fdw, maximum: 4,782.2 µg/g fdw).

µg/ person/ day*		**µg/ person/ day***		**µg/kg bw/day***		**µg/kg bw/day ***	
Mean		**P97.5th**		**Mean**		**P97.5th**	
Min	Max	Min	Max	Min	Max	Min	*Max*
360	*5200*	*1300*	*1800*	*5.5*	*79*	*20*	*290*

*rounded 2.s.f

41. The exposure data in table 5 should be treated with caution because it is based on consumption data from a limited number of consumers, particularly the 97.5th percentile estimates. Another important caveat is that

the use of unprocessed seaweed biomass is a conservative approach for exposure assessments which is likely to lead to an overestimation. The minimum and maximum seaweed iodine values are only based on 16 samples. The effects of cooking and processing as well as bioavailability are not taken into account for this assessment as the data from EFSA 2019 is based on freeze dried samples of seaweed (EFSA, 2019).

Risk characterisation

42. In 2003, the EVM set a guidance level for iodine of 15 µg/kg bw/day that would not be expected to cause adverse effects in the majority of the population. It should be noted that this is a guidance level only as there was insufficient data from human or animal studies to establish a Safe Upper Level for iodine. Therefore, its applicability to maternal health is uncertain. The exposure estimates in Table 2 are below the guidance value. As seen in table 5, the estimated mean exposure for seaweed based on the minimum value of 333.0 µg/g fdw of iodine was 5.5 µg/kg and is below the guidance value. The estimated mean exposure for seaweed based on the maximum value of 4782.2 µg/g fdw of iodine was 79 µg/kg bw/day and is above the set guidance value. The estimated 97.5th percentile exposures for seaweed based on the minimum and maximum values of 333.0 µg/g and 4782.2 µg/g fdw iodine was 20 and 288 µg/kg bw/day, respectively. The estimated exposures are above the guidance value.

43. JECFA established a provisional Maximum Tolerable Daily Intake (PMTDI) of 17 µg/kg bw/day for iodine from all sources, based on the same longer- term studies in adults used by SCF in 2002 to support the TUL. The exposure estimates in Table 2 are below the PMTDI. As seen in table 5, the estimated mean exposure for seaweed based on the minimum value of 333.0 µg/g fdw of iodine is below the PMTDI. The estimated mean exposure for seaweed based on the maximum value of 4782.2 µg/g fdw of iodine is above the PMTDI. The 97.5th percentile exposure estimates for seaweed based on the minimum (333.0 µg/g fdw) and maximum iodine (4782.2 µg/g fdw) values are above the PMTDI.

44. The SCF established a UL of 600 µg/day for pregnant and lactating women based on of lack of adverse effects at significantly higher exposures (SCF, 2000). The exposure estimates in table 2 are below the UL. The estimated mean exposure for seaweed based on the minimum value of 333.0 µg/g fdw of iodine was below the UL. The estimated mean exposure based on the maximum value of 4782.2 µg/g fdw iodine was above the UL. The estimated 97.5th percentile exposures for seaweed based on the minimum

(333.0 µg/g fdw) and maximum iodine (4782.2 µg/g fdw) values are above the UL.

Conclusions of the Committee

45. Iodine is essential in the diet to produce thyroid hormones which are involved in cell metabolism, growth and development. However, both exposure to excess iodine and iodine deficiency in pregnancy may cause adverse effects on maternal and fetal thyroid function, birth outcomes, offspring growth and development.

46. Iodine status in the individual is difficult to assess since healthy people excrete excess iodine in urine so it is not a good marker for individual exposure. However, iodine deficiency and excess can be identified in a population by looking at the distribution of urinary iodine.

47. Iodine intake from the diet is within the HBGVs set by bodies such as EFSA, JECFA and the EVM for adults and would not be a risk to maternal health.

48. However, exposure to excess iodine in seaweed consumers (particularly those at the upper percentile) could pose a risk to maternal health. A risk benefit exercise should be performed to assess this due to the relatively narrow window between nutritional need and potential adverse effects.

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