The Director General

Maisons-Alfort, 21 July 2020

OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

on "maximum cadmium levels for seaweed intended for human consumption"[1]

ANSES undertakes independent and pluralistic scientific expert assessments.
ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.
It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are published on its website. This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 2 March 2020 shall prevail.

On April 4, 2017, ANSES received a formal request from the French Directorate General for Competition, Consumer Affairs and Fraud Control to conduct the following expert appraisal: request for an opinion on maximum cadmium levels for seaweed intended for human consumption.

1. BACKGROUND AND PURPOSE OF THE REQUEST

The consumption of edible seaweed is an emerging phenomenon in France and Europe, driven in particular by the popularity of Japanese restaurants and the consumption of sushi.

European Union regulations do not currently stipulate maximum cadmium levels in edible seaweed intended for direct human consumption or used as an ingredient in foodstuffs.

Regulation (EC) No 1881/2006[2] provides for maximum cadmium levels of 3.0 mg.kg^{-1} in food supplements as sold, consisting exclusively or mainly of dried seaweed or products derived from seaweed.

In addition, following its meetings of 14 June 1988, 13 December 1988 and 9 January 1990, the French High Council for Public Health (CSHPF) issued a list of edible seaweed authorised for human consumption, together with recommendations on maximum levels of trace metal elements. The CSHPF recommended a cadmium concentration in edible seaweed below 0.5 mg.kg^{-1} dry weight.

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[1] Cancels and replaces the opinion of 02 March 2020 (the changes to the text are listed in the table in Appendix 3).

[2] Regulation (EC) No 1881/2006 as amended setting maximum levels for certain contaminants in foodstuffs.

As observed by the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF) following sampling and analysis of edible seaweed, this cadmium concentration recommended by the CSHPF is often exceeded.

The information provided by the supervisory ministries in the formal request letter indicated that "*the results of the analyses available in the 'CONTAMINE' database show that the maximum cadmium concentration recommended by the CSHPF (0.5 mg.kg^{-1} dry weight) is very often exceeded*.

In 2013: six of the 13 seaweed samples analysed had a cadmium concentration above 0.5 mg.kg^{-1} dry weight:

- *1 sample of nori seaweed from Argentina: 9.4 mg.kg^{-1};*
- *2 samples of wakame seaweed from China: 1.7 and 2.2 mg.kg^{-1};*
- *3 samples of dried seaweed from China: 2.6, 3 and 3.1 mg.kg^{-1}.*

In 2014: two of the nine seaweed samples analysed had a cadmium concentration above 0.5 mg.kg^{-1} dry weight, with:

- *1 sample of nori seaweed of unknown origin: 2.1 mg.kg^{-1};*
- *1 sample of wakame seaweed from Japan: 2.9 mg.kg^{-1}.*

In 2015: four of the six seaweed samples analysed had a cadmium concentration above 0.5 mg.kg^{-1} dry weight, with:

- *1 sample of nori seaweed from China: 2.8 mg.kg^{-1};*
- *1 sample of roasted seaweed from China: 1.9 mg.kg^{-1};*
- *1 sample of dried seaweed from China: 1.7 mg.kg^{-1};*
- *1 sample of dried mixed seaweed from France: 1 mg.kg^{-1}.*

These findings were confirmed by the results of analyses provided by the Centre for Study and Promotion of Algae (CEVA) and attached to the formal request. Of the 343 seaweed samples analysed, 108 (31%) contained cadmium concentrations above 0.5 mg.kg^{-1} dry weight.
The DGCCRF's services are experiencing difficulties in managing the exceeded concentrations observed and defining the action to be taken. Indeed, it is difficult to conclude that there is a potential risk to consumer safety solely on the basis of the value recommended by the CSHPF (which is particularly old – dating from 1990 – and may not have been established on the basis of a rigorous risk assessment) being exceeded. Moreover, this value is contested by operators that struggle to comply with it."

ANSES was asked for an opinion on maximum cadmium levels in light of the value for seaweed intended for human consumption recommended by the CSHPF in 1990.

In particular, ANSES's opinion was sought on:

- *the advisability of retaining the conclusions of the French High Council for Public Health, issued at its meetings of 14 June 1988 and 9 January 1990, recommending a maximum cadmium concentration in edible seaweed of 0.5 mg.kg^{-1} dry weight;*
- *defining a cadmium concentration above which seaweed should not be placed on the market. The way in which seaweed is consumed could, where appropriate, be taken into account in order to determine differentiated levels;*
- *the advisability of defining recommendations for seaweed consumption.*

2. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French standard NF X 50-110 "Quality in Expert Appraisals – General requirements of Competence for Expert Appraisals (May 2003)".

The collective expert appraisal was carried out by the Expert Committee on "Assessment of physical and chemical risks in food" (CES ERCA). The methodological and scientific aspects of the work were presented to the CES between May 2017 and July 2019. The work was adopted by the CES ERCA at its meeting on 11 July 2019.

ANSES analyses interests declared by experts before they are appointed and throughout their work in order to prevent risks of conflicts of interest in relation to the points addressed in expert appraisals. The experts' declarations of interests are made public via the ANSES website (www.anses.fr). Two experts from the CES ERCA had what were regarded as major personal connections with the assessment of this topic and did not therefore participate in the collective scientific expert appraisal associated with this formal request.

The following data were attached to the formal request:

- *Contamination data provided by the Centre for Study and Promotion of Algae (CEVA);*
- *Study of the consumption of edible seaweed in France published by the AGROCAMPUS OUEST fisheries unit in 2014;*
- *Study of the French edible seaweed market published by the AGROCAMPUS OUEST fisheries unit in 2014:*
  - Volume 1: Overview of distribution to stores;
  - Volume 2: Catalogue and analysis of existing products.

As part of this assessment, a hearing with CEVA took place on 13 November 2018, which provided additional information for the seaweed contamination study.

3. ANALYSIS AND CONCLUSIONS OF THE CES ERCA

3.1. Edible seaweed

3.1.1. The seaweed sector

3.1.1.1. Production

The seaweed sector is highly diversified, in terms of production and exploitation.

Every year, France produces between 40,000 and 70,000 tonnes of fresh seaweed (14% of European production). In comparison, global production in 2010 was 20 million tonnes (compared to two million tonnes produced in 1970), 95% of which was produced by phycoculture[3] in Asia (FAO, 2014).

The geographic origin of the seaweed and its production method are rarely included on the product label. Only 1% of French production is intended for human consumption (CEVA, 2014) while globally, seaweed intended for direct human consumption (as a vegetable) accounts for between 20 and 45% of production.

Two techniques are currently used to produce seaweed for human consumption: manual harvesting of shore seaweed and seaweed farming. In France, as in other European countries, production is still essentially based on the collection of seaweed from the natural environment. The advantage of manual harvesting is that it enables the diversity of seaweed to be exploited. A good practice guide was published by the trade association Inter Bio Bretagne in 2011 (Philippe, 2011). At the global

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[3] Phycoculture, or seaweed farming, is the mass cultivation of seaweed for industrial and commercial purposes.

level, seaweed farming accounts for more than 95% of the seaweed produced (FAO statistics, 2014). Although France has the know-how and knowledge to develop seaweed farming, production remains limited for the moment in terms of players and volumes (Le Bras *et al.* 2015). The main species cultivated in France are kelp such as Devil's apron (*Saccharina latissima*), wakame (*Undaria pinnatifida*) and dabberlocks (*Alaria esculenta*).

3.1.1.2. Use

Seaweed has many applications in:

- the cosmetics industry;
- agriculture, as a fertiliser or an ingredient in the manufacture of livestock feed;
- the agrifood, chemistry and microbiology industries, as phycocolloids (alginates, agar-agar, carrageenans), which account for 75% of the macroalgae market (produced and imported);
- the food sector, in which certain species of seaweed can be consumed as a vegetable, or processed (dried, salted, etc.) or consumed as a food supplement.

In practice, the same species of seaweed can have several uses. *Laminaria japonica*, for example, is used to produce alginates, but also for human food where it is known as kombu. The same is true for several other species. It is therefore difficult to know precisely what proportion of global production is intended for which use (Le Bras *et al.* 2014). However, it is estimated that seaweed for direct human consumption (as a vegetable) constitutes between 20 and 45% of total global production, while the phycocolloid industry consumes between 40 and 70% of global production, and other applications such as agricultural supplies or cosmetics use between 10 and 15% of the total tonnage (Le Bras *et al.* 2014).

Since the 1960s, the technological properties of seaweed extracts have primarily been promoted by the food processing sector. Due to their varied rheological behaviours, they are widely used in processed foods as texturising additives.

3.1.1.3. Consumption

Some seaweed species can be consumed as vegetables. Several processes can be used to preserve seaweed: it can be dried, frozen, bottled, salted or served fresh.

Seaweed consumption is traditional in many Asian countries. In Japan, it is estimated that 1.5 to 2.5 kg of seaweed is consumed per person and per year (Zava and Zava, 2011). The consumption of edible seaweed is an emerging phenomenon in France and Europe, driven in particular by the growth of Japanese restaurants and the consumption of certain types of sushi. In this context, a national study of edible seaweed consumption was undertaken in 825 people across France (Le Bras *et al.,* 2014). This study examined consumer behaviour and motivations, as well as the population's perception of edible seaweed and barriers to consumption. Its results showed that more than half of the population (58%) consumes edible seaweed at least once a year. However, only 20% consume it regularly (at least once a month), including a small proportion of consumers (9%) who have incorporated seaweed into their diet, consuming it at least once a week. A large share of consumers (91%) eat seaweed exclusively in the context of Japanese food. The IDEALG study (Le Bras *et al.* 2014) showed that 22% of consumers are not aware of consuming seaweed, especially when consuming Asian products.

The main edible seaweed species used for human nutrition in France (Le Bras *et al.* 2014) are as follows:

- Thongweed or sea spaghetti (*Himanthalia elongata*);
- Sea lettuce or ulva (*Ulva* spp.);
- Dulse (*Palmaria palmata*);
- Nori (*Porphyra* spp.);
- Wakame (*Undaria pinnatifida*);
- Devil's apron (*Saccharina latissima*, formerly *Laminaria saccharina*).

According to the European Food Safety Authority (EFSA, 2016), in Europe, average consumption of seaweed food products ranges from 0.05 to 211 $g.d^{-1}$ and of sushi from 4.46 to 80.71 $g.d^{-1}$ for all surveys included in the EFSA Comprehensive Food Consumption database. Consumption of edible seaweed is reported either as a food alone (nori (*Porphyra spp*.), wakame (*Undaria pinnatifida*) and Devil's apron (*Saccharina latissima*)) or incorporated as an ingredient (sushi). It was noted, however, that the number of consumers reported in this database is very low.

In this formal request, the scope of the expert appraisal covers edible seaweed:

- Intended for direct human consumption;
- Used as an ingredient in foodstuffs;
- Used in food supplements.

3.1.2. Seaweed species considered for human consumption in France

The species considered have been identified as living in a marine biotope and are referred to as "seaweed" by the general public (Le Bras *et al*., 2014). They correspond to microalgae, macroalgae and halophytes. The generic term "seaweed" will be used repeatedly in this Opinion.

In France, initially, significant consumption histories prior to the entry into force of the Novel Food Regulation (Regulation (EC) No 258/97[4]) and a number of assessments by the CSHPF (CSHPF Opinion, 1997) were used to draw up a list of seaweed suitable for human consumption. Twelve macroalgae species and one microalgae species received favourable opinions from the CSHPF (CSHP, 1997) for use in human food as a vegetable or condiment. Other seaweed species then received favourable opinions from AFSSA[5] and authorisation according to Regulation (EC) No 258/97 (UE, 1997). The other species considered have been taken from the list of plants authorised in food supplements from the Ministerial Order of 24 June 2014[6], broadened to include the list from the Belfrit project[7], as well as the DGCCRF list of eligible plants under Article 15 of Decree No 2006-352 of 20 March 2006 on food supplements[8].

All of the macroalgae, microalgae and halophytes likely to be consumed in France (ANSES, 2018) are listed in the following table.

Table 1. List of macroalgae, microalgae and halophytes likely to be consumed in France

Scientific name	**Common name**	**Seaweed type**	**Status***
Alaria esculenta (L.) Grev.	Dabberlocks	brown	Edible seaweed "Plants" Order

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[4] Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients.

[5] French Food Safety Agency.

[6] The Ministerial Order of 24 June 2014, referred to as the "Plants" Order, establishes the list of plants other than fungi authorised in food supplements, as well as the conditions for their use. In this Order, "plants" are whole plants including seaweed and microalgae. The seaweed species included in the list in Annex I of the "Plants" Order are known as plant species that can be consumed as a food, condiment, food supplement or food ingredient.

[7] Harmonised list of 1025 plants identified in Belgium, France and Italy as being eligible for use in food supplements.

[8] https://www.economie.gouv.fr/files/files/directions_services/dgccrf/securite/teleicare/Table-Plantes.pdf

Scientific name	**Common name**	**Seaweed type**	**Status***
Ascophyllum nodosum (L.) Le Jolis	Knotted wrack	brown	Edible seaweed "Plants" Order
Chondrus crispus Stackhouse	Irish moss, carrageen	red	Edible seaweed "Plants" Order
Corallina officinalis L.	-	red	Belfrit Art-15
Enteromorpha spp.	Green laver	green	Edible seaweed
Fucus serratus L.	Toothed wrack	brown	Edible seaweed "Plants" Order
Fucus vesiculosus L.	Bladder wrack	brown	Edible seaweed "Plants" Order
Gelidium corneum (Hudson) J.V.Lamouroux	Agar-agar	red	"Plants" Order
G. amansii J.V.Lamouroux	-	red	"Plants" Order
G. sesquipedale (Clemente) Thuret	-	red	"Plants" Order
Gracilaria gracilis (Stackhouse) Steentoft, L.M. Irvine & Farnham	Ogonori	red	"Plants" Order
Gracilaria verrucosa (Hudson) Papenfuss	Gracilaria, ogo, ogonori	red	Edible seaweed
Himanthalia elongata (L.) S.F.Gray	Thongweed, sea spaghetti	brown	Edible seaweed "Plants" Order
Hizikia fusiformis (Harvey) Okamura	-	brown	Belfrit
Laminaria digitata (L.) J.V.Lamouroux	Oarweed	brown	Edible seaweed "Plants" Order
Laminaria hyperborea (Gunnerus) Foslie	-	brown	"Plants" Order
Laminaria palmata Bory	-	brown	Belfrit Art-15
Macrocystis pyrifera (L.) C.Agardh	Kelp	brown	"Plants" Order
Mastocarpus stellatus (Stackh.) Guiry	False Irish moss	red	"Plants" Order
Padina pavonica (L.) Thivy	-	brown	Edible seaweed
Palmaria palmata (L.) F.Weber & D.Mohr	Dulse	red	Edible seaweed "Plants" Order
Phymatolithon calcareum (Pallas) W.H.Adey & D.L.McKibbin ex Woelkering & L.M.Irvine Syn.[9] *Lithothamnium calcareum*	-	red	"Plants" Order, Belfrit and Art-15 Edible seaweed
Porphyra dioica J.Brodie & L.M.Irvine	Nori	red	Edible seaweed
Porphyra laciniata (Lightfoot) C.Agardh	Nori	red	Edible seaweed
Porphyra leucosticta Thuret	Nori	red	Edible seaweed
Porphyra purpurea (Roth) C.Agardh	Nori	red	Edible seaweed
Poryphora tenera (Kjellman) N.Kikuchi, M.Miyata, M.S.Hwang & H.G.Choi	Nori	red	Edible seaweed
Poryphora umbilicalis Kützing	Nori	red	Edible seaweed "Plants" Order
Poryphora yezoensis (Ueda) M.S.Hwang & H.G.Choi	Nori	red	Edible seaweed
Pyropia tenera (Kjellman) N.Kikuchi, M.Miyata, M.S.Hwang & H.G.Choi	Nori	red	Belfrit Art-15
Saccharina latissima (L.) C.E.Lane, C.Mayes, Druehl & G.W.Saunders Syn. *Laminaria saccharina*	Sugar kelp, sea belt, Devil's apron	brown	Edible seaweed "Plants" Order

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[9] Syn.: corresponds to an obsolete previous name

Scientific name	Common name	Seaweed type	Status*
Saccharina japonica (Areschoug) C.E.Lane, C.Mayes, Druehl & G.W.Saunders Syn. *Laminaria japonica*	Kombu	brown	Edible seaweed "Plants" Order
Sargassum fusiforme (Harvey) Setchell	Hijiki	brown	"Plants" Order
Ulva lactuca L.	Sea lettuce, ulva	green	Edible seaweed "Plants" Order
Undaria pinnatifida (Harvey) Suringar	Wakame	brown	Edible seaweed "Plants" Order
Crambe maritima L.	Sea kale	halophyte	Belfrit
Crithmum maritimum L.	Rock samphire Sea fennel	halophyte	"Plants" Order
Salicornia spp.	Glasswort	halophyte	Halophytes
Dunaliella salina (Dunal) Teodoresco	-	microalgae	"Plants" Order
Haematococcus pluvialis Flotow, syn. *Haematococcus lacustris* (Girod-Chantrans) Rostafinski	-	microalgae	"Plants" Order
Odontella aurita (Lyngbye) C.Agardh	-	microalgae	Edible seaweed
Parachlorella kessleri (Fott & Nováková) Krienitz, E.H.Hegewald, Hepperle, V.Huss, T.Rohr & M.Wolf	-	microalgae	Art-15
Aphanizomenon flos-aquae Ralfs ex Bornet & Flahault	Blue-green Klamath Lake alga, AFA	microalgae	"Plants" Order
Auxenochlorella protothecoides (Krüger) Kalina & Puncochárová	-	microalgae	Art-15
Auxenochlorella pyrenoidosa (H.Chick) Molinari & Calvo-Pérez	-	microalgae	Art-15
Chlorella vulgaris Beijerinck	Chlorella	microalgae	"Plants" Order
Chlorella sorokiniana Shihira & R.W.Krauss	-	microalgae	Art-15
Scenedesmus vacuolatus Shihira & Krauss	-	microalgae	Art-15
Arthrospira major (Kützing ex Gomont) W.B.Crow Syn.: *Spirulina major* Kützing ex Gomont	Spirulina	microalgae	Edible seaweed "Plants" Order
Arthrospira maxima Setchell & N.L.Gardner Syn.: *Spirulina maxima* (Setchell & N.L.Gardner) Geitler	Spirulina	microalgae	Edible seaweed "Plants" Order
Arthrospira fusiformis (Voronikhin) Komarek & J.W.G.Lund) Syn.: *Spirulina platensis* (Gomont) Geitler	Spirulina	microalgae	Edible seaweed "Plants" Order
Spirulina P.J.F.Turpin ex M.Gomont	Spirulina	microalgae	Art-15

* The status of seaweed, microalgae and halophytes:
- edible seaweed according to CEVA, based on the consumption history, or on CSHPF or ANSES opinions;
- seaweed included in the list of the "Plants" Order, the Belfrit list or the DGCCRF "Article 15" (Art-15) list.

3.1.2.1. **Microalgae**

Freshwater, terrestrial and marine microalgae are unicellular organisms belonging to the groups of cyanobacteria and microscopic algae.

Spirulina, whose name refers to cyanobacteria of the *Arthrospira* (formerly *Spirulina*) genus, is the microalgae most commonly used as a food ingredient or supplement due to its consumption history in third countries and its nutritional potential. In France, spirulina is marketed in bulk, as a powder, or as a food supplement in the form of capsules or tablets (Cornillier, Korsia-Meffre, and Senart 2008). Since it contains almost no iodine, the risk of excess iodine intake from this microalgae seems negligible. Furthermore, aside from the risk of contamination, spirulina does not pose any health risks at the doses usually used (ANSES, 2016b).

3.1.2.2. **Macroalgae**

Marine macroalgae are multicellular plant-like organisms. Unlike microalgae, most of them are sedentary in nature. They can cover large spaces forming fields or forests, often compared to those of the terrestrial system. However, due to a need for light, colonisation of seawater by most macroalgae is limited to coastal areas and a depth of around 30 metres. Marine macroalgae vary greatly in colour and have a wide variety of biological structures ranging from simple filaments just a few centimetres long to thalli[10] with lengths of several tens of metres (Kornprobst, 2005).

Macroalgae are divided into three groups (phyla) based on their pigmentation: green seaweed (close to the surface), brown seaweed (intermediate depths) and red seaweed (maximum depth of 200 metres).

They are known for their ability to concentrate heavy metals and iodine (Besada *et al.* 2009). Kelp are those that concentrate the most iodine. This iodine-concentrating capacity depends on the species, location, farming conditions and development cycle (Teas *et al.* 2004).

3.1.2.3. **Halophytes**

Halophytes are higher plants that grow in salty environments such as coastal soils and saline inland soils. Three species are likely to be consumed in France: *Crambe maritima* (common name: sea kale), *Crithmum maritimum* (common names: sea fennel and rock samphire) and *Salicornia* spp. (common names: glasswort, marsh samphire).

3.1.3. The French edible seaweed market

There are two types of products on the French market: firstly, Asian-style products reflecting the context of consumption of exotic products, and secondly, French-style products adapting to Western culinary culture (Le Bras *et al.* 2015).

The table below presents the edible seaweed products identified on the French market.

Table 2. Categorisation of seaweed food products (source: Le Bras *et al.* 2015)

Product category	Product sub-category	
Raw products	Nori sheets	Mainly Asian-style products
	Dried seaweed flakes	Mainly Asian- and French-style products
	Whole dried seaweed	Mainly Asian- and French-style products
	Fresh seaweed (in brine)	Mainly French-style products
	Bottled seaweed	Mainly French-style products
	Lactic-acid fermented seaweed	Mainly French-style products
Soups	Miso soups	Mainly Asian-style products
	Soups	Mainly French-style products

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[10] Thalli: Vegetative tissue of lower plants without leaves, stems or roots

Product category	Product sub-category	
	Noodle soups	Mainly Asian-style products
Spreads	Tartars	Mainly French-style products
	Rillettes	Mainly French-style products
Beverages	Tea	Mainly French-style products
	Beers	Mainly French-style products
Condiments	Stocks	Mainly French-style products
	Flavourings	Mainly Asian- and French-style products
	Salts	Mainly French-style products
	Mustards	Mainly French-style products
	Butters	Mainly French-style products
Seaweed salads	Fresh seaweed	Mainly Asian- and French-style products
	Frozen seaweed	Mainly Asian-style products
Biscuits	Crackers	Mainly Asian-style products
	Sweet biscuits	Mainly French-style products
	Energy bars	Mainly French-style products
Ready meals	Sushi	Mainly Asian-style products
	Canned fish	Mainly French-style products
	Tofu	Mainly French-style products
Pasta	Pasta	Mainly French-style products
Other	Undetermined	Mainly French-style products
	Starches	Mainly French-style products
	Sushi kits	Mainly Asian-style products

3.1.4. Identified hazards associated with seaweed intended for human consumption

The composition of edible seaweed raises the question of the risk to consumers associated with excess iodine intake and the identification of exogenous contaminants (chemical, microbiological) (NIFES, 2016) (ANSES, 2018).
Trace elements (mainly cadmium, arsenic, mercury, lead and tin), plant protection product residues, marine toxins and cyanobacterial toxins are all contaminants that can be found in seaweed (ANSES,

2016b). Seaweed is a bioindicator of marine environmental quality (Almela *et al.*, 2006; NIFES, 2016).
Following an internal request, ANSES previously assessed the risk of excess iodine intake from the consumption of seaweed in foodstuffs (ANSES, 2018).

The composition of seaweed can influence contaminant levels (NIFES, 2016). Fresh seaweed contains 70-90% water (Arne Jensen, 1993; Stévant *et al.*, 2017; Qing Chen *et al.*, 2018; Roleda *et al.*, 2019). The chemical composition of seaweed is characterised by high levels of specific polysaccharides in the structural components of the seaweed. The types of polysaccharides differ between brown, red and green macroalgae; alginate being the major component of brown macroalgae. Polysaccharides have a propensity to bind to metals, which can affect both metal concentrations and the availability of these metals bound to the seaweed. Seaweed generally has low lipid levels and therefore low concentrations of lipophilic compounds.

The concentrations of metals in macroalgae vary between species. However, within species, variations in metal concentrations appear to be site-specific, related to seaweed growth rates, and differ from one part of the seaweed to another. The presence of a large surface area of the seaweed in contact with water also facilitates the absorption of contaminants (NIFES, 2016). In addition, environmental factors (location, temperature, salinity, light, etc.) can influence the level of seaweed contamination (NIFES, 2016, Roleda *et al.*, 2019).

At the regulatory level, Regulation (EC) No 629/2008, amending Regulation (EC) No 1881/2006[2], lays down maximum cadmium levels of 3.0 mg.kg^{-1} in food supplements as sold, consisting exclusively or mainly of dried seaweed or products derived from seaweed. In addition, at its meetings of 14 June 1988 and 9 January 1990, the CSHPF issued recommendations for maximum values for iodine and trace elements in edible seaweed (Table 3). It also defined microbiological criteria to ensure the safety of edible seaweed.

Table 3. Maximum values for trace elements and iodine in seaweed used as a vegetable or condiment recommended by the CSHPF, in mg.kg^{-1} dry matter (DM)

Element	***Maximum levels (mg.kg^{-1} DM)***
Inorganic arsenic	3
Cadmium	0.5
Mercury	0.1
Lead	5
Tin	5
Iodine	2000

Lastly, the European Commission is currently recommending[11] that Member States, in cooperation with food and feed industry operators, monitor the presence of arsenic, cadmium, iodine, lead and mercury in seaweed, halophytes and products based on seaweed, during the years 2018, 2019 and 2020. This monitoring should cover edible halophytes including *Salicornia europaea* and *Tetragonia tetragonoides*, as well as a wide variety of seaweed species reflecting consumption habits and animal feed uses, including *Ecklonia bicyclis* (arame), *Fucus vesiculosus* (bladderwrack), *Palmaria palmata* (dulse), *Hizikia fusiforme* (hijiki or hiziki), *Chondrus crispus* (Irish moss, carrageen moss), *Laminaria digitata* (oarweed, tangleweed, sea girdle), *Laminaria japonica/Saccharina japonica* (kombu), *Porphyra* and *Pyropia* spp. (nori, red seaweed of both genera), *Ascophyllum nodosum* (rockweed, knotted wrack), *Ulva* spp. (sea lettuce, ulva), *Himanthalia elongata* (thongweed, sea spaghetti), *Fucus serratus* (toothed wrack, serrated wrack), *Codium* spp. (codium, sponge seaweed), *Saccharina latissima* (Devil's apron, sugar kelp, sea belt), *Undaria pinnatifida* (wakame, sea mustard) and *Alaria esculenta* (dabberlocks/badderlocks, winged kelp) to enable an accurate

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[11] Commission Recommendation (EU) 2018/464 of 19 March 2018 on the monitoring of metals and iodine in seaweed, halophytes and marine algae-based products.

estimation of exposure. Occurrence data on the substances concerned should also be gathered for food additives based on seaweed, in particular E 400, E 401, E 403, E 404, E 405, E 406, E 407, E 407a and E 160a(iv).

3.2. Dietary risk assessment of cadmium identified in seaweed intended for consumption

3.2.1. Toxicological characteristics of cadmium

Cadmium (Cd) is a ubiquitous trace metal element (TME) found in the various environmental compartments (soil, water, air) due to its natural presence in the Earth's crust and to anthropogenic inputs (industrial and agricultural activities).

According to the World Health Organization, the general population is mainly exposed through active and passive inhalation of tobacco smoke and consumption of contaminated food and water (WHO, 2010). Cadmium has bioaccumulative behaviour and is a food-chain contaminant of potential concern (EFSA, 2009).

Prolonged oral exposure to cadmium induces nephropathy, bone fragility and reproductive disorders. Cadmium and its compounds have been classified as "carcinogenic to humans" (Group 1, mainly lung, prostate and kidney) by the International Agency for Research on Cancer (IARC, 2012a).

In 2009, EFSA lowered the provisional tolerable weekly intake (PTWI) from 7 µg.kg $bw^{-1}.wk^{-1}$ to a tolerable weekly intake (TWI) of 2.5 µg.kg $bw^{-1}.wk^{-1}$ (0.36 µg Cd.kg $bw^{-1}.d^{-1}$), in both cases based on the observation of kidney effects following chronic exposure to cadmium. The TWI was established using a benchmark dose (BMD) approach by modelling the relationship between the urinary concentration of cadmium and that of β-2-µglobulin, which is a good marker of renal tubular damage (EFSA, 2009a).

In 2019, ANSES (ANSES, 2019) identified bone effects as the most relevant critical effects, based on the epidemiological studies by Engström *et al.* (2011 and 2012). Engström *et al.* (2011 and 2012) found a correlation between exposure to cadmium and a reduction in bone density (possibly increasing the risk of osteoporosis or fractures) in Swedish women aged 56 to 69 (2688 individuals). This association was also demonstrated in men (age > 69 years) in the study by Wallin *et al.*, 2016. The relationship between prolonged cadmium exposure and the risk of osteoporosis or bone fractures based on the articles by Engström *et al*. (2011 and 2012) was analysed. The urinary cadmium concentration of 0.5 $\mu g.g^{-1}$ creatinine was regarded as the no observed adverse effect level (NOAEL) and was chosen as the toxicological point of departure.
The oral toxicity reference value (TRV) was established using the Kjellström and Nordberg (1978) kinetic model. This model was used to relate urinary cadmium concentrations to oral exposure values and to estimate the changes in the maximum urinary cadmium concentration (in $\mu g.g^{-1}$ creatinine according to age) since birth that should not be exceeded, in order to avoid exceeding 0.5 $\mu g.g^{-1}$ creatinine in adulthood.
A tolerable daily intake (TDI) of 0.35 µg Cd.kg $bw^{-1}.d^{-1}$ or a TWI of 2.45 µg Cd.kg $bw^{-1}.wk^{-1}$ resulting in a urinary cadmium concentration of 0.5 $\mu g.g^{-1}$ creatinine, in a 60-year-old adult, assuming that ingestion is the sole source of cadmium exposure, has now been established.

3.2.2. Assessment and characterisation of the dietary risk from cadmium identified in seaweed

The study of a maximum cadmium concentration in seaweed was based on a consumer exposure assessment.

Based on the available consumption data, individual body weights and contamination data, consumer exposure can be estimated and compared with the toxicity reference value to assess the health risk from cadmium in seaweed.

3.2.2.1. Study of data on cadmium contamination of edible seaweed

CEVA has compiled all the existing data on seaweed contamination from 1984 to 2016. These data come from scientific publications and scientific studies coordinated by CEVA. In addition, ANSES's "CONTAMINE" database lists the results of seaweed samples added since 2010 as part of the annual monitoring and control plan for contamination of certain foodstuffs by trace metal elements set up by the DGCCRF.

3.2.2.1-1 Study of the CEVA contamination database

The dataset contains 343 analytical results on at least one of these elements: cadmium, lead, mercury, arsenic, inorganic arsenic and iodine, according to the categories, families and species of seaweed analysed (brown, red, green, macroalgae, microalgae, halophytes) and their origins.

Sampling of data on cadmium contamination of seaweed

The dataset includes 343 results on seaweed analysed for cadmium in Europe and Asia between 1984 and 2016. Only 186 results of cadmium contamination of seaweed analysed between 1996 and 2016 could be studied, based on the results of studies coordinated by CEVA and one scientific publication (Rodenas de la Rocha *et al.*, 2009); studies of the remaining 157 results were not available or usable (non-validated analytical methods).

Study of the analysis methods and data quality

The information on the 186 samples enabled the analytical methods used and their performance criteria to be evaluated and assessed.

Limits of detection (LOD) and limits of quantification (LOQ) were not specified for some results. In general, these limits were between 0.03 and 0.06/0.15 mg.kg^{-1} dry weight, respectively. Although there were indications regarding expression of the measurement uncertainty, the results compiled in the database sometimes lacked information, making it impossible to determine whether this was the expanded uncertainty U. According to Regulation (EC) No 333/2007[12] "The analytical result shall be reported as x +/- U whereby x is the analytical result and U is the expanded measurement uncertainty, using a coverage factor of 2 which gives a level of confidence of approximately 95% (U = 2u)". Although there were indications regarding uncertainty, it was not always specified whether this concerned the expanded uncertainty.

Ultimately, 180 cadmium analysis results in seaweed were usable.

These 180 seaweed samples included cadmium contamination results from the analysis of 124 brown macroalgae (69%), 35 red macroalgae (19.4%), 18 green macroalgae (10%) and 3 halophytes (glasswort, 1.7%).

It is possible to confirm that the characteristics of the seaweed sample are not too far removed from those of the seaweed consumed by the French population. Several parameters can be compared, such as mode of consumption, seaweed group, species and place of origin. The comparison of these

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[12] Commission Regulation (EC) No 333/2007 of 28 March 2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs

different parameters was based on French data from the national study of edible seaweed consumption conducted by Le Bras *et al.* (2014, 2015).

Considering Table 2, which categorises all seaweed-based food products (Asian- and/or French-style), Le Bras *et al.* (2014, 2015) reported that out of 746 linear referenced products (of which 54% were classified as Asian-style and 46% as French-style products), 50% were associated with the consumption of raw seaweed in dried form (whole or flaked). All seaweed in the CEVA sample was analysed in its raw, dried form.

According to Le Bras *et al.* (2014, 2015), the main species used in the production of Asian-style seaweed products were nori (red macroalgae) and wakame (brown macroalgae), which were found in 74% and 30% of products, respectively. Concerning French-style products, dulse (red macroalgae), sea lettuce (green macroalgae), nori (red macroalgae) and wakame (brown macroalgae), found in about 30-35% of products, were the most commonly used seaweed species. On the other hand, kombu (brown macroalgae) was one of the least used seaweed species. In the sample from the CEVA database, the families of brown and red macroalgae were in the majority (up to 88.4% of the dataset). Wakame (brown macroalgae) was the main species found in the sample (10%), followed by sea lettuce (green macroalgae) (8%) and dulse (7.7%) (red macroalgae). On the other hand, thongweed (brown macroalgae) accounted for nearly 10% of the dataset. Nori (red macroalgae) represented less than 3% of the sample. Kombu (brown macroalgae) was also less represented (2%), as was glasswort (halophyte) (< 2%).
In addition, mixtures of species were common in French-style products, as 35% of products contained a mixture of two or more species. The most common mixture consisted of dulse, sea lettuce and nori. No species mixtures were sampled in the CEVA database.

Concerning the indication of the geographical origin of products, this was sometimes imprecise, or even non-existent on certain products according to Le Bras *et al.* (2014, 2015), who reported that 80% of French-style seaweed-based food products were produced in France. The quality of the data relating to geographical origin was highly variable. 96% of the samples in the CEVA database were sourced in France.

However, the comparability of the sample from the CEVA database with the seaweed consumed by the French population related to the national study of edible seaweed consumption remains limited.

Data on cadmium contamination of seaweed

The cadmium data were only analysed by seaweed group and using the upper bound (UB) approach. Data processing covered the 180 samples analysed for cadmium between 1996 and 2016. Thirty-five out of 180 values were reported as being < LOQ of 0.15 (n = 32) or 0.06 mg.kg^{-1} dry weight (n = 3). The "lower than" value was therefore used in the calculations (e.g. < 0.06 was replaced by 0.06).

The table below presents the analysis of data on cadmium contamination in the seaweed categories of the CEVA database.

Table 4. Analysis of cadmium concentrations (mg.kg^{-1} dry matter (DM)) in the seaweed categories of the CEVA database

	Total	Brown macroalgae	Red macroalgae	Green macroalgae*	Halophytes*
n	180	124	35	18	3
Cadmium concentrations (mg.kg^{-1} dry matter (DM))					
Median	0.21	0.27	0.12	0.13	0.17
Mean	0.41	0.46	0.39	0.14	0.18

	Total	Brown macroalgae	Red macroalgae	Green macroalgae*	Halophytes*
95th percentile	1.44	1.00	2.94	-	-
Min	0.01	0.01	0.03	0.03	0.16
Max	3.18	2.95	3.18	0.60	0.21
Breakdown of numbers according to classes of cadmium concentrations (mg.kg^{-1} DM) below or above the CSHPF reference value of 0.5 mg.kg^{-1} DM					
concentration < 0.5	141	89	32	17	3
0.5 < concentration < 1	20	19	0	1	0
1 < concentration < 2	14	14	0	0	0
2 < concentration < 3	3	2	1	0	0
3 < concentration < 4	2	0	2	0	0
4 < concentration < 5	0	0	0	0	0
concentration > 5	0	0	0	0	0

Total: all seaweed categories combined; Brown macroalgae: seaweed belonging to the brown macroalgae group; Red macroalgae: seaweed belonging to the red macroalgae group; Green macroalgae: seaweed belonging to the green macroalgae group; Halophytes: related to glasswort.

***Due to the small number of samples, the 95th percentile was not calculated.**

For the data as a whole, the mean and median cadmium contamination levels of all seaweed categories combined were 0.41 and 0.21 mg.kg^{-1} dry matter, respectively (min-max 0.01-3.18 mg.kg^{-1} dry weight).

Red and brown macroalgae were the most contaminated with cadmium, with mean values above 0.39 mg.kg^{-1} dry matter compared to mean values below 0.20 mg.kg^{-1} dry matter for the other two categories (green macroalgae and halophytes).

A maximum concentration of 3.18 mg Cd.kg^{-1} dry matter was observed in a sample of red macroalgae (nori) from Japan. With 3.07 mg Cd.kg^{-1} dry matter, another sample of red macroalgae (nori from Korea) had contamination above 3 mg Cd.kg^{-1} dry matter. These results came from a scientific publication (Rodenas de la Rocha *et al.*, 2009). In view of the analysis of the expanded measurement uncertainty, neither of these two samples would exceed the threshold of 3 mg Cd.kg^{-1} provided for in Regulation (EC) No 1881/2006[2] in food supplements containing dried seaweed.

Three other samples had cadmium contamination above 2 mg.kg^{-1} dry matter. These were one sample of red macroalgae (nori from France with a concentration of 2.88 mg Cd.kg^{-1} dry matter) and two samples of brown macroalgae (1 sample of wakame from France with a concentration of 2.07 mg Cd.kg^{-1} dry matter, and one sample of kombu from Japan with a concentration of 2.95 mg Cd.kg^{-1} dry matter).

Only the samples from the halophyte category (analysis of glasswort only) did not exceed the CSHPF reference value of 0.5 mg Cd.kg^{-1} dry matter (n = 3).

For the green macroalgae analysed, only 1 sample out of 18 analysed had a concentration above 0.5 mg Cd.kg^{-1} dry matter (0.6 mg Cd.kg^{-1} dry matter identified in a sample of sea lettuce from France).

A total of 39 results (22%) out of the 180 seaweed samples analysed exceeded the concentration of 0.5 mg Cd.kg^{-1} dry matter recommended by the CSHPF. The exceeded concentrations were mostly observed for the brown macroalgae category (35 out of 124 samples, of which 33 had contamination levels between 0.5 and 2 mg Cd.kg^{-1} dry matter) while the highest contamination levels, above 2 or even 3 mg Cd.kg^{-1} dry matter, were observed for three red macroalgae.

However, in order to compare it with the reference value, knowledge of the expanded uncertainty U of each result is needed.

3.2.2.1-2 Study of the "CONTAMINE" contamination database

The CONTAMINE database contains 525 results on concentrations of cadmium, lead, arsenic (total and inorganic) and mercury (total) in seaweed.

__Sampling of data on cadmium contamination of seaweed__

The dataset contains 131 results of cadmium contamination of seaweed (macroalgae, spirulina, glasswort), including seaweed used as such (fresh, dried or roasted), as a food ingredient (agar-agar, beverages) and as a food supplement ingredient, sampled in France between 2009 and 2017 and analysed between 2010 and 2018.

__Study of the analysis methods and data quality__

The 131 samples were analysed by four COFRAC-accredited laboratories of the DGCCRF's Joint Laboratory Service (SCL) (L67 (n = 53), L33 (n = 75), L59 (n = 1) and L974 (n = 2)), mainly by electrothermal atomic absorption spectrometry, but also by induced plasma mass spectrometry (ICP-OES/MS) (n = 33).
Limits of detection (LOD) and limits of quantification (LOQ) (between 0.0002 and 0.035 mg.kg^{-1} total weight) are given when concentrations are below these limits. Although there were indications regarding expression of the measurement uncertainty, the results compiled in the database sometimes lacked clarity on whether the information did indeed refer to the expanded uncertainty U, and on its expression, where certain values were probably expressed in % and others in mg.kg^{-1}.

Out of these 131 analysed samples (all of which were usable), 39 analytical results concerned macroalgae (brown, red, green) used as such, while 11 and 3 analytical results respectively concerned microalgae (spirulina only) and halophytes (glasswort only). The seaweed category was unspecified or unknown for 20 of the analysed samples. Fifty-three analytical results concerned food supplements containing seaweed. Two samples of seaweed mixtures, 1 sample of seaweed powder, 1 sample of agar-agar and 1 sample of seaweed-based beverage were also analysed for cadmium.
The groups analysed, in increasing order of percentage, were as follows:
Food supplements (FS) (40.5%) > unknown seaweed (15.3%) > brown macroalgae (13%) = red macroalgae (13%) > microalgae (spirulina) (8.4%) > green macroalgae (3.8%) > halophytes (glasswort) (2.3%; n = 3) > seaweed mixtures (1.5%; n = 2) > powder, agar-agar and beverages (0.8% each (n = 1 each)).

It is possible to confirm that the characteristics of the seaweed sample are not too far removed from those of the seaweed consumed by the French population, when they are known. The following parameters related to mode of consumption, seaweed group, species, and place of origin were compared, based on national data from the national study of edible seaweed consumption conducted by Le Bras *et al.* (2014, 2015).

Considering Table 2 categorising all seaweed-based food products (Asian- and/or French-style), Le Bras *et al.* (2014, 2015) reported that out of 746 linear referenced products (of which 54% were classified as Asian-style and 46% as French-style products), 50% were associated with the consumption of raw seaweed in dried form (whole or flaked). Almost 50% of the samples in the CONTAMINE dataset were analysed in their raw, dried form.

According to Le Bras *et al.* (2014, 2015), the main species used in the production of Asian-style seaweed products were nori (red macroalgae) and wakame (brown macroalgae), which were found in 74% and 30% of products, respectively. Concerning French-style products, dulse (red macroalgae), sea lettuce (green macroalgae), nori (red macroalgae) and wakame (brown macroalgae), found in about 30-35% of products, were the most commonly used seaweed species. On the other hand, kombu (brown macroalgae) was one of the least used seaweed species. In the sample from the CONTAMINE database, the families of brown and red macroalgae were in the majority (up to 26% of the dataset). Nori (red macroalgae) was the main species found in the sample (8%), followed by wakame (brown macroalgae) (7%) and dulse (red macroalgae) (6%). Sea lettuce (green macroalgae) accounted for 5% of the dataset. Kombu (brown macroalgae) was also less represented (1.5%), as was glasswort (halophyte) (2.3%).
In addition, mixtures of species were common in French-style products, as 35% of products contained a mixture of two or more species. The most common mixture consisted of dulse, sea lettuce and nori. Two samples of species mixtures were collected from the CONTAMINE database, including a mixture of dulse, sea lettuce and nori.

Concerning the indication of the geographical origin of products, this was sometimes imprecise, or even non-existent on certain products according to Le Bras *et al.* (2014, 2015), who reported that 80% of French-style seaweed-based food products were produced in France. The quality of the data relating to geographical origin was highly variable. 52% of the seaweed sampled in CONTAMINE originated from France, and nearly 37% originated from Asia (China, Japan, Korea).

However, the comparability of the sample from the CONTAMINE database with the seaweed consumed by the French population related to the national study of edible seaweed consumption remains limited.

__Data on cadmium contamination of seaweed__

The cadmium data were analysed by seaweed group and using the upper bound (UB) approach. Data processing covered the 131 samples analysed for cadmium, except for the single samples of powder, agar-agar and beverages. Twenty-six results out of the 131 samples analysed were not quantified (n = 17) or detected (n = 9) (LOD/LOQ between 0.001 and 0.090 mg/kg). The dataset was converted to mg.kg^{-1} dry matter where necessary, by applying a conversion factor for data provided as wet weight. The choice of this factor was based on a review of the literature (Arne Jensen, 1993; Stévant *et al.*, 2017; Qing Chen *et al.*, 2018; Roleda *et al.*, 2019) and assumed an average dry matter content of 20% in fresh seaweed. This conversion to dry matter enables these data to be compared with those of CEVA.

The table below presents the analysis of data on cadmium contamination in the seaweed categories of the CONTAMINE database.

Table 5. Analysis of cadmium concentrations (mg.kg^{-1} dry matter (DM)) in the seaweed categories of the CONTAMINE database.

	Total	Unknown	Brown macroalgae*	Red macroalgae*	Green macroalgae*	Microalgae*	Halophytes*	Mixtures*	FS
n	75	20	17	17	5	11	3	2	53
Cadmium concentrations (mg.kg^{-1} dry matter (DM))									
Median	0.230	0.360	0.365	1.10	0.140	0.028	0.045	0.534	0.051
Mean	1.07	1.32	1.14	1.59	1.11	0.029	0.122	0.534	0.112
95th percentile	2.90	-	-	-	-	-	-	-	0.500
Min	0.001	0.008	0.022	0.007	0.055	0.001	0.035	0.077	0.004
Max	9.4	4.6	4.4	9.4	4.250	0.088	0.285	0.990	0.588
Breakdown of numbers according to classes of cadmium concentrations (mg.kg^{-1} DM) below or above the CSHPF reference value of 0.5 mg.kg^{-1} DM									
concentration < 0.5	46	11	9	8	3	11	3	1	50
0.5 < concentration < 1	2	0	0	0	0	0	0	1	3
1 < concentration < 2	9	2	4	3	1	0	0	0	0
2 < concentration < 3	12	4	3	5	0	0	0	0	0
3 < concentration < 4	2	2	0	0	0	0	0	0	0
4 < concentration < 5	3	1	1	0	1	0	0	0	0
concentration > 5	1	0	0	1	0	0	0	0	0

Total: all seaweed categories combined, except food supplements, agar-agar, beverages and seaweed powder; Unknown: seaweed whose parent group is not specified; Brown macroalgae: seaweed belonging to the group of brown macroalgae; Red macroalgae: seaweed belonging to the group of red macroalgae; Green macroalgae: seaweed belonging to the group of green macroalgae; Microalgae: related to spirulina in CONTAMINE; Halophytes: related to glasswort in CONTAMINE; Mixtures: mixtures of dried seaweed; FS: food supplements containing dried seaweed.
***Due to the small number of samples, the 95th percentile was not calculated.**

For the data as a whole, the mean and median cadmium contamination levels of all seaweed categories combined, excluding food supplements, agar-agar, beverages and seaweed powder, were 1.07 and 0.23 mg.kg^{-1} DM, respectively (min-max 0.001-9.4 mg Cd.kg^{-1} dry matter).

Red, brown macroalgae and unknown seaweed were the most contaminated with cadmium, with mean values above 1.14 mg.kg^{-1} dry matter.
A maximum cadmium level of 9.4 mg.kg^{-1} dry matter was observed in a sample of red macroalgae (wild *Porphyra* flakes, nori) from Argentina. This was the only sample that exceeded the concentration of 5 mg Cd.kg^{-1} dry matter. Three other samples exceeded the concentration of 4 mg Cd.kg^{-1} dry matter, including a green macroalgae (4.25 mg Cd.kg^{-1} dry matter, related to a farmed seaweed for human consumption corresponding to sea lettuce from France), a brown macroalgae (4.4 mg Cd.kg^{-1} dry matter in a dried wakame seaweed from China) and an unknown seaweed (4.6 mg Cd.kg^{-1} dry matter in a seaweed from China). Two other samples of unknown seaweed (wild seaweed-silver seaweed from China; roasted sushi seaweed from Korea) had cadmium levels above 3 mg Cd.kg^{-1} dry matter. A third sample of unknown seaweed (farmed seaweed, roasted seaweed from China) had a level of 2.99 mg Cd.kg^{-1} dry matter. A total of 12 seaweed samples had

concentrations between 2 and 3 mg Cd.kg^{-1} dry matter (red macroalgae (n = 5), brown macroalgae (n = 3), unknown seaweed (n = 4)).
Contamination levels of the halophyte and microalgae groups did not exceed the CSHPF reference value of 0.5 mg Cd.kg^{-1} dry matter. However, the number of samples analysed was small (n < 12). Lastly, cadmium concentrations in the single samples of powder, agar-agar and seaweed-based beverages did not exceed this reference value of 0.5 mg Cd.kg^{-1} dry matter.

A total of 29 out of 75 seaweed samples analysed, all seaweed categories combined, excluding food supplements, agar-agar, beverages and seaweed powder (i.e. 38%), exceeded the reference value of 0.5 mg Cd.kg^{-1} dry matter recommended by the CSHPF, with groups of red macroalgae (n = 9), brown macroalgae (n = 8), green macroalgae (n = 2) and seaweed with unknown classification (n = 9). A sample of a seaweed mixture had cadmium concentrations that exceeded the reference value of 0.5 mg Cd.kg^{-1} dry matter recommended by the CSHPF but was below 1 mg Cd.kg^{-1} dry matter.

Regarding the levels of cadmium contamination observed in food supplements containing dried seaweed, these did not exceed the maximum cadmium levels of 3.0 mg.kg^{-1} in food supplements as sold, consisting exclusively or mainly of dried seaweed or products derived from seaweed, laid down in Regulation (EC) No 1881/2006[2].

However, it should be noted that in order to compare it with the reference value, knowledge of the expanded uncertainty U of each result is needed, because according to Regulation (EC) No 333/2007[13] "The analytical result shall be reported as x +/- U whereby x is the analytical result and U is the expanded measurement uncertainty, using a coverage factor of 2 which gives a level of confidence of approximately 95% (U = 2u)." Although there were indications regarding uncertainty, it was not always specified whether this concerned the expanded uncertainty.

3.2.2.1-3 Summary

The table below summarises the cadmium concentrations observed in seaweed intended for human consumption for the entire dataset used in this formal request (from the CEVA and CONTAMINE databases).

Table 6. Summary of cadmium concentrations observed in seaweed intended for human consumption from the entire dataset available for the formal request

		Cadmium concentrations (mg.kg^{-1} dry matter (DM))			
		Min	**Mean**	**95th percentile**	**Max**
Unprocessed seaweed (all species combined)	N = 255	0.001	0.604	2.700	9.400
Food supplements containing dried seaweed	N = 53	0.004	0.112	0.500	0.588

For the data as a whole, the mean cadmium contamination level for all seaweed categories combined, unprocessed, was 0.604 mg.kg^{-1} (min-max 0.001-9.4 mg Cd.kg^{-1} dry matter). Regarding food supplements containing dried seaweed, it was 0.112 mg.kg^{-1} (min-max 0.004-0.588 mg Cd.kg^{-1} dry matter).
The data show that the reference value of 0.5 mg Cd.kg^{-1} dry matter recommended by the CSHPF was frequently exceeded (26% of the samples in the total dataset), mainly observed for brown and

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[13] Commission Regulation (EC) No 333/2007 of 28 March 2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs

red macroalgae samples. Higher cadmium levels were found in seaweed belonging to the brown and red macroalgae groups.
These findings, particularly in terms of the CSHPF guideline value being frequently exceeded and the higher levels of cadmium contamination of seaweed species belonging to the brown and red macroalgae groups, were also observed in the literature (Almela *et al.*, 2006; Superior Health Council, 2015; NIFES, 2016; Paz *et al.*, 2018; Roleda *et al*., 2019).

The usable data on lead, arsenic (total and inorganic) and mercury (total) contamination of seaweed were also investigated and are presented in Annex 2.

3.2.2.2. Study of data on edible seaweed consumption

Data on the consumption of edible seaweed and seaweed-based ingredients, as well as on food supplements containing seaweed, were taken from the third Individual and National Study on Food Consumption (INCA 3) (ANSES, 2017).

Data on food consumption relating to foods and ingredients: INCA 3 study

The INCA 3 study was conducted between February 2014 and September 2015 with a representative sample of individuals living in metropolitan France (excluding Corsica). A total of 5855 individuals, broken down into 2698 children from birth to age 17 and 3157 adults between the ages of 18 and 79, participated in the study. The individuals were selected according to a three-stage random sampling method (geographical units, households and then individuals), from the 2011 annual census of the population, complying with a geographical stratification (region, size of the urban area) in order to ensure representativeness for the entire country. Two independent samples were established: a "Children" sample (from birth to 17 years of age) and an "Adults" sample (18 to 79 years).
Information on the food consumption of individuals was collected over three non-consecutive days (2 weekdays and 1 weekend day) spread over around three weeks, using the 24h recall method for individuals aged 15 to 79 years, and the 24h record method (via a food picture book) for individuals aged 0 to 14 years. For the three selected days, the individuals were asked to describe their food consumption by identifying all the foods and beverages consumed during the previous day and night. Of the 5855 individuals participating in the study, 4114 (1993 children and 2121 adults) validated the consumption part by taking part in at least two food interviews.
In parallel with the INCA 3 study, a research and development agreement was set up with the Research Centre for the Study and Monitoring of Living Conditions (CREDOC) to break down into ingredients the complex foods reported as home-made and mentioned most often in the INCA 3 study (example: apple pie = pastry dough, custard, apples). Each recipe provided by CREDOC corresponded to an average generic recipe resulting from a combination of the five most consulted recipes on the Internet. The precise methodology defined by ANSES enabled the recipe breakdown to be standardised in order to ensure that the generic recipes reflected the likely home-made recipes for these foods (ANSES, 2017).

Data on food supplements: INCA 3 study

The data on food supplement consumption collected in the INCA 3 study did not strictly follow the regulatory definition, but also included drugs that can provide nutrients, and plant extracts. Data on food supplement consumption was collected for the 5855 participants in the INCA 3 study. For each product mentioned, the name, brand, form of presentation, place of purchase, frequency of consumption and quantity consumed were documented.
Concerning the data on food supplement composition, the packaging of the food supplements consumed was collected by the investigators when they had the opportunity to do so. The information available on the packaging (name, brand, manufacturer, form of presentation, dosage, list of

ingredients, list of constituents, etc.) was entered into a database. Not all the food supplements mentioned in the INCA 3 study (1102 different products based on brand, name and form of presentation) yet appear in the database, which is currently being finalised internally.

Identification of foods and ingredients regarded as edible seaweed

The edible seaweed species identified in France (see Section 3.1.2) were compared to the lists of foods mentioned in the INCA 3 study, to the ingredients used in CREDOC's recipe breakdowns, and to the lists of constituents and ingredients of food supplements currently available, in order to identify foods and ingredients regarded as edible seaweed, as well as food supplements containing seaweed.

Foods labelled "seaweed" and "glasswort" in the INCA 3 study were selected as edible seaweed. The food agar-agar used as such was not considered in the study of food consumption in the INCA 3 report published in June 2017 and has not been taken into account in responding to this formal request.
On the basis of the data transmitted by CREDOC, recipes mentioned at least once as having been home-made and including seaweed were considered, such as "dairy-based desserts and cooked desserts", "fruit jams" (unsweetened or with reduced sugar content), "jellied flans", "makis" and "California rolls", systematically including seaweed in their composition. As agar-agar had not been taken into account, only "makis" and "California rolls" were retained for the remainder of the assessment.
Lastly, from the data available in the database of food supplement composition, about 30 products were identified as containing at least one edible seaweed.

Estimating data on edible seaweed consumption

On the basis of the few data available for each case, i.e. seaweed consumed as a food, seaweed consumed as a food ingredient or seaweed consumed as a food supplement ingredient, the following were estimated separately for adults and children:

- Number of consumption occasions;
- Consumer rates (with a 95% confidence interval);
- Number of consumers.

This ultimately led to the quantities of seaweed consumed as a food, ingredient or food supplement being estimated at the individual level.

Results

Table 7 shows the number of consumption occasions, consumer rates and mean consumption of edible seaweed as a food, food ingredient and food supplement ingredient in adults and children obtained from the INCA 3 study.

Consumption occasion and consumption rates of edible seaweed were very low among adults (0.3% of consumers), and even lower among children (0.07% of consumers). The "seaweed" item was the main representative of edible seaweed consumed, with the consumption of "glasswort" seeming minor.

Consumption of edible seaweed was in the form of ingredients more often than food, although consumption occasions and consumer rates were low.

Consumption of seaweed via food supplements was also relatively low, close to 1% in adults and less than 0.1% in children.

Table 7. Number of consumption occasions, consumer rates and mean consumption of edible seaweed as a food, food ingredient and food supplement ingredient in adults and children according to the INCA 3 study (2014-2015)

Sample	**INCA 3 name**	**Number of consumers**	**Consumer rates (95% CI)**	**Number of consumption occasions**	**Mean consumption**
Adults (n = 2121)	Seaweed ("Seaweed" + "Glasswort")	10	0.30% (0.1% - 0.8%)	14	6.1 g
Children (n = 1993)	Seaweed ("Seaweed" + "Glasswort")	4	0.07% (0.02% - 0.2%)	4	5.4 g
Adults (n = 2121)	Edible seaweed as a food ingredient	33	1.7% (1.1% - 2.6%)	42	0.47 g
Children (n = 1993)	Edible seaweed as a food ingredient	16	0.4% (0.2% - 0.7%)	75	0.36 g
Adults (n = 3157)	Edible seaweed as a food supplement ingredient	29	0.7% (0.4% - 1.1%)	30	198 mg
Children (n = 2698)	Edible seaweed as a food supplement ingredient	3	0.06% (0.02% - 0.25%)	3	295 mg

Combining all forms of edible seaweed intakes (food, ingredient, food supplement), 2.5% of adults and 0.5% of children reported a consumption occasion in the INCA 3 study of at least one seaweed-based food or food supplement (see Table 8).

Table 8. Number of consumption occasions and consumer rates of edible seaweed in all forms combined (food, recipe ingredients and food supplement ingredients) in adults and children according to the INCA 3 study (2014-2015)

Sample	**Number of consumption occasions**	**Consumer rates (95% CI)**
Adults (n = 2121)	53	2.50% (1.8% - 3.5%)
Children (n = 1993)	112	0.50% (0.3% - 0.8%)

In conclusion, few consumption data for edible seaweed or food products including seaweed could be derived from the INCA 3 study (ANSES, 2017). Given the changes in the eating habits of French consumers, a survey is needed to specifically investigate the frequency, mode of consumption and quantity of seaweed consumed by type of seaweed used according to the food product, in the French population. A more accurate qualitative and quantitative collection of these data would help refine the results and recommendations for the consumption of edible seaweed.

3.2.2.3. Assessment of dietary exposure to cadmium identified in edible seaweed

Preamble

Apart from smoking, the main source of exposure to cadmium in the general population is food (EFSA, 2009a, 2012a). Cadmium is bioaccumulative and is a food-chain contaminant of potential concern. According to ANSES's opinion and report on its second Total Diet Study (TDS2) of June 2011 (ANSES, 2011a), the tolerable weekly intake (TWI) defined by EFSA in 2009 was exceeded in 0.6% of adults and 15% of children. Cadmium is a ubiquitous element found in a large proportion of foods. The main foods identified as contributing to cadmium exposure were bread and dried bread products, potatoes and related products, and vegetables (ANSES, 2011a, b). The TDS2 study recommended implementing or strengthening management measures aimed at limiting levels of exposure to cadmium.

More recently, the conclusions of the Infant Total Diet Study (iTDS) published in September 2016 (ANSES, 2016a) confirmed those of the TDS2, i.e. that a health risk associated with cadmium cannot be ruled out for children under three years of age. In the iTDS, the main contributors to cadmium exposure for children over the age of five months were the same as those identified for the general population. ANSES had concluded that the recommendations issued to reduce dietary exposure of the general population were also relevant for children under three years of age, to limit the accumulation of cadmium from a very early age.

Estimating dietary exposure to cadmium from consumption of edible seaweed

The input data for estimating dietary cadmium exposure for seaweed consumers are explained in the following table:

Table 9. Input data for estimating dietary cadmium exposure for seaweed consumers

	Contamination input data		Consumption input data	
	Source	**N**	**Source**	**N***
Scenario for seaweed consumed as a food	CEVA (1996-2016) and CONTAMINE (2010-2018) dataset	N = 255 cadmium concentrations in unprocessed seaweed (all species combined)	INCA 3 study	N = 14 consumption occasions for seaweed as a food ("Seaweed" + "Glasswort") in adults
Scenario for seaweed consumed as an ingredient in foodstuffs	CEVA (1996-2016) and CONTAMINE (2010-2018) dataset	N = 255 cadmium concentrations in unprocessed seaweed (all species combined)	INCA 3 study	N = 42 and 75 consumption occasions for seaweed as a food ingredient in adults and children respectively
Scenario for seaweed consumed as a food supplement ingredient	CONTAMINE dataset (2010-2018)	N = 53 cadmium concentrations in food supplements containing dried seaweed	INCA 3 study	N = 30 consumption occasions for seaweed as a food supplement ingredient in adults
Scenario for seaweed consumed in all forms combined (food, ingredient, food supplement)	CEVA (1996-2016) and CONTAMINE (2010-2018) dataset	N = 310 cadmium concentrations in unprocessed seaweed (all species combined) and in food supplements containing dried seaweed	INCA 3 study	N = 53 and 75** consumption occasions for seaweed in all forms combined in adults and children respectively

* Consumption occasions

** Due to the low number of consumers of seaweed used as such or as a food supplement ingredient in the child population, only consumers of ingredients were taken into account in this assessment.

Input data on cadmium contamination levels in seaweed, when censored in the dataset, were expressed with a high (conservative) assumption using the upper bound (UB) approach. This is because the dataset has no information on the values of the limits of detection. In the UB scenario, "not detected" or "not quantified" results were replaced by the limit of quantification (LOQ).

Concerning the consumption data, due to the small dataset available:

- Individual consumption occasions were taken into account, not consumers as such;
- Only the consumption occasions of adult consumers of seaweed as a food or food supplement ingredient were considered for estimating the associated cadmium exposures.

Dietary exposure to cadmium in seaweed consumers was estimated on the basis of the following consumption scenarios, considering:

1) Seaweed consumed directly as a food, without processing, as such;
2) Seaweed consumed as an ingredient in foodstuffs (maki, California roll);
3) Seaweed consumed as a food supplement ingredient;
4) Seaweed consumed in all its forms (food, ingredient, food supplement).

For each scenario, dietary exposure to cadmium was estimated using a probabilistic approach.
The principle of this approach is to generate a probability distribution of possible exposure values. This method consists in randomly selecting a large number of possible contamination and consumption values according to a probability distribution assigned to them from the available data[14]. This approach makes it possible to take into account the various factors that go into calculating exposure (contamination, consumption, body weight) and to include their distributions in the calculation.

Thus, for each act of consumption and each food, 100,000 contamination and consumption values were randomly selected in probability distributions defined from the available data (see Table 10). This procedure yielded 100,000 exposure values describing an exposure distribution from which conventional parameters such as the mean, median and percentiles of the distribution, along with their confidence intervals, could be calculated. This approach was applied for each sub-population (children aged 3 to 17, adults), and each scenario (seaweed, ingredients, food supplements, all sources combined).

Table 10. Defined probability distributions for the available data

Variable	Fitted distribution
Contamination of seaweed as a food	Inverse-Gaussian[a] (0.62695;0.2202)
Consumption of seaweed as a food in adults	Inverse-Gaussian (0.086378;0.012977)
Contamination of seaweed as an ingredient	Inverse-Gaussian (0.62695;0.2202)
Consumption of seaweed as an ingredient in adults	Log-normal[b] (0.0096244;0.0078926)
Consumption of seaweed as an ingredient in children	Log-normal (0.010748;0.0058055)
Contamination of FS containing seaweed	Log-normal (0.15225;0.58499)
Consumption of FS containing seaweed	Log-normal (38.486;3464)
Exposure to background levels in adults	Log-logistic[c] (-0.023257;0.17141;5.5617)

[a] Inverse-Gaussian distribution (mu, lambda); [b] Log-normal distribution (mean, standard deviation), [c] Log-logistic distribution (gamma, beta, alpha)

Simulations were performed using @Risk 7.5 and R software (R fitdistrplus package).

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[14] The assigned probability distribution is the one that best fits the available data according to statistical criteria.

The same approach was used to calculate dietary exposure of seaweed consumers to inorganic arsenic, methylmercury and lead, based on the available distributions of contamination for these trace elements in seaweed. The results of the analysis of contamination data and estimated exposure of seaweed consumers are presented in Annex 2.

3.2.2.4. Health risk associated with exposure to cadmium in seaweed

Dietary exposure to cadmium in seaweed was compared with the tolerable daily intake (TDI) for cadmium of 0.35 µg Cd.kg $bw^{-1}.d^{-1}$ selected by ANSES (ANSES, 2019).

Estimated dietary exposure to cadmium in seaweed consumers according to scenario and contribution of mean exposure relative to the tolerable daily intake for cadmium

The table below presents the exposure results for each scenario for adult seaweed consumers and only for the "Ingredient" scenario for children, based on the combination of the distributions of cadmium contamination observed in seaweed and the acts of seaweed consumption available in INCA 3 (see Table 9).
For adult seaweed consumers, exposure to cadmium via seaweed consumed as a food represented on average about 16% of the TDI, and between 1.6 and 1.7% when seaweed was consumed as a food ingredient or food supplement. Cadmium from all seaweed sources (food, ingredient, food supplement) represented on average around 19% of the TDI. Seaweed consumed as such accounted for most of this intake, making it a major contributor.
For children consuming seaweed, the mean cadmium intake from seaweed as a food ingredient was less than 2% of the TDI.
It should be remembered that these estimates were made under the UB hypothesis, the most protective because it is the most conservative.

Table 11. Estimated dietary exposure to cadmium in seaweed consumers by scenario and contribution of mean exposure relative to the TDI for cadmium

	Adults			Children		
	Mean	**P95**	**% TDI**	**Mean**	**P95**	**% TDI**
Exposure to seaweed as a food in µg/kg bw/d	**0.05**	**0.20**	**15.5%**			
Exposure to seaweed as a food ingredient in µg/kg bw/d	**0.006**	**0.023**	**1.6%**	**0.006**	**0.024**	**1.7%**
Exposure to seaweed as a FS[15] ingredient in µg/kg bw/d	**0.006**	**0.005**	**1.7%**			
Exposure to seaweed in all forms combined (food + ingredients + FS) in µg/kg bw/d	**0.07**	**0.22**	**18.8%**	**0.006**	**0.024**	**1.7%**

Considering the CSHPF limit value of 0.5 mg cadmium.kg^{-1} dry matter as the maximum contamination level of unprocessed seaweed as a food or condiment, the estimates of mean dietary exposure to cadmium in seaweed consumers showed a contribution relative to the tolerable daily intake of cadmium of up to 15.4% of the TDI when seaweed is consumed in all its forms (food, ingredient, food supplement) (see Table 12), meaning that it remains a major contributor. Mean exposure to cadmium when seaweed was consumed as a food ingredient or food supplement was 1.3% of the TDI, in both cases.

For children consuming seaweed, the mean cadmium intake from seaweed as a food ingredient was 1.4% of the TDI.

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[15] Food supplement

Table 12. Estimated dietary exposure to cadmium in seaweed consumers by scenario and contribution of mean exposure relative to the TDI for cadmium, considering the limit value of 0.5 mg cadmium.kg^{-1} dry matter of seaweed recommended by the CSHPF

	Adults			**Children**		
	Mean	**P95**	**% TDI**	**Mean**	**P95**	**% TDI**
Exposure to seaweed as a food in µg/kg bw/d	**0.045**	**0.19**	**12.7%**			
Exposure to seaweed as a food ingredient in µg/kg bw/d	**0.0046**	**0.012**	**1.3%**	**0.0048**	**0.01**	**1.4%**
Exposure to seaweed as a FS[16] ingredient in µg/kg bw/d	**0.005**	**0.005**	**1.3%**			
Exposure to seaweed in all forms combined (food + ingredients + FS) in µg/kg bw/d	**0.054**	**0.21**	**15.4%**	**0.0048**	**0.01**	**1.4%**

Estimated maximum cadmium concentration in seaweed for the seaweed-consuming population relative to the TDI of 0.35 µg Cd.kg bw^{-1}.d^{-1}

The maximum cadmium concentration in seaweed consumed as such was calculated so as not to increase the initial dietary cadmium exposure of seaweed consumers.
To do this, the distribution of cadmium exposure of the general adult population estimated in TDS2 (ANSES, 2011a) was taken into account, reflecting the baseline exposure of the population, also known as the "background exposure", i.e. cadmium exposure from the entire diet. It should be noted that this overall exposure, without consumption of edible seaweed, already exceeded EFSA's TDI of 0.36 µg Cd.kg bw^{-1}.d^{-1} (EFSA, 2009a) in the general population (0.6% of adults and 15% of children in the TDS2) with, among adult consumers, an estimated mean exposure of 0.15 µg.kg bw^{-1}.d^{-1} and a P95 of 0.27 µg.kg bw^{-1}.d^{-1}, and among child consumers, a mean exposure of 0.24 µg.kg bw^{-1}.d^{-1} and a P95 of 0.45 µg.kg bw^{-1}.d^{-1} (ANSES, 2011a).
This calculation could not be performed for children as they were not included in the "Seaweed" scenario.

This back-calculation[17] was performed using a probabilistic approach similar to that used for the exposure calculation, but here taking into account the baseline exposure distribution of the population. The result is presented as a distribution of the maximum cadmium concentration in unprocessed seaweed intended for human consumption that ensures that the TDI is not exceeded by adding an additional source of cadmium represented by seaweed.

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[16] Food supplement

[17] $ML = \frac{(TRV - Background) x Body\ weight}{Consumption}$

Figure 1 shows the distribution of the maximum cadmium concentration in unprocessed seaweed used as a vegetable or condiment and its confidence interval derived from the back-calculation under the probabilistic approach, as a function of the percentile of the population for which exposure is not expected to exceed the TDI for cadmium when considering the entire diet. The red curve in Figure 1 shows the estimated values of maximum cadmium concentrations in unprocessed seaweed used as a vegetable or condiment, derived from the probabilistic calculation described above for values of the probability of exceeding the TDI between 0.05 and 0.25. These maximum concentrations correspond to percentages of consumers exceeding the TDI between 5% (left of the graph) and 25% (right of the graph) or, equivalently, to percentages of consumers not exceeding the TDI between 95% (left of the graph) and 75% (right of the graph). The y-axis shows the maximum concentration values and the x-axis shows the corresponding probability values. The blue dashed lines in Figure 1 represent the 95% confidence intervals of the estimated maximum concentration values. Calculations were performed considering the entire diet.

The estimated value at the 5th percentile of this distribution was equal to 0.35 mg.kg^{-1} dry matter with a 95% confidence interval of [0.18,1.09] (Figure 1). This maximum level ensures that 95% of the population consuming unprocessed seaweed used as a vegetable or condiment will not exceed the TDI for cadmium even when simultaneously exposed to other dietary sources of cadmium. However, as the confidence interval includes the maximum concentration of 0.5 mg Cd.kg^{-1} dry matter of seaweed, it is possible that this concentration prevents 95% of the population from exceeding the TDI for cadmium.

Ninety-four samples of unprocessed seaweed, all species combined, out of 255 samples from the contamination dataset used (from the CEVA and CONTAMINE databases) exceeded the concentration of 0.35 mg.kg^{-1} dry matter of seaweed (i.e. 36.8% of the dataset).

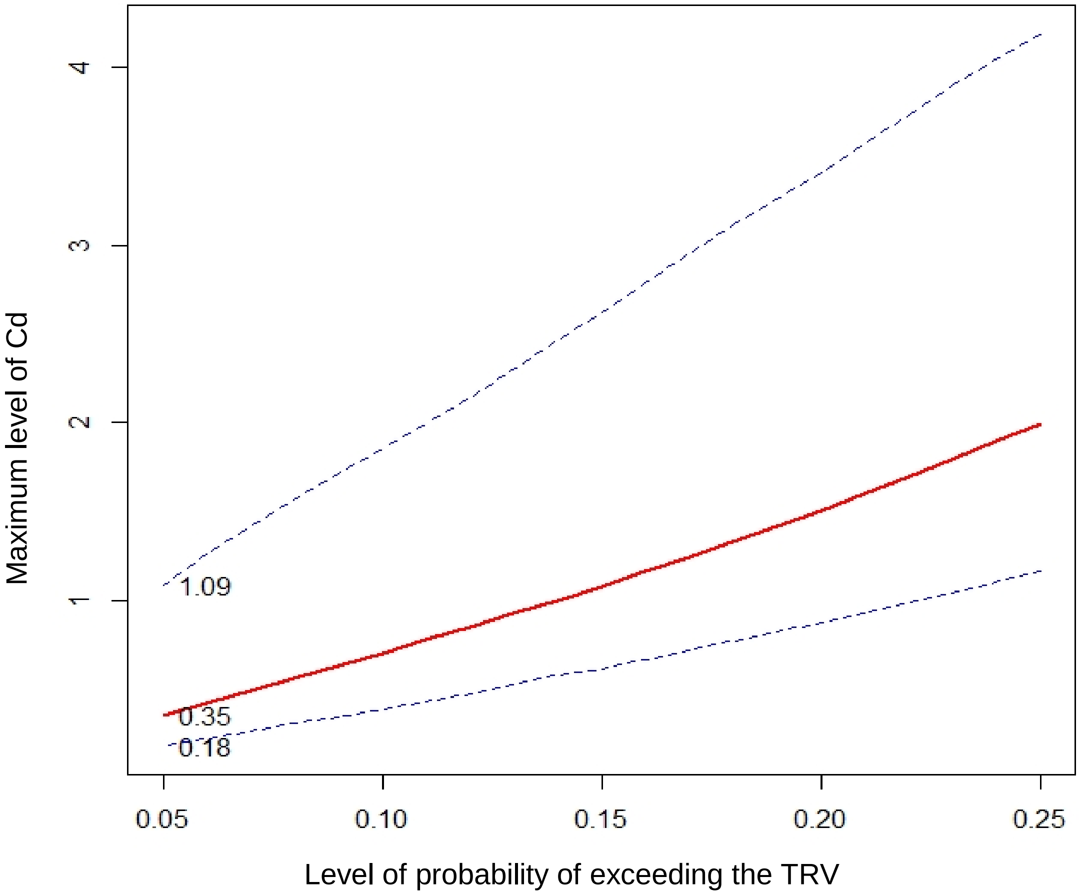

Figure 1. Distribution of the maximum cadmium concentration in unprocessed seaweed used as a vegetable or condiment (mg.kg^{-1} DM) and its confidence interval, as a function of the percentile of the population for which exposure is not expected to exceed the TDI for cadmium when considering the entire diet (explained in the text above).
It should be noted that this back-calculation incorporates two different population samples related firstly to seaweed consumers based on INCA 3 consumption data, and secondly to background levels of exposure to cadmium through the total diet (not including seaweed) of the general population based on INCA 2 consumption data.

Considering the maximum cadmium concentration in edible unprocessed seaweed used as a vegetable or condiment of 0.5 mg.kg^{-1} dry matter recommended by the CSHPF, based on this back-calculation, it appears that the cadmium exposure of the seaweed-consuming population would not exceed the TDI in 93% of cases, taking into account other dietary sources of cadmium.

Lastly, a cadmium concentration of 0.35 mg.kg^{-1} dry matter of unprocessed seaweed used as a vegetable or condiment would, in terms of dietary exposure of consumers of seaweed in all its forms (food, ingredient, food supplement), contribute on average 11.5% of the TDI for cadmium (Table 13), compared to 18.8% with the cadmium contamination distributions observed in seaweed and 15.4% for the maximum concentration of 0.5 mg Cd.kg^{-1} dry matter of seaweed recommended by the CSHPF.

Table 13. Estimated dietary exposure to cadmium in seaweed consumers by scenario considering a maximum concentration in seaweed of 0.35 mg.kg^{-1} dry matter and comparing the contributions of mean exposure to the TDI for cadmium in consumers as a function of concentrations in seaweed

	Adults					Children				
	Maximum concentration in seaweed of 0.35 mg Cd.kg^{-1} dry matter calculated in this work			Maximum concentration in seaweed of 0.5 mg Cd.kg^{-1} dry matter recommended by the CHSPF	Distribution of observed Cd concentrations in seaweed	Maximum concentration in seaweed of 0.35 mg Cd.kg^{-1} dry matter calculated in this work			Maximum concentration in seaweed of 0.5 mg Cd.kg^{-1} dry matter recommended by the CHSPF	Distribution of observed Cd concentrations in seaweed
	Mean	**P95**	**% TDI**	**% TDI**	**% TDI**	**Mean**	**% TDI**	**% TDI**	**% TDI**	**% TDI**
Exposure to seaweed as a food in µg/kg bw/d	**0.03**	**0.13**	**8.9%**	**12.7%**	**15.5%**					
Exposure to seaweed as a food ingredient in µg/kg bw/d	**0.003**	**0.008**	**0.9%**	**1.3%**	**1.6%**	**0.003**	**0.007**	**1.0%**	**1.4%**	**1.7%**
Exposure to seaweed as a FS[18] ingredient in µg/kg bw/d	**0.006**	**0.005**	**1.6%**	**1.3%**	**1.7%**					
Exposure to seaweed in all forms combined (food + ingredients + FS) in µg/kg bw/d	**0.04**	**0.15**	**11.5%**	**15.4%**	**18.8%**	**0.003**	**0.007**	**1.0%**	**1.4%**	**1.7%**

3.2.3. Dealing with uncertainties

When assessing consumer exposure to cadmium through the consumption of edible seaweed, some uncertainties were identified. The experts qualified their impacts on the estimation of consumer exposure and the maximum recommended cadmium concentration in seaweed intended for human consumption.

Table 14. Uncertainties in the assessment of dietary exposure to cadmium associated with the consumption of edible seaweed and impacts on the estimation of exposure and the maximum recommended cadmium concentration

Sources of uncertainty	Impact on exposure estimation
Contamination input data	
- Limits of Detection (LOD) not specified for some results -> Analysis according to the conservative UB assumption	**+**
- Expanded uncertainty U unknown for certain results	**+/-**
- Representativeness of samples	**-**

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[18] Food supplement

Sources of uncertainty	**Impact on exposure estimation**
Consumption input data	
- Limited knowledge on the frequency, mode of consumption and quantity of seaweed consumed by type of seaweed	**-**
- Inadequate knowledge of recipes to take into account all seaweed-based ingredients	**-**
Exposure estimate input data	
- Inclusion of consumption occasions given the quantity of data	**+**
- Failure to include children's consumption data for exposure estimates related to the consumption of unprocessed seaweed and food supplements containing seaweed given the quantity of data	**-**
Estimating a maximum cadmium concentration in seaweed intended for human consumption	
- Back-calculations incorporating two different population samples related to seaweed consumers based on INCA 3 consumption data, and to background levels of exposure to cadmium through the total diet of the general population based on INCA 2 consumption data	**+/-**

+: Uncertainty that may lead to an overestimation of exposure; -: Uncertainty that may lead to an underestimation of exposure

3.3. Conclusions and recommendations

In the general population, a risk to consumers associated with cadmium, a ubiquitous element found in a large proportion of foods, could not be ruled out in the second Total Diet Study (ANSES, 2011a), with the tolerable weekly intake defined by EFSA in 2009 (2.5 µg Cd.kg $bw^{-1}.wk^{-1}$) being exceeded by 0.6% in adults and 15% in children. Indeed, overall mean consumer exposure (known as background exposure) to cadmium was high and estimated to be 0.15 and 0.24 µg.kg $bw^{-1}.d^{-1}$ in adult and child consumers, respectively (ANSES, 2011a). Establishing or strengthening management measures aimed at limiting levels of exposure to cadmium in the general population is therefore necessary.
In adult seaweed consumers, mean dietary exposure to cadmium contributes up to 19% of the tolerable daily intake (TDI) for cadmium of 0.35 µg Cd.kg $bw^{-1}.d^{-1}$ adopted by ANSES (ANSES, 2019) through the consumption of edible seaweed in all its forms (food, ingredient, food supplement). Seaweed consumed as such accounts for the majority of this intake. Indeed, among adult seaweed consumers, exposure to cadmium from seaweed consumed as a food represented on average about 16% of the TDI, and between 1.6 and 1.7% when seaweed was consumed as a food ingredient or food supplement.

Because of firstly, the high exposure of the general population to the ubiquitous element cadmium, and secondly, some uncertainties identified when assessing dietary exposure to cadmium associated with edible seaweed consumption, in terms of data quality and quantity (related to data on seaweed contamination and consumption), it is difficult to produce a robust estimate of the cadmium exposure associated with seaweed consumption, as well as the maximum cadmium concentration in seaweed intended for human consumption.
It is therefore recommended that the maximum cadmium concentration in seaweed should be as low as possible.

On the basis of the exposure scenarios constructed and simulated using a probabilistic approach according to the associated hypotheses and identified limits, some answers can be provided with regard to the questions asked in the formal request.

3.3.1. Recommendations on maximum cadmium levels for seaweed intended for human consumption

In particular, ANSES's opinion was sought on:

1) *"the advisability of retaining the conclusions of the French High Council for Public Health, issued at its meetings of 14 June 1988 and 9 January 1990, recommending a maximum cadmium concentration in edible seaweed of 0.5 mg.kg^{-1} dry weight"*

Considering the maximum cadmium concentration in edible unprocessed seaweed used as a vegetable or condiment of 0.5 mg.kg^{-1} dry matter recommended by the CSHPF, it appears that the cadmium exposure of the seaweed-consuming population would not exceed the TDI in 93% of cases, taking into account the background exposure from the rest of the diet.
This concentration of 0.5 mg.kg^{-1} dry matter in unprocessed seaweed used as a vegetable or condiment recommended by the CSHPF would, on average, in terms of dietary exposure of consumers of seaweed in all its forms (food, ingredient, food supplement), contribute up to 15.4% of the TDI for cadmium, making it a major contributor.

However, the analysis of data on cadmium contamination of unprocessed seaweed intended for human consumption showed that this value in edible seaweed of 0.5 mg.kg^{-1} dry matter was frequently exceeded, representing about 26% of the samples in the available dataset (mostly in seaweed belonging to the brown and red macroalgae groups). The mean cadmium contamination for all categories of unprocessed seaweed observed in the dataset used for the formal request was 0.604 mg.kg^{-1} dry matter (min-max 0.001-9.4 mg Cd.kg^{-1} dry matter).

Furthermore, the levels of cadmium contamination observed in food supplements containing dried seaweed in the dataset used for the formal request did not exceed the maximum cadmium level of 3.0 mg.kg^{-1} laid down in Regulation (EC) No 1881/2006 for food supplements as sold, consisting exclusively or mainly of dried seaweed or products derived from seaweed (mean cadmium concentration observed in the dataset used for the formal request of 0.112 mg.kg^{-1} (min-max 0.004-0.588 mg Cd.kg^{-1} dry weight)).

2) *"defining a cadmium concentration above which seaweed should not be placed on the market. The way in which seaweed is consumed could, where appropriate, be taken into account in order to determine differentiated levels"*

Given that a health risk for the French population from cadmium through total diet cannot be ruled out (ANSES, 2011a), the lowest possible maximum cadmium concentration in seaweed is recommended.
Considering the assumptions of the back-calculation through a probabilistic approach, and taking the entire diet into account, it appears that the level of cadmium contamination must remain below 0.35 mg.kg^{-1} dry matter [0.18,1.09] of unprocessed seaweed used as a vegetable or condiment, all species combined, to avoid the cadmium exposure of the seaweed-consuming population exceeding the TDI in 95% of cases.
A cadmium concentration of 0.35 mg.kg^{-1} dry matter of seaweed as an unprocessed food would, in terms of dietary exposure of consumers of seaweed in all its forms (food, ingredient, food supplement), contribute on average 11.5% of the TDI for cadmium, compared to 15.4% for a maximum concentration of 0.5 mg Cd.kg^{-1} dry matter of seaweed. However, as the confidence

interval includes the maximum concentration of 0.5 mg Cd.kg^{-1} dry matter of seaweed, it is possible that this concentration prevents 95% of the population from exceeding the TDI for cadmium.

It should be pointed out that cadmium contamination is higher in seaweed belonging to the groups of brown and red macroalgae, which are widely consumed (examples: makis, soups, etc.).

3) "*the advisability of defining recommendations for seaweed consumption*."

Due to the small dataset on edible seaweed consumption derived from the INCA 3 study (ANSES, 2017) used for estimating cadmium exposure, it is difficult to formulate recommendations on edible seaweed consumption according to the type of seaweed and mode of consumption. Given the changes in the eating habits of French consumers, a survey is needed to specifically investigate the frequency, mode of consumption and quantity of seaweed consumed by type of seaweed used according to the food product, in the French population. A more accurate qualitative and quantitative collection of these data would help refine the results and recommendations for the consumption of edible seaweed.

3.3.2. Recommendations on the advisability of defining maximum levels of contaminants (trace elements) identified in seaweed intended for human consumption

The consumption of edible seaweed as such or incorporated as a food ingredient or as a food supplement can expose consumers to other contaminants besides cadmium, which was the subject of this formal request. Seaweed has a high polysaccharide composition, which is characterised by an affinity to bind to trace metal elements present in the environment. Due to their natural and anthropogenic origins, besides cadmium, trace elements such as arsenic, mercury and lead are found in seaweed (Almela *et al.*, 2006; Superior Health Council, 2015; NIFES, 2016; Paz *et al.*, 2018; Roleda *et al*., 2019). The CEVA and CONTAMINE contamination databases have the advantage of also containing results on levels of arsenic (total and inorganic), mercury (total) and lead contamination analysed in seaweed. An assessment of consumer exposure by substance to arsenic, mercury and lead was therefore carried out with the aim of issuing recommendations with regard to these trace elements identified in edible seaweed, in order to protect consumer health, given the emerging consumption of this foodstuff.

The assessment is provided in Annex 2 of this opinion.

Apart from the observation, only for cadmium, that the maximum value in edible seaweed recommended by the CSHPF was frequently exceeded – an observation also made in the literature (Almela *et al*., 2006; Superior Health Council, 2015; NIFES, 2016; Paz *et al,*2018; Roleda *et al.*, 2019) – the analysis of contamination data for inorganic arsenic, mercury and lead showed very few cases of the values recommended by the CSHPF being exceeded (see Table 3, Section 3.1.4 and Annex 2).

The assessment covered lead, inorganic arsenic and methylmercury, according to the toxicological characteristics of the forms of the chemical species and the available and usable results on contamination levels from the CONTAMINE database.
Excluding seaweed consumption, a health risk to consumers associated with exposure to inorganic arsenic, methylmercury (through fish and seafood consumption) and lead through total diet cannot be ruled out, according to ANSES's second Total Diet Study (ANSES, 2011a).

Estimating exposure to these trace elements following consumption of edible seaweed (based on the constructed scenarios for cadmium) in this work showed that:

- The share of mean exposure to inorganic arsenic in consumers of seaweed in all its forms (food, ingredients, food supplements) contributes between 2 and 54% of the benchmark values established by JECFA for estimating the risk from inorganic arsenic (0.3 and 8 µg.kg bw^{-1}.d^{-1} respectively). Seaweed consumed as such accounts for the majority of this intake.
- The mean exposure to methylmercury in consumers of seaweed in all its forms (food, ingredients, food supplements) contributes 3% of the PTWI of 1.3 µg.kg bw^{-1}.wk^{-1}.
- The share of mean exposure to lead in consumers of seaweed in all its forms (food, ingredients, food supplements) contributes 78% for adults and 8% for children of the benchmark values established by EFSA for estimating the risk from lead intake (0.63 µg.kg bw^{-1}.d^{-1} and 0.50 µg.kg bw^{-1}.d^{-1} for adults and children, respectively).
  Seaweed consumed as such accounts for the majority of this intake.

The data on contamination of seaweed intended for human consumption showed that inorganic arsenic, mercury and lead were not detected or quantified in 53%, 80% and 40% of the samples, respectively. The exposure estimate was based on the UB assumption, which maximises the calculations.

Because of firstly, the high exposure of the general population to these trace elements, and secondly, some uncertainties identified when assessing dietary exposure (as with cadmium) associated with edible seaweed consumption, in terms of data quality and quantity (related to data on seaweed contamination and consumption), it is difficult to produce a robust estimate of exposure to these contaminants associated with seaweed consumption, as well as their maximum concentrations in seaweed intended for human consumption.
It is therefore recommended that the maximum concentration of these trace elements in seaweed should be as low as possible.
Lastly, it was noted that the seaweed hijiki (*Hizikia fusiforme*, a brown macroalgae), was identified in the literature among all seaweed species as particularly accumulative of inorganic arsenic (Almela *et al*., 2006; EFSA, 2009b, 2014; Esther *et al.*, 2014; Superior Health Council, 2015; NIFES, 2016; Roleda *et al.*, 2019); the other seaweed species generally contained more of the organic form of arsenic. Almela *et al.* (2006), EFSA (2009b, 2014), Esther *et al*. (2014), the Superior Health Council (2015), NIFES (2016) and Roleda *et al.* (2019) indicated a potentially high risk to consumers from consumption of this species, which accumulates high levels of inorganic arsenic. Some health agencies recommend avoiding consumption of this species of hijiki (*Hizikia fusiforme*) seaweed (FSA, 2004; EFSA 2009b, 2014; Superior Health Council, 2015). This species, which is likely to be found on the consumer's plate (see Table 1), was not found among the samples taken and analysed in the annual monitoring and control plans in France, and should be included in them.

4. AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety endorses the CES ERCA's conclusions.

The DGCCRF asked ANSES to conduct an expert appraisal on maximum cadmium (Cd) levels for seaweed intended for human consumption.

The consumption of edible seaweed in different forms (as a food, food ingredient or food supplement ingredient) is still a recent development in consumption habits in France, as well as in Europe. The seaweed consumed in this way is varied in terms of its origin (local and imported) and types (brown, red, green, macroalgae, microalgae, halophytes, etc.), which may have specific characteristics in terms of contaminant levels.

Due in particular to its high levels of polysaccharides (molecules that have a high binding affinity to trace metal elements (TMEs)) and the presence of these elements in the oceans, either naturally or enhanced by anthropogenic activities, seaweed can contain significant levels of different TMEs. However, some TMEs are already subject to ANSES recommendations following risk assessments resulting from total diet studies based on calculated exposure levels, independent of any seaweed consumption (the INCA 2 study did not identify any that were statistically significant).

To date, only cadmium levels in seaweed used in food supplements are governed by European regulations (Regulation (EC) No 1881/2006 as amended). In France, the CSHPF (since replaced by the HCSP) had in 1990 issued a list of seaweed that could be authorised for human consumption, together with recommendations on maximum levels (in weight/kg dry matter) for the following TMEs: inorganic arsenic (3 mg.kg^{-1}), cadmium (0.5 mg.kg^{-1}), mercury (0.1 mg.kg^{-1}) and lead (5 mg.kg^{-1}).

Moreover, based on the same observation that "seaweed and halophytes form an increasingly important contribution to the consumption patterns of certain EU consumers", in March 2018 the European Commission issued a recommendation (Recommendation (EU) 2018/464) to Member States to gather monitoring data and provide them to EFSA, in order to "assess whether the contribution of arsenic, cadmium, iodine, lead and mercury from seaweed and halophytes to the total exposure of these substances, would necessitate the establishment of MLs for arsenic, cadmium and lead for these commodities or the amendment of the MRL for mercury for algae and prokaryotic organisms or any action to be taken related to the exposure to iodine from these products."

On the basis of the available sampling data (just under 500 samples from the results of the centralised monitoring and control plans in CONTAMINE on the one hand, and a CEVA survey on the other), which the experts considered to be of limited comparability with the seaweed actually consumed, the experts calculated an exposure contribution – for seaweed consumers – in terms of percentage of the health reference values for cadmium, lead, mercury and arsenic.

At this stage of the analysis, the Agency had already observed that a non-negligible fraction of seaweed exceeded the maximum values established by the CHSPF. For these different TMEs, the calculated fraction represented by the estimated exposure of seaweed consumers relative to the health reference values was respectively: 3% (mercury), 19% (cadmium), between 3% and 54% (arsenic) and 80% (lead). The contribution of food supplements containing seaweed was always minor among adult consumers. In addition, there were too few data on the consumption of seaweed as a food and as a food supplement ingredient in children.

Therefore, given that a risk to consumers associated with cadmium, lead, mercury and arsenic could not be ruled out in light of the second Total Diet Study (TDS2), the experts reiterated their recommendation to strengthen management measures to limit exposure of the general population to these elements. In this respect, adding potentially significant intakes by incorporating in the diet foods that increase this exposure should therefore be taken into consideration in this aim of limiting exposure, which in particular requires concentrations to be reduced as much as possible.

Specifically regarding cadmium, which was the main subject of the formal request, the experts developed a probabilistic approach to best account for the sources of variability in cadmium exposure (both for basic and added consumption). This approach, supplemented by a back-calculation method, led them to identify the cadmium concentration of 0.35 mg.kg^{-1} dry matter (confidence interval: [0.18,1.09]), which should ensure that the seaweed-consuming population does not exceed the tolerable daily intake (TDI) of cadmium in 95% of cases. In this case, the contribution of seaweed consumers relative to the TDI is therefore reduced from 19% (related to the distribution of cadmium concentrations observed in seaweed) to 11,5% with a maximum concentration in seaweed of 0.35 mg Cd.kg^{-1} dry matter, while a contribution of 15.5% of the TDI is observed with the maximum concentration in seaweed of 0.5 mg Cd.kg^{-1} dry matter recommended by the CSHPF. The experts stressed that cadmium contamination was higher for brown and red macroalgae.

The expert appraisal highlighted the risk of higher overexposure to chemical contaminants from combining consumption of seaweed with that of other foods, such as combining consumption of the hijiki (*Hizikia fusiforme*) seaweed, an accumulator of inorganic arsenic, with that of rice contaminated by inorganic arsenic.

Regarding all contaminants taken together, the Agency emphasises that in situations where health reference values are exceeded for a fraction of the population, it is up to the competent authority to identify and define the appropriate management levers for foods that are new entrants to the existing supply: implementation of maximum levels based on control statistics in an ALARA approach (e.g. by setting a P95 type value), use of existing limit levels in other food categories (e.g. vegetables) or specific provisions for different categories that make a greater contribution (specific recommendations or maximum levels).

Lastly, the experts considered that the weakness of the consumption dataset (from the INCA 3 study) made it impossible to establish consumption recommendations according to the type of seaweed and mode of consumption. They recommended implementation of a survey to increase data on frequency, quantity consumed and mode of consumption according to the types of seaweed. These data will be used to obtain a more precise estimate of exposure associated with the various types of seaweed consumption for the populations concerned and, where appropriate, of TME concentration limits in edible seaweed.

The Agency underlines that this recommendation is more broadly in line with the one issued by the European Union in March 2018, which is likely to be followed by proposals for maximum levels established at European level in the framework of relevant regulations.

Dr Roger Genet

KEYWORDS

Algues, alimentation humaine, contaminants, cadmium
Algae, food, contaminants, cadmium

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ANNEX 1

Presentation of the participants

PREAMBLE: The expert members of the Expert Committees and Working Groups or designated rapporteurs are all appointed in a personal capacity, *intuitu personae*, and do not represent their parent organisation.

RAPPORTEURS

Mr David MAKOWSKI – Research Director – expertise in statistics and modelling

EXPERT COMMITTEE

The work covered in this report was monitored and adopted by the following Expert Committee (CES):

CES on "Assessment of physical-chemical risks in food" – 11 July 2019

Chair

Mr Bruno LE BIZEC – University Professor – expertise in analytical chemistry

Vice-Chairs

Mr Fabrice NESSLANY – Laboratory Director – expertise in toxicology

Ms Karine TACK – Researcher – expertise in analytical and environmental chemistry, health risk assessment

Members

Mr Claude ATGIE – University Professor – expertise in toxicology

Mr Pierre-Marie BADOT – University Professor – expertise in contaminant transfer and ecotoxicology

Ms Marie-Yasmine DECHRAOUI BOTTEIN – Researcher in Environmental Toxicology – expertise in marine biotoxins

Ms Martine CLAUW – University Professor – expertise in toxicology

Mr Nicolas DELCOURT – University Lecturer, Hospital Pharmacist – expertise in biochemistry and clinical toxicology

Ms Christine DEMEILLIERS – University Lecturer – expertise in toxicology

Mr Erwan ENGEL – Research Director – expertise in analytical chemistry

Mr Jérôme GAY-QUEHEILLARD – University Lecturer – expertise in digestive impacts, metabolism, immunity; health impacts of pesticides

Mr Petru JITARU – Laboratory Manager – expertise in analytical chemistry

Ms Sonia KHIER – University Lecturer – expertise in pharmacokinetics

Ms Emilie LANCE – University Lecturer – expertise in ecotoxicology and cyanotoxins

Ms Caroline LANIER – University Lecturer – expertise in assessment of health risks associated with the environment and food

Ms Raphaële LE GARREC – University Lecturer – expertise in toxicology

Mr Ludovic LE HEGARAT – Laboratory Manager – expertise in toxicology

Mr Nicolas LOISEAU – Researcher – expertise in toxicology

Mr David MAKOWSKI – Research Director – expertise in statistics and modelling

Mr Eric MARCHIONI – University Professor – expertise in analytical chemistry

Mr Jean-François MASFARAUD – University Lecturer – expertise in contaminant transfer and ecotoxicology

Mr César MATTEI – University Lecturer – expertise in toxicology

Mr Alain-Claude ROUDOT – University Professor – expertise in mathematical modelling, exposure assessment

Mr Yann SIVRY – University Lecturer – expertise in analytical chemistry

Ms Paule VASSEUR – Professor Emeritus – expertise in toxicology

ANSES PARTICIPATION

Coordination and scientific contributions

Ms Géraldine CARNE – Scientific Project Leader – ANSES

Scientific contribution

Ms Eleni ANASTASIS – ANSES

Ms Nawel BEMRAH – Scientific Project Manager – ANSES

Ms Sandrine CARRILLO – Scientific Project Leader – ANSES

Mr Thierry GUERIN – Head of the Chemical Contaminants in Food Department – ANSES

Mr Petru JITARU – Head of the Metal and Mineral Trace Elements Unit – ANSES

Ms Karine VIN – Study and Scientific Support Coordinator – ANSES

Administrative secretariat

Ms Angélique LAURENT – ANSES

HEARINGS WITH EXTERNAL EXPERTS

Ms Hélène MARFAING – Agri-food and Nutrition Project Leader at the Centre for Study and Promotion of Algae (CEVA), interviewed on 13 November 2018

Mr Ronan PIERRE – Head of the Innovation and Products Unit at the Centre for Study and Promotion of Algae (CEVA), interviewed on 13 November 2018

ANNEX 2

Assessment of consumer exposure to trace elements (arsenic, mercury, lead) identified in seaweed intended for human consumption

The consumption of edible seaweed as such or incorporated as a food ingredient or as a food supplement can expose consumers to other contaminants besides cadmium, which was the subject of this formal request. Seaweed has a high polysaccharide composition, which is characterised by an affinity to bind to trace elements present in the environment. Due to their natural and anthropogenic origins, besides cadmium, trace elements such as arsenic, mercury and lead have been identified in seaweed (Almela *et al.*, 2006; Superior Health Council, 2015; NIFES, 2016; Paz *et al.*, 2018; Roleda *et al.*, 2019). The CEVA and CONTAMINE contamination databases have the advantage of also containing results on levels of arsenic (total and inorganic), mercury (total) and lead contamination analysed in seaweed. An assessment of consumer exposure by substance to arsenic, mercury and lead was therefore carried out, with the aim of making recommendations for these trace elements identified in edible seaweed, in order to protect consumer health, given the emerging consumption of this foodstuff.

- **Arsenic**

Hazard characterisation

Arsenic (As) is a metalloid found widely in the Earth's crust (2 mg.kg^{-1} on average) and very prevalent in certain delta regions. It also comes from anthropogenic inputs (industrial activities, fossil fuel combustion, former agricultural uses, etc.). It exists in different chemical forms, organic or inorganic, and in four valence states [(-3), (0), (+3) and (+5)]. Arsenic speciation – the form in which it is found – determines its behaviour in the environment, bioavailability and toxicity.

Arsenic, which is usually rapidly and almost completely absorbed after ingestion, is distributed in the liver, kidney, spleen and lung, and secondarily in the skin and skin appendages. It is then detoxified primarily in the liver, with varying effectiveness depending on the individual's species, age, sex or nutritional status, and is excreted in the urine primarily as dimethylarsinic acid and monomethylarsonic acid.
In addition, inorganic arsenic and its methyl metabolites readily cross the placental barrier and the immature blood-brain barrier of the foetus.
Chronic ingestion of arsenic may result in a broad spectrum of non-neoplastic effects including skin lesions, neurotoxicity, cardiovascular, respiratory and gastrointestinal diseases, immunological, haematological and glucose metabolism disorders, and impaired reproduction and development. The occurrence of these effects is dependent on the chemical form of the arsenic and the level of exposure. Inorganic arsenic is a proven human carcinogen, classified in Group 1 by the IARC on the basis of epidemiological evidence of induction of skin, lung and bladder cancers (IARC, 2012b).
Taking as a reference point the carcinogenic effects of the ingestion of inorganic arsenic on the skin, lung and bladder and considering the limited data on exposure of the populations studied (measurements of total arsenic in drinking water), in 2009 EFSA selected a $BMDL_{01}$ ranging[19] from 0.3 to 8 µg.kg bw^{-1}.d^{-1} (EFSA, 2009b) based on modelling of dose-response relationships in key epidemiological studies, without specifying any margins of exposure beyond which a risk could be ruled out. In addition, although the carcinogenicity of inorganic arsenic is probably a threshold mechanism of action rather than direct genotoxicity, a threshold dose was not defined due to uncertainties in the shape of the dose-response relationship. Consequently, EFSA recommended

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[19] Depending on the adverse effects selected (lung, bladder or skin cancers)

assessing the health risk on the basis of the margins of dietary exposure of the population and the reference points identified by epidemiology. In 2011, JECFA selected a $BMDL_{0.5}$ ranging from 2 to 7 µg.kg $bw^{-1}.d^{-1}$ based on an increase in lung cancer (JECFA, 2011b). This falls within the range of values adopted by EFSA.

For organic arsenic, there are insufficient data to establish a TRV.

According to the second Total Diet Study (ANSES 2011a), in both adults and children, the major contributors to total arsenic exposure are fish (30% and 42%, respectively) and shellfish (17% and 7%, respectively). Water also appears to be a significant contributor (8% in adults and 6% in children), as well as milk in children (6%). Water is the major contributor to inorganic arsenic exposure in both adults and children. This study indicated that the possibility of a risk associated with exposure to inorganic arsenic could not be excluded for certain groups of consumers and that efforts to reduce dietary intake of inorganic arsenic should continue. The Infant Total Diet Study (ANSES, 2016a), for its part, indicated a situation of concern for children under 3 years of age. In addition, it appears necessary to implement routine analytical methods to quantify the different forms of arsenic speciation in order to refine exposure, and to continue efforts.

EFSA (2009b, 2014) identified seaweed as a major contributor to consumer exposure to total arsenic. Seaweed was identified by EFSA as a matrix containing high levels of arsenic contamination, mainly in the form of organic arsenic (more specifically in the form of arsenosugar[20]); with the exception of the brown macroalgae hiziki or hijiki (*Hizikia fusiforme*), which contains very high levels of inorganic arsenic. Almela *et al.* (2006), Esther *et al.* (2014), Superior Health Council (2015), NIFES (2016) and Roleda *et al.* (2019) also made similar observations.
EFSA (2014) selected as its speciation hypothesis that 1% of the total arsenic analysed in seaweed is assumed to be in inorganic form, excluding the hijiki species that specifically accumulates inorganic arsenic.

Contamination

The data from the monitoring and control plans compiled in CONTAMINE have analytical information for this element (analytical methods, performance criteria, etc.), from which it is possible to assess the quality of the data and constitute a means for exploiting the contamination levels observed in seaweed.

This dataset contains 120 results of analysed contamination levels of total arsenic and 41 results of analysed contamination levels of inorganic arsenic in seaweed, including seaweed used as such, as a food ingredient and a food supplement ingredient, sampled in France between 2009 and 2017 and analysed between 2010 and 2018.
The samples were analysed by laboratories accredited according to ISO/IEC 17025 (59% of samples) or by laboratories with in-house accreditation (17.5% of data). In 23.5% of cases, laboratories were classified as accredited without any information on the type of accreditation (ISO 17025 or in-house).
Seaweed samples were analysed by electrothermal atomic absorption spectrometry and also by inductively coupled plasma mass spectrometry (ICP-OES/MS) methods, producing data of satisfactory quality for this type of analysis.

Limits of Detection (LOD) and Limits of Quantification (LOQ) are given when concentrations are below these limits. Although there were indications regarding expression of the measurement uncertainty, the results compiled in the database sometimes lacked clarity on whether the

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[20] Carbohydrate compounds containing arsenic

information did indeed refer to the expanded uncertainty U, and on its expression, where in some cases they were probably expressed in % and others in mg.kg^{-1}.

Ultimately, all 120 results of analysed contamination levels of total arsenic and 41 results of analysed contamination levels of inorganic arsenic in seaweed were usable.

The groups analysed for total arsenic, in increasing order of percentage, were as follows:
Food supplements (FS) (44%) > unknown seaweed (17.5%) > brown macroalgae (12.5%) > red macroalgae (10.8%) > microalgae (spirulina) (6.6%) > green macroalgae (3.3%) > halophytes (glasswort) (2.5%) > seaweed mixtures (0.8%; n = 1) > powder, agar-agar and beverages (0.8% each (n = 1 each)).

The groups analysed for inorganic arsenic, in increasing order of percentage, were as follows:
Unknown seaweed (30%) > brown macroalgae (24.3%) > red macroalgae (19.5%) > microalgae (spirulina) (12.1%) > food supplements (FS) (7.3%) > green macroalgae (4.8%) > seaweed mixtures (2.4%; n = 1) > halophytes (glasswort) (0%) > powder, agar-agar and beverages (0%).

However, the comparability of the sample from the CONTAMINE database with the seaweed consumed by the French population related to the national study of edible seaweed consumption (Le Bras *et al.*, 2014, 2015) remains limited.

The data were then analysed by seaweed group and using the upper bound (UB) approach. Data processing covered all samples analysed for total and inorganic arsenic, except for the single samples of powder, agar-agar and beverages. Thirty-nine results out of 120 samples analysed for total arsenic were not quantified (n = 31) or detected (n = 8) (LOD/LOQ between 0.04 and 2.65 mg.kg^{-1}) and 22 results out of 41 samples analysed for inorganic arsenic were not quantified (n = 21) or detected (n = 1) (LOD/LOQ between 0.08 and 1 mg.kg^{-1}). The dataset was converted to mg.kg^{-1} dry matter where necessary, by applying a conversion factor for data provided as wet weight. The choice of this factor was based on a review of the literature (Arne Jensen, 1993; Stévant *et al.*, 2017; Qing Chen *et al.*, 2018; Roleda *et al.*, 2019) and assumed an average dry matter content of 20% in fresh seaweed.

The table below presents the analysis of data on total and inorganic arsenic contamination in the seaweed categories of the CONTAMINE database.

Table 2-1. Analysis of total arsenic concentrations (mg.kg^{-1} dry matter (DM)) in the seaweed categories of the CONTAMINE database

	Total	**Unknown**	**Brown macroalgae**	**Red macroalgae**	**Green macroalgae**	**Microalgae**	**Halophytes**	**Mixtures**	**FS**
n	120	21	15	13	4	8	3	1	53
				Total arsenic concentrations (mg.kg^{-1} dry matter (DM))					
Median	2.89	14.5	23.5	14.6	10.1	0.18	0.25	10.9	0.66
Mean	10.3	15.1	22.4	15.2	14.7	0.22	0.21	10.9	5.92
Min	0.035	0.040	0.075	0.052	1.55	0.035	0.055	10.9	0.11
Max	50.0	50.0	45.0	35.4	37.0	0.55	0.34	10.9	48.7

Total: all seaweed categories combined; Unknown: seaweed whose parent group is not specified; Brown macroalgae: seaweed belonging to the group of brown macroalgae; Red macroalgae: seaweed belonging to the group of red macroalgae; Green macroalgae: seaweed belonging to the group of green macroalgae; Microalgae: related to spirulina in CONTAMINE; Halophytes: related to glasswort in CONTAMINE; Mixtures: mixtures of dried seaweed; FS: food supplements containing dried seaweed.

Table 2-2. Analysis of inorganic arsenic concentrations (mg.kg^{-1} dry matter (DM)) in the seaweed categories of the CONTAMINE database

	Total	Unknown	Brown macroalgae	Red macroalgae	Green macroalgae	Microalgae	Halophytes	Mixtures	FS
n	41	12	10	8	2	5	0	1	3
Inorganic arsenic concentrations (mg.kg^{-1} dry matter (DM))									
Median	0.50	0.56	0.50	0.21	0.50	0.10	0	5.30	0.10
Mean	1.48	0.86	3.95	0.38	0.50	0.09	0	5.30	0.35
Min	0.039	0.10	0.100	0.039	0.50	0.08	0	5.30	0.10
Max	20.0	3.80	20.0	1.20	0.50	0.10	0	5.30	0.86
Breakdown of numbers according to classes of inorganic arsenic concentrations (mg.kg^{-1} DM) below or above the CSHPF reference value of 3 mg.kg^{-1} DM									
concentration < 3	37	11	8	8	2	5	0	0	3
3 < concentration < 4	1	1	0	0	0	0	0	0	0
concentration > 4	3	0	2	0	0	0	0	1	0

Total: all seaweed categories combined; Unknown: seaweed whose parent group is not specified; Brown macroalgae: seaweed belonging to the group of brown macroalgae; Red macroalgae: seaweed belonging to the group of red macroalgae; Green macroalgae: seaweed belonging to the group of green macroalgae; Microalgae: related to spirulina in CONTAMINE; Halophytes: related to glasswort in CONTAMINE; Mixtures: mixtures of dried seaweed; FS: food supplements containing dried seaweed.

For the data as a whole, the mean and median total arsenic contamination levels for all seaweed categories were 10.2 and 2.89 mg.kg^{-1} DM, respectively (min-max 0.035-50 mg.kg^{-1} dry matter).
Brown macroalgae were the most contaminated with total arsenic, with a mean value of 22.4 mg.kg^{-1} dry matter. Next came the groups of red and green macroalgae, which were significantly more contaminated (mean total arsenic concentration above 14 mg.kg^{-1} dry matter) than the groups of microalgae and halophytes, which had mean total arsenic concentrations of 0.22 and 0.21 mg.kg^{-1} dry matter, respectively.
In the form of inorganic arsenic, for the data as a whole, the mean and median contamination levels for all seaweed categories were 1.48 and 0.50 mg.kg^{-1} DM, respectively (min-max 0.039-20 mg.kg^{-1} dry weight). Brown macroalgae had the highest mean inorganic arsenic concentration (3.95 mg.kg^{-1} dry matter). The seaweed mixture sample had an inorganic arsenic concentration of 5.30 mg.kg^{-1} dry matter.

The food supplement group (n = 53) had a mean total arsenic concentration of 5.92 mg.kg^{-1} dry weight (min-max 0.11-48.7 mg.kg^{-1} dry weight).
The food supplement group (n = 3) had a mean inorganic arsenic concentration of 0.35 mg.kg^{-1} dry weight (min-max 0.10-0.86 mg.kg^{-1} dry weight).

A maximum total arsenic level of 50 mg.kg^{-1} dry matter was observed in a sample of dried seaweed of unknown identification originating in Korea.
A maximum inorganic arsenic level of 20 mg.kg^{-1} dry matter was observed in a sample of kombu brown macroalgae originating in France.

A total of 4 out of 41 seaweed samples analysed for inorganic arsenic for all seaweed categories combined (i.e. 10%) exceeded the value of 3 $mg.kg^{-1}$ dry matter recommended by the CSHPF (see Table 3, Section 3.1.4), with brown macroalgae (n = 2) (kombu brown macroalgae originating in France), seaweed with unknown classification (n = 1) (origin France) and seaweed mixtures (n = 1) (origin France).

However, it should be noted that in order to compare it with the reference value, knowledge of the expanded uncertainty U of each result is needed, because according to Regulation (EC) No 333/2007[21] "The analytical result shall be reported as x +/- U whereby x is the analytical result and U is the expanded measurement uncertainty, using a coverage factor of 2 which gives a level of confidence of approximately 95% (U = 2u)." Although there were indications regarding uncertainty, it was not always specified whether this concerned the expanded uncertainty.

Exposure

Consumer exposure to inorganic arsenic only through ingestion of edible seaweed was estimated. The estimates were based on the exposure scenarios for edible seaweed consumption developed for the cadmium study and described in Section 3.2.2.3. Similarly, the input data were based on seaweed consumption data derived from the INCA 3 study (ANSES, 2017) considering the consumption occasions of adult seaweed consumers for the scenarios related to the consumption of unprocessed seaweed and seaweed incorporated as a food supplement ingredient, and the consumption occasions of child and adult consumers for the scenario related to the consumption of seaweed as a food ingredient. These consumption data were combined with contamination data from analytical results for inorganic arsenic, to ultimately arrive at an estimated contribution of exposure of seaweed consumers relative to the available benchmark values for inorganic arsenic. The uncertainties identified in the assessment of dietary exposure to cadmium associated with edible seaweed consumption (see Section 3.2.3) also apply to this inorganic arsenic-related contaminant.

Table 2-3. Estimated dietary exposure to inorganic arsenic from consumption of edible seaweed by scenario and contribution of mean exposure relative to the benchmark values (BMDLs as defined by JECFA) for inorganic arsenic

	Adults				**Children**			
	Mean	**P95**	**% of the benchmark value of 0.3 µg/kg bw/d**	**% of the benchmark value of 8 µg/kg bw/d**	**Mean**	**P95**	**% of the benchmark value of 0.3 µg/kg bw/d**	**% of the benchmark value of 8 µg/kg bw/d**
Exposure to seaweed as a food in µg/kg bw/d	**0.14**	**0.41**	**45.80%**	**1.70%**				
Exposure to seaweed as a food ingredient in µg/kg bw/d	**0.014**	**0.059**	**4.70%**	**0.18%**	**0.015**	**0.062**	**4.90%**	**0.18%**
Exposure to seaweed as a FS ingredient in µg/kg bw/d	**0.01**	**0.015**	**3.30%**	**0.12%**				

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[21] Commission Regulation (EC) No 333/2007 of 28 March 2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs

	Adults				Children			
	Mean	**P95**	**% of the benchmark value of 0.3 µg/kg bw/d**	**% of the benchmark value of 8 µg/kg bw/d**	**Mean**	**P95**	**% of the benchmark value of 0.3 µg/kg bw/d**	**% of the benchmark value of 8 µg/kg bw/d**
Exposure to seaweed in all forms combined (food + ingredients + FS) in µg/kg bw/d	**0.16**	**0.493**	**53.80%**	**2%**	**0.015**	**0.062**	**4.90%**	**0.18%**

The table above presents the exposure results for each scenario for adult seaweed consumers and only for the "Ingredient" scenario for children.

For adults, based on the benchmark values of 0.3 and 8 µg.kg bw^{-1}.d^{-1}, exposure to inorganic arsenic via seaweed consumed as a food represented on average about 46% and 2% of the TDI, respectively, and less than 5% and less than 0.2%, respectively, when seaweed was consumed as an ingredient or food supplement. Inorganic arsenic contributed by all sources of seaweed represented on average nearly 54% and 2% of the benchmark values of 0.3 and 8 µg.kg bw^{-1}.d^{-1}, respectively.

In children, the mean intake of inorganic arsenic from seaweed as an ingredient was less than 5% and 0.2% of the 0.3 and 8 µg.kg bw^{-1}.d^{-1} benchmarks, respectively.

It should be remembered that these calculations were estimated under the UB assumption.

Conclusions

The seaweed hijiki (*Hizikia fusiforme*, a brown macroalgae), was identified in the literature among all seaweed species as particularly accumulative of inorganic arsenic specifically (Almela *et al.*, 2006; EFSA, 2009b, 2014; Esther *et al.*, 2014; Superior Health Council, 2015; NIFES, 2016; Roleda *et al.*, 2019); the other seaweed species generally contained more of the organic form of arsenic. Almela *et al.* (2006), EFSA (2009b, 2014), Esther *et al*. (2014), the Superior Health Council (2015), NIFES (2016) and Roleda *et al.* (2019) indicated a potentially high risk to consumer health from consumption of this species, which accumulates high levels of inorganic arsenic. This risk is even higher when this consumption is combined with that of rice contaminated by inorganic arsenic. Moreover, some agencies recommend avoiding consumption of this species of hijiki (*Hizikia fusiforme*) seaweed (FSA, 2004; EFSA 2009b, 2014, Superior Health Council, 2015). Although this seaweed is primarily consumed on the Asian market, it is also identified as a species likely to be consumed by French consumers (see Table 1). It can indeed find its way onto the European market through restaurants, food supplements, etc.

This species was not identified among the seaweed analysed for arsenic in the contamination dataset available for this formal request. Sampling of the species hijiki (*Hizikia fusiforme*) likely to be found on the consumer's plate and testing for inorganic arsenic for this species should be encouraged in the annual monitoring and control plans in France.

Estimating inorganic arsenic exposure from edible seaweed consumption showed that the mean exposure to this contaminant in consumers of seaweed in all its forms (food, ingredients, food supplements) contributes 54% and 2% of the benchmark values of 0.3 to 8 µg.kg bw^{-1}.d^{-1}, respectively. Seaweed consumed as such accounts for the majority of this intake.

Initially, a health risk to consumers associated with exposure to inorganic arsenic cannot be ruled out, according to ANSES's second Total Diet Study (ANSES, 2011a). Overall mean consumer exposure (background exposure) to inorganic arsenic was high and estimated to be 0.27 and 0.38 µg.kg bw^{-1}.d^{-1} in adult and child consumers, respectively (ANSES, 2011a). The situation was even considered a concern for children under 3 years of age, according to the Infant Total Diet Study

(ANSES, 2016a). Efforts to reduce dietary intakes of inorganic arsenic should therefore be continued. Analysis of the data on inorganic arsenic contamination in seaweed intended for human consumption showed that inorganic arsenic was not detected or quantified in 53% of the dataset samples, as well as a mean and median concentration (1.48 and 0.50 $mg.kg^{-1}$ dry matter) 2 to 6 times lower than the CSHPF reference value of 3 mg $Asi.kg^{-1}$ dry matter.
It is therefore recommended that the maximum concentration of inorganic arsenic in seaweed should be as low as possible.

In addition, to reduce exposure to inorganic arsenic through edible seaweed consumption, the Superior Health Council (2015) recommends that cooking water be discarded, since arsenic tends to migrate into cooking water. Almela *et al*. (2006), Esther *et al*. (2014), Superior Health Council (2015) and Roleda *et al.* (2019) made the same observations, also noting that preparing seaweed by washing and boiling it tends to reduce arsenic levels in seaweed intended for human consumption. Nevertheless, the effects of seaweed preparation (washing, boiling) on arsenic levels in this matrix should be studied further, in order to obtain more robust data.

Lastly, the toxicological characterisation of arsenic in seaweed (organic form: arsenosugars, arsenolipids, etc. and inorganic form), as well as the identification and quantitative analysis of all arsenic species, remain to be defined and then taken into account by legislation to regulate arsenic levels in seaweed intended for food consumption.

- **Mercury**

Hazard characterisation

Mercury (Hg) is a metallic element naturally present in the Earth's crust (0.02 $mg.kg^{-1}$), which has the characteristic of being in liquid form under normal temperature and pressure conditions. Mercury is used in a wide range of industries (batteries, electrical cables and switches, measuring devices, dental amalgams, lamps), leading to releases into the environment that are compounded by waste incineration. It exists in different chemical, organic or inorganic forms. Methylmercury, the main form of organic mercury, is bioaccumulative and becomes highly concentrated in the food chain.
Inorganic mercury's toxicity leads to kidney damage, neurotoxicity and cardiovascular disorders. In 2010, JECFA established a new provisional tolerable weekly intake (PTWI) for inorganic mercury of 0.004 mg.kg $bw^{-1}.wk^{-1}$ (4 µg.kg $bw^{-1}.wk^{-1}$), based on kidney effects in rats, which applies to exposure to total mercury in food excluding fish and other seafood (JECFA, 2011a).
Via the oral route, the central nervous system is the main target organ for organic mercury, especially during foetal development. The toxic effects are impaired sensory functions (sight, hearing), motor coordination, memory, attention and learning. JECFA has set a PTWI for methylmercury of 1.6 µg.kg $bw^{-1}.wk^{-1}$, based on epidemiological studies on the relationship between maternal exposure and the neurological development of the child. This value was established on the basis of neurodevelopmental toxicity observed in cohorts of children living in the Seychelles and the Faroe Islands, where both mothers and children were exposed to methylmercury (JECFA, 2004). In 2012, EFSA proposed a new PTWI of 1.3 µg.kg $bw^{-1}.wk^{-1}$ based on a re-analysis of the ongoing cohorts in the Seychelles and the Faroe Islands and new data from these cohorts. This PTWI referred to a no observed adverse effect level (NOAEL) of 11.5 $mg.kg^{-1}$ in maternal hair and was based on the neurological development of the child. This NOAEL is the mean between the new NOAEL from the cohort in the Seychelles (11 $mg.kg^{-1}$ maternal hair) and the $BMDL_{05}$ from the cohort in the Faroe Islands (12 $mg.kg^{-1}$ maternal hair) (EFSA, 2012b).
The PTWI of 1.3 µg.kg $bw^{-1}.wk^{-1}$ (i.e. 0.19 µg.kg $bw^{-1}.d^{-1}$) established by EFSA was selected and applied to the population as a whole (including the vulnerable population) to assess the risk from methylmercury.
It applies to exposure to methylmercury through the consumption of fish and other seafood products.

According to the second Total Diet Study (ANSES, 2011a) and Infant Total Diet Study (ANSES, 2016a), a health risk associated with dietary exposure to methylmercury cannot be excluded, in particular from the consumption of fish and other seafood products.

Contamination

The data from the monitoring and control plans compiled in CONTAMINE have analytical information for this element (analytical methods, performance criteria, etc.), from which it is possible to assess the quality of the data and constitute a means for exploiting the contamination levels observed in seaweed.

This dataset contains 100 results of analysed contamination levels of total mercury in seaweed, including seaweed used as such, as a food ingredient and as a food supplement ingredient, sampled in France between 2009 and 2017 and analysed between 2010 and 2018.

The samples were analysed by laboratories accredited according to ISO/IEC 17025 (56% of samples) or by laboratories with in-house accreditation (22% of data). In 22% of cases, laboratories were classified as accredited without any information on the type of accreditation (ISO 17025 or in-house).

Seaweed samples were analysed by electrothermal atomic absorption spectrometry and also by inductively coupled plasma mass spectrometry (ICP-OES/MS) methods, producing data of satisfactory quality for this type of analysis.

Limits of Detection (LOD) and Limits of Quantification (LOQ) are given when concentrations are below these limits. Although there were indications regarding expression of the measurement uncertainty, the results compiled in the database sometimes lacked clarity on whether the information did indeed refer to the expanded uncertainty U, and on its expression, where in some cases they were probably expressed in % and others in mg.kg^{-1}.

Ultimately, all 100 results of analysed contamination levels of total mercury in seaweed were usable.

The groups analysed for total mercury, in increasing order of percentage, were as follows:
Food supplements (FS) (48%) > unknown seaweed (13%) = brown macroalgae (13%) > red macroalgae (10%) > microalgae (spirulina) (7%) > green macroalgae (3%) > halophytes (glasswort) (2%) > seaweed mixtures (2%) > powder, agar-agar and beverages (1% each (n = 1 each)).

However, the comparability of the sample from the CONTAMINE database with the seaweed consumed by the French population related to the national study of edible seaweed consumption (Le Bras *et al.*, 2014, 2015) remains limited.

The data were then analysed by seaweed group and using the upper bound (UB) approach. Data processing covered all samples analysed for total mercury, except for the single samples of powder, agar-agar and beverages. Eighty results out of 100 samples analysed for total mercury were not quantified or detected (LOD/LOQ between 0.0003 and 0.16 mg.kg^{-1}). The dataset was converted to mg.kg^{-1} dry matter where necessary, by applying a conversion factor for data provided as wet weight. The choice of this factor was based on a review of the literature (Arne Jensen, 1993; Stévant *et al.*, 2017; Qing Chen *et al.*, 2018; Roleda *et al.*, 2019) and assumed an average dry matter content of 20% in fresh seaweed.

The table below presents the analysis of data on total mercury contamination in the seaweed categories of the CONTAMINE database.

Table 2-4. Analysis of total mercury concentrations (mg.kg^{-1} dry matter (DM)) in the seaweed categories of the CONTAMINE database

	Total	Unknown	Brown macroalgae	Red macroalgae	Green macroalgae	Microalgae	Halophytes	Mixtures	FS
n	100	13	13	10	3	7	2	2	48
Total mercury concentrations (mg.kg^{-1} dry matter (DM))									
Median	0.017	0.02	0.023	0.010	0.050	0.015	0.063	0.080	0.015
Mean	0.037	0.03	0.024	0.014	0.046	0.040	0.063	0.080	0.04
Min	0.0010	0.010	0.010	0.010	0.014	0.010	0.050	0.010	0.001
Max	0.38	0.1	0.050	0.027	0.075	0.10	0.075	0.15	0.2
Breakdown of numbers according to classes of total mercury concentrations (mg.kg^{-1} DM) below or above the CSHPF reference value of 0.1 mg.kg^{-1} DM									
concentration < 0.1	97	13	13	10	3	7	2	1	47
0.1 < concentration < 0.5	3	0	0	0	0	0	0	1	1
concentration > 0.5	0	0	0	0	0	0	0	0	0

Total: all seaweed categories combined; Unknown: seaweed whose parent group is not specified; Brown macroalgae: seaweed belonging to the group of brown macroalgae; Red macroalgae: seaweed belonging to the group of red macroalgae; Green macroalgae: seaweed belonging to the group of green macroalgae; Microalgae: related to spirulina in CONTAMINE; Halophytes: related to glasswort in CONTAMINE; Mixtures: mixtures of dried seaweed; FS: food supplements containing dried seaweed.

For the data as a whole, the mean and median total mercury contamination levels for all seaweed categories were 0.037 and 0.017 mg.kg^{-1} DM, respectively (min-max 0.001-0.38 mg.kg^{-1} dry matter). Among the families of seaweed, the groups of halophytes (glasswort), green macroalgae and mixtures were the most contaminated by total mercury, with mean values of 0.063, 0.046 and 0.08 mg.kg^{-1} dry matter, respectively. The red macroalgae group had lower levels of total mercury, with a mean concentration of 0.014 mg.kg^{-1} dry matter.

The food supplement group (n = 48) had a mean total mercury concentration of 0.04 mg.kg^{-1} dry weight (min-max 0.001-0.2 mg.kg^{-1} dry weight).

A maximum total mercury level of 0.38 mg.kg^{-1} dry weight was observed in a sample of seaweed and soy beverage originating in Switzerland.

A total of 3 out of 100 seaweed samples analysed for total mercury for all forms of seaweed combined (i.e. 3%) exceeded the value of 0.1 mg.kg^{-1} dry matter recommended by the CSHPF (see Table 3, Section 3.1.4). These samples corresponded to a sample of dried seaweed mixtures originating in France, a sample of food supplements containing dried seaweed originating in France, and the sample of seaweed and soy beverage originating in Switzerland.

However, it should be noted that in order to compare it with the reference value, knowledge of the expanded uncertainty U of each result is needed, because according to Regulation (EC) No 333/2007[22] "The analytical result shall be reported as x +/- U whereby x is the analytical result and U is the expanded measurement uncertainty, using a coverage factor of 2 which gives a level of confidence of approximately 95% (U = 2u)." Although there were indications regarding uncertainty, it was not always specified whether this concerned the expanded uncertainty.

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[22] Commission Regulation (EC) No 333/2007 of 28 March 2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs

Exposure

The estimates were based on the exposure scenarios for edible seaweed consumption developed for the cadmium study and described in Section 3.2.2.3. Similarly, the input data were based on seaweed consumption data derived from the INCA 3 study (ANSES, 2017) considering the consumption occasions of adult seaweed consumers for the scenarios related to the consumption of unprocessed seaweed and seaweed incorporated as a food supplement ingredient, and the consumption occasions of child and adult consumers for the scenario related to the consumption of seaweed as a food ingredient. To estimate exposure, these consumption data were combined with the usable contamination data in the dataset available for the formal request. The analyses concerned total mercury. Speciation assumptions were applied by EFSA to data on total mercury contamination, in order to estimate the share of organic and inorganic mercury in food (EFSA, 2012b). For seaweed, there are no specific speciation assumptions. For purely theoretical and protective purposes, the most toxic form of the chemical species identified for fish and seafood was used for the estimation, assuming that 100% of the mercury was present in the methylmercury form (most conservative hypothesis). Only consumer exposure to methylmercury and the contribution relative to the toxicity reference value following ingestion of edible seaweed was estimated.
The uncertainties identified in the assessment of dietary exposure to cadmium associated with the consumption of edible seaweed (see Section 3.2.3) also apply to this methylmercury-related contaminant.

Table 2-5. Estimated dietary exposure to methylmercury from consumption of edible seaweed by scenario and contribution of mean exposure relative to the toxicity reference value for methylmercury

	Adults			**Children**		
	Mean	**P95**	**% TDI**	**Mean**	**P95**	**% TDI**
Exposure to seaweed as a food in µg/kg bw/d	**0.004**	**0.011**	**1.9%**			
Exposure to seaweed as a food ingredient in µg/kg bw/d	**0.0004**	**0.001**	**0.23%**	**0.0005**	**0.0011**	**0.25%**
Exposure to seaweed as a FS ingredient in µg/kg bw/d	**0.002**	**0.003**	**0.92%**			
Exposure to seaweed in all forms combined (food + ingredients + FS) in µg/kg bw/d	**0.006**	**0.017**	**3.03%**	**0.0005**	**0.0011**	**0.25%**

The table above presents the exposure results for each scenario for adult seaweed consumers and only for the "Ingredient" scenario for children.
For adults, exposure to methylmercury from seaweed consumed as a food represents on average less than 2% of the TDI and less than 1% when seaweed is consumed as an ingredient or food supplement. Methylmercury from all sources of seaweed represents on average 3% of the TDI.

For children, the mean methylmercury intake from seaweed as an ingredient was less than 0.25% of the TDI.
It should be remembered that these calculations were estimated under the UB assumption.

Conclusions

The analyses of seaweed concerned total mercury. There are insufficient data to make assumptions about seaweed-related mercury speciation in order to more robustly estimate the exposure of seaweed consumers. The form of the chemical species of mercury in seaweed should therefore be identified and investigated, and then taken into account by legislation to regulate mercury levels in seaweed intended for food consumption.
For purely theoretical and protective purposes, the most toxic form of the chemical species identified for fish and seafood was used for the estimation, assuming that 100% of the mercury was present in the methylmercury form (most conservative hypothesis).
Estimating methylmercury exposure from edible seaweed consumption showed that the mean exposure to this contaminant in consumers of seaweed in all its forms (food, ingredients, food supplements) contributes 3% of the PTWI of 1.3 µg.kg bw^{-1}.wk^{-1} (i.e. 0.19 µg.kg bw^{-1}.d^{-1}).
Initially, a health risk to consumers associated with exposure to methylmercury cannot be ruled out, according to ANSES's second Total Diet Study (ANSES, 2011a), particularly related to the consumption of fish and seafood products. Indeed, overall mean consumer exposure (background exposure) to methylmercury was high and estimated to be 0.19 and 0.27 µg.kg bw^{-1}.d^{-1} in adult and child consumers, respectively (ANSES, 2011a). Efforts to reduce dietary intakes of methylmercury should therefore be continued.
Analysis of the data on mercury contamination in seaweed intended for human consumption showed that mercury was not detected or quantified in 80% of the dataset samples, as well as a mean and median concentration (0.037 and 0.017 mg.kg^{-1} dry matter) 2 to 5 times lower than the CSHPF reference value of 0.1 mg Hg.kg^{-1} dry matter.
It is therefore recommended that the maximum mercury concentration in seaweed should be as low as possible.

- **Lead**

Hazard characterisation

Lead (Pb) is a ubiquitous metal naturally present in the Earth's crust (10 mg.kg^{-1} on average). Its intensive use by humans (mining and industrial activities: smelters, batteries, pigments, alloys, ammunition, etc.) has led to widespread dispersion in the environment. It is mainly found in the forms Pb^0 and Pb^{2+}, and also in some cases Pb^{4+}. Humans are mainly exposed to it through the food and water they consume, but also via air, soil and dust.

In humans, the main target organ is the central nervous system, especially during development in the foetus and young child. In the event of massive intoxication, signs of lead poisoning appear (neurobehavioural disorders). An inversely proportional relationship has been demonstrated between blood lead levels and IQ scores (Budtz-Jorgensen *et al.*, 2013, Canfield *et al.*, 2003, Lanphear *et al.*, 2005).

In adults, lead has effects on the kidneys (increased prevalence of chronic kidney disease) and the cardiovascular system (increase in systolic blood pressure). Inorganic lead is classified by the IARC in Group 2A "probably carcinogenic to humans": this form is predominantly found in the environment (EFSA, 2013). Regarding organic lead, its carcinogenic effect has not been demonstrated to date, and it is therefore classified by the IARC in Group 3 "not classifiable as to its carcinogenicity to humans" (IARC, 2006).

Because of the developmental effects and placental transfer[23], pregnant women and young children are considered the populations most vulnerable to the effects of lead. Children and women of childbearing age are therefore specific populations for whom lead exposure needs to be assessed.

EFSA identified three critical blood lead levels and used pharmacokinetic modelling to derive reference intakes – two in adults, and one in children, pregnant women and women of childbearing age. They were respectively 15 µg.L^{-1} for nephrotoxic effects (equivalent to an oral intake of 0.63 µg.kg bw^{-1}.d^{-1}), 36 µg.L^{-1} for cardiovascular effects (i.e. 1.5 µg.kg bw^{-1}.d^{-1}) and 12 µg.L^{-1} for neurodevelopmental effects (i.e. 0.5 µg.kg bw^{-1}.d^{-1}) (EFSA, 2013). To assess the risk in children, EFSA used a BMDL$_{01}$ of 0.5 µg.kg bw^{-1}.d^{-1} and considered the risk to be negligible when the MOS (margin of safety)[24] was greater than 10. The High Council of Public Health also retained the critical blood lead level of 12 µg.L^{-1} associated with an exposure dose of 0.5 µg.kg bw^{-1}.d^{-1} (HCSP, 2014).
These neurodevelopmental effects (quantified through the decrease in one IQ point in the child population) were not selected by ANSES to define the critical blood lead level value because the experts considered that the decrease in the IQ point cannot be used for a quantitative health risk assessment (ANSES, 2013). ANSES considered that the critical blood lead level set at 15 µg.L^{-1} was valid for the general population, including children, and for all critical effects identified to date (including effects on the nervous system). This blood lead level of 15 µg.L^{-1} (corresponding to an oral exposure of 0.63 µg.kg bw^{-1}.d^{-1}) is associated with a 10% increase in the prevalence of chronic kidney disease[25]. No kidney effect was observed in children (under 12 years of age) for blood lead levels below 50 µg.L^{-1}, but the effects observed on the kidney in adults may be the result of lifetime exposure from childhood (NTP, 2012).
In view of current international discussions, the values of 0.5 (BMDL$_{01}$) and 0.63 µg.kg bw^{-1}.d^{-1} (BMDL$_{10}$), corresponding to critical blood lead levels of 12 and 15 µg.L^{-1} respectively, were taken into account in this study. For risk assessment purposes, the risk is negligible when the MOS (margin of safety)[23] is greater than 10.

According to the second Total Diet Study (ANSES, 2011a) and the Infant Total Diet Study (ANSES, 2016a), a health risk associated with dietary exposure to lead cannot be excluded. Efforts to reduce dietary intakes of lead should therefore be continued.

Contamination

The data from the monitoring and control plans compiled in CONTAMINE have analytical information for this element (analytical methods, performance criteria, etc.), from which it is possible to assess the quality of the data and constitute a means for exploiting the contamination levels observed in seaweed.

This dataset contains 132 results of analysed contamination levels of lead in seaweed, including seaweed used as such, as a food ingredient and a food supplement ingredient, sampled in France between 2009 and 2017 and analysed between 2010 and 2018.

The samples were analysed by laboratories accredited according to ISO/IEC 17025 (55% of samples) or by laboratories with in-house accreditation (22% of data). In 23% of cases, laboratories were classified as accredited without any information on the type of accreditation (ISO 17025 or in-house).

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[23] During pregnancy, free lead (bone stock and lead ingested by the mother) can cross the placental barrier and be stored in the brain and skeleton of the foetus.

[24] In the case of substances characterised by a BMDL, characterisation of the risk involved calculating a margin of exposure (MOE) for genotoxic carcinogenic substances, or a margin of safety (MOS) for non-genotoxic substances whose effects appear from a certain threshold. These margins of exposure or safety correspond to the ratio between a critical exposure (BMDL, for example) and the mean exposure of the population or exposure at a high percentile. These margins were then compared to a critical margin defined when the BMDL was established by national and international bodies, in order to conclude as to the risk to the population.

[25] Defined as the persistence for more than three months of a glomerular filtration rate of less than 60 mL/min/1.73 m^2 body surface area

Seaweed samples were analysed by electrothermal atomic absorption spectrometry and also by inductively coupled plasma mass spectrometry (ICP-OES/MS) methods, producing data of satisfactory quality for this type of analysis.

Limits of Detection (LOD) and Limits of Quantification (LOQ) are given when concentrations are below these limits. Although there were indications regarding expression of the measurement uncertainty, the results compiled in the database sometimes lacked clarity on whether the information did indeed refer to the expanded uncertainty U, and on its expression, where in some cases they were probably expressed in % and others in mg.kg^{-1}.

Ultimately, all 132 results of the analysed lead contamination levels in seaweed were usable.

The groups analysed for lead, in increasing order of percentage, were as follows:
Food supplements (FS) (40.9%) > unknown seaweed (15.1%) > brown macroalgae (13.6%) > red macroalgae (12.1%) > microalgae (spirulina) (8.3%) > green macroalgae (3.8%) > halophytes (glasswort) (2.3%) > seaweed mixtures (1.5%; n = 2) > powder, agar-agar and beverages (0.7% each (n = 1 each)).

However, the comparability of the sample from the CONTAMINE database with the seaweed consumed by the French population related to the national study of edible seaweed consumption (Le Bras *et al.*, 2014, 2015) remains limited.

The data were then analysed by seaweed group and using the upper bound (UB) approach. Data processing covered all samples analysed for lead, except for the single samples of powder, agar-agar and beverages. Fifty-four results out of 132 samples analysed for lead were not quantified (n = 38) or detected (n = 16) (LOD/LOQ between 0.02 and 0.2 mg.kg^{-1}). The dataset was converted to mg.kg^{-1} dry matter where necessary, by applying a conversion factor for data provided as wet weight. The choice of this factor was based on a review of the literature (Arne Jensen, 1993; Stévant *et al.*, 2017; Qing Chen *et al.*, 2018; Roleda *et al.*, 2019) and assumed an average dry matter content of 20% in fresh seaweed.

The table below presents the analysis of data on lead contamination in the seaweed categories of the CONTAMINE database.

Table 2-6. Analysis of lead concentrations (mg.kg^{-1} dry matter (DM)) in the seaweed categories of the CONTAMINE database

	Total	**Unknown**	**Brown macroalgae**	**Red macroalgae**	**Green macroalgae**	**Microalgae**	**Halophytes**	**Mixtures**	**FS**
n	132	20	18	16	5	11	3	2	54
Lead concentrations (mg.kg^{-1} dry matter (DM))									
Median	0.30	0.36	0.61	0.17	0.48	0.08	0.60	0.92	0.39
Mean	0.72	0.42	0.55	0.20	1.39	0.10	0.53	0.92	1.16
Min	0.010	0.068	0.021	0.060	0.220	0.010	0.200	0.830	0.16
Max	13.3	1.3	1.5	0.4	3.2	0.2	0.8	1.0	13.3
Breakdown of numbers according to classes of lead concentrations (mg.kg^{-1} DM) below or above the CSHPF reference value of 5 mg.kg^{-1} DM									
concentration < 5	130	20	18	16	5	5	0	2	52
5 < concentration < 6	1	0	0	0	0	0	0	0	1
concentration > 6	1	0	0	0	0	0	0	0	1

Total: all seaweed categories combined; Unknown: seaweed whose parent group is not specified; Brown macroalgae: seaweed belonging to the group of brown macroalgae; Red macroalgae: seaweed belonging to the group of red macroalgae; Green macroalgae: seaweed belonging to the group of green macroalgae; Microalgae: related to spirulina in CONTAMINE; Halophytes: related to glasswort in CONTAMINE; Mixtures: mixtures of dried seaweed; FS: food supplements containing dried seaweed.

For the data as a whole, the mean and median lead contamination levels for all seaweed categories were 0.72 and 0.30 mg.kg^{-1} DM, respectively (min-max 0.01-13.3 mg.kg^{-1} dry matter).
Among the families of seaweed, the groups of brown and green macroalgae and mixtures were the most contaminated by lead, with mean values of 0.55, 1.39 and 0.92 mg.kg^{-1} dry matter respectively. The halophyte group had a mean lead concentration of 0.53 mg.kg^{-1} dry matter. The microalgae group had lower levels of lead, with a mean concentration of 0.10 mg Pb.kg^{-1} dry matter.

The food supplement group (n = 53) had a high mean lead concentration compared to the other matrices, of 1.16 mg.kg^{-1} dry weight (min-max 0.16-13.3 mg.kg^{-1} dry weight).

A maximum lead level of 13.3 mg.kg^{-1} dry weight was observed in a sample of food supplements containing dried seaweed (*Fucus Vesiculosus*) and green clay originating in France.

A total of 2 out of 132 seaweed samples analysed for lead for all forms of seaweed combined exceeded the value of 5 mg.kg^{-1} dry matter recommended by the CSHPF (see Table 3, Section 3.1.4). These two samples corresponded to seaweed incorporated in the form of food supplements originating in France.

However, it should be noted that in order to compare it with the reference value, knowledge of the expanded uncertainty U of each result is needed, because according to Regulation (EC) No 333/2007[26] "The analytical result shall be reported as x +/- U whereby x is the analytical result and U is the expanded measurement uncertainty, using a coverage factor of 2 which gives a level of confidence of approximately 95% (U = 2u)." Although there were indications regarding uncertainty, it was not always specified whether this concerned the expanded uncertainty.

Exposure

Consumer exposure to lead from ingestion of edible seaweed was estimated. The estimates were based on the exposure scenarios for edible seaweed consumption developed for the cadmium study and described in Section 3.2.2.3. Similarly, the input data were based on seaweed consumption data derived from the INCA 3 study (ANSES, 2017) considering the consumption occasions of adult seaweed consumers for the scenarios related to the consumption of unprocessed seaweed and seaweed incorporated as a food supplement ingredient, and the consumption occasions of child and adult consumers for the scenario related to the consumption of seaweed as a food ingredient. To estimate exposure, these consumption data were combined with the analysed data on lead contamination in seaweed in the usable dataset available for the formal request. The uncertainties identified in the assessment of dietary exposure to cadmium associated with the consumption of edible seaweed (see Section 3.2.3) also apply to this lead-related contaminant.

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[26] Commission Regulation (EC) No 333/2007 of 28 March 2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs

Table 2-7. Estimated dietary exposure to lead from consumption of edible seaweed by scenario and contribution of mean exposure relative to the benchmark values for lead in adults (0.63 µg.kg bw^{-1}.d^{-1}) and children (0.50 µg.kg bw^{-1}.d^{-1}) (considering a MOS of 10)

	Adults			**Children**		
	Mean	**P95**	**% of the benchmark value**	**Mean**	**P95**	**% of the benchmark value**
Exposure to seaweed as a food in µg/kg bw/d	**0.04**	**0.15**	**62.5%**			
Exposure to seaweed as a food ingredient in µg/kg bw/d	**0.004**	**0.015**	**6.34%**	**0.004**	**0.015**	**8.33%**
Exposure to seaweed as a FS ingredient in µg/kg bw/d	**0.006**	**0.019**	**9.1%**			
Exposure to seaweed in all forms combined (food + ingredients + FS) in µg/kg bw/d	**0.05**	**0.176**	**77.9%**	**0.004**	**0.015**	**8.33%**

The table above presents the exposure results for each scenario for adult seaweed consumers and only for the "Ingredient" scenario for children.
For adults, exposure to lead from seaweed consumed as a food represented on average less than 63% of the 0.63 benchmark value µg.kg bw^{-1}.d^{-1} (considering a MOS of 10). This percentage was 6 and 9% when the seaweed was consumed as an ingredient or food supplement, respectively. Lead from all sources of seaweed represented on average 78% of this benchmark value.
In children, the mean lead intake from seaweed as an ingredient represented 8% of the benchmark value of 0.50 µg.kg bw^{-1}.d^{-1} (considering a MOS of 10).
It should be remembered that these calculations were estimated under the UB assumption.

Conclusions

Estimating lead exposure from edible seaweed consumption showed that the mean exposure to this contaminant in consumers of seaweed in all its forms (food, ingredients, food supplements) contributed 78% in adults and 8% in children of the benchmark value of 0.63 µg.kg bw^{-1}.d^{-1} for adults and 0.50 µg.kg bw^{-1}.d^{-1} for children (considering a MOS of 10). Seaweed consumed as such accounts for the majority of this intake.
Initially, a health risk to consumers associated with exposure to lead cannot be ruled out, according to the second Total Diet Study (ANSES, 2011a) and the Infant Total Diet Study (ANSES, 2016a). Indeed, overall mean consumer exposure (background exposure) to lead was high and estimated to be 0.20 and 0.26 µg.kg bw^{-1}.d^{-1} in adult and child consumers, respectively (ANSES, 2011a), considering a MOS greater than 10. Efforts to reduce dietary intakes of lead should therefore be continued. Analysis of the data on lead contamination in seaweed intended for human consumption showed that lead was not detected or quantified in 40% of the dataset samples. No samples of unprocessed seaweed of any species exceeded the CSHPF reference value of 5 mg Pb.kg^{-1} dry matter (mean and median lead concentrations for all seaweed categories were 0.72 and 0.30 mg.kg^{-1} DM, 7 to 16 times lower than the CSHPF reference value).
It is therefore recommended that the maximum lead concentration in seaweed should be as low as possible.

ANNEX 3

Track changes made to the 02 March 2020 version

Page number	Modification made
Page 34	Correction of the value quoted in the sentence: « In this case, the contribution of seaweed consumers relative to the TDI is therefore reduced from 19% (related to the distribution of cadmium concentrations observed in seaweed) to 13% with a maximum concentration in seaweed of 0.35 mg Cd.kg^{-1} dry matter » by « In this case, the contribution of seaweed consumers relative to the TDI is therefore reduced from 19% (related to the distribution of cadmium concentrations observed in seaweed) to 11,5% with a maximum concentration in seaweed of 0.35 mg Cd.kg^{-1} dry matter »