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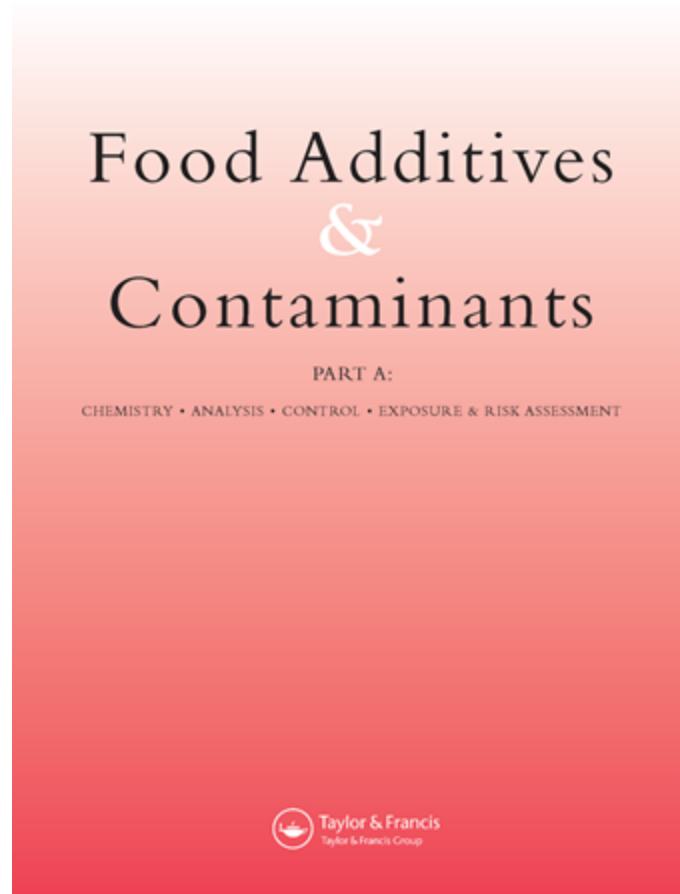
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Probabilistic determination of a maximum acceptable level of contaminant to reduce the risk of overexposure for a novel or emerging food: the case of cadmium in edible seaweed in the French population

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Abstract:	<p>European and French populations are overexposed to cadmium (Cd) through their foods. The risk of increased cadmium exposure for consumers needs to be limited by reduced maximum limits (ML) for novel foodstuffs such as edible seaweed in France. The objective was to derive a low and protective cadmium concentration in edible seaweeds to limit cadmium overexposure in consumers. To do so, we applied a probabilistic approach to the data collected on French seaweed consumers, taking into account other sources of exposure for cadmium. This approach led to the identification of a cadmium concentration which should ensure that the seaweed-consuming population does not exceed the tolerable daily intake (TDI) of cadmium according to a probability of cases, when simultaneously exposed to other cadmium dietary sources. Considering the 5% of the population exceeding TDI, the estimated ML is equal to 0.35 mg Cd kg⁻¹ dry matter of seaweed as an unprocessed food with a 95% confidence interval of [0.18,1.09]. The proposed approach is generic and could be applied to other relevant food / substance pairs when considering the setting of MLs in the regulatory system. It ensures better protection of consumer health.</p>

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Probabilistic determination of a maximum acceptable level of contaminant to reduce the risk of overexposure for a novel or emerging food: the case of cadmium in edible seaweed in the French population

Géraldine Carne^{1*}, David Makowski², Sandrine Carrillo¹, Thierry Guérin³, Petru Jitaru⁴, J-C Jean-cedric Reninger¹, Gilles Rivière¹ and Nawel Bemrah¹

¹ANSES, Risk Assessment Department, 14 rue Pierre et Marie Curie, F-94701 Maisons-Alfort Cedex, France ; ²INRAE AgroParisTech University Paris-Saclay, UMR MIA, 16 rue Claude Bernard, 75231 Paris, France ; ³ANSES, Strategy and Programmes Department, F-94701 Maisons-Alfort Cedex, France ; ⁴ANSES, Laboratory for Food Safety, 14 rue Pierre et Marie Curie, F-94701 Maisons-Alfort Cedex, France

*Corresponding Author - Carne G, French Agency for Food, Environmental and Occupational Health & Safety (ANSES), Risk Assessment Department, 14 rue Pierre et Marie Curie, F-94701 Maisons-Alfort Cedex, France . geraldine.carne@anses.fr

Abstract

European and French populations are overexposed to cadmium (Cd) through their foods. The risk of increased cadmium exposure for consumers needs to be limited by reduced maximum limits (ML) for novel foodstuffs such as edible seaweed in France. The objective was to derive a low and protective cadmium concentration in edible seaweeds to limit cadmium overexposure in consumers. To do so, we applied a probabilistic approach to the data collected on French seaweed consumers, taking into account other sources of exposure for cadmium. This approach led to the identification of a cadmium concentration which should ensure that the seaweed-consuming population does not exceed the tolerable daily intake (TDI) of cadmium according to a probability of cases, when simultaneously exposed to other cadmium dietary sources. Considering the 5% of the population exceeding TDI, the estimated ML is equal to 0.35 mg Cd kg⁻¹ dry matter of seaweed as an unprocessed food with a 95% confidence interval of [0.18,1.09].

The proposed approach is generic and could be applied to other relevant food / substance pairs when considering the setting of MLs in the regulatory system. It ensures better protection of consumer health.

Keywords: Maximum limit, overexposure, emerging consumption, risk assessment, cadmium, seaweed, France

Introduction

The exposure of the general population to cadmium (Cd) due to the consumption of a large panel of foods contaminated to cadmium is a matter of concern in Europe and France (EFSA 2012; ANSES 2011a, 2019). Apart from tobacco, food is the main source of cadmium exposure. Cadmium is an ubiquitous trace metal element found in various environmental compartments (soil, water, air) due to its natural presence in the Earth's crust and to anthropogenic inputs (industrial and agricultural activities). Prolonged oral exposure to cadmium induces nephropathy, bone fragility and reproductive disorders (EFSA 2009; ANSES 2011a, 2019; Leconte *et al.* 2021). 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 2012).

Average exposure of adults in Europe is slightly higher than the tolerable weekly intake (TWI) of $2.5 \mu\text{g Cd kg bw}^{-1} \text{wk}^{-1}$ defined in 2009 by European Food Safety Authority (EFSA) (2009). Subgroups of the European population such as vegetarians, children, smokers and people living near contaminated areas may exceed the TWI by a factor of approximately two, (EFSA 2012). In France, according to the second Total Diet Study (TDS2) of the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) (2011a), this TWI is exceeded in 0.6% of adults and 15% of children. The part of the French population overexposed to cadmium by the entire diet reaches 1.1% of adults and 18.5% of children in 2019 after revision by ANSES of health-based guidance value (HBGV) for cadmium into a Tolerable Daily Intake (TDI) of $0.35 \mu\text{g Cd kg bw}^{-1} \text{d}^{-1}$ (ANSES 2019; Leconte *et al.* 2021). These results clearly indicate that dietary exposure to cadmium needs to be reduced for the general population.

One of the levers of action is setting of maximum limits for cadmium in dietary contributors. Regulators establish regulatory limits according to the As Low As Reasonably Achievable (ALARA) principle, by setting a threshold of exclusion from the distribution of contamination (example: percentile 95 (P95)). This principle allows, on the one hand, to protect

the consumer by excluding the most contaminated batches of food, and on the other hand, to limit the percentage of excluded batches to an economically bearable level.

The introduction of a novel food to the total diet can increase cadmium intake. The risk of increased cadmium exposure for consumers needs to be limited by a reduced maximum concentration for the new entrant. The relevant case of edible seaweed consumers in France illustrates the situation.

In France, the consumption of seaweed increased in the last years due to the increase of Asian foods, promoted by the popularity of Japanese restaurants and the consumption of makis, and also because of the nutritional benefits perceived by the population (Le Bras *et al.* 2014). Seaweeds are also used in cosmetics industry, agriculture (as a fertiliser or livestock feed), agrifood, chemistry and microbiology industries (as phycocolloids such as alginates, agar-agar, carrageenans). They can also be eaten as vegetables served fresh, dried, frozen, bottled, salted through processes used to preserve seaweed. Seaweeds are also incorporated as ingredients in foodstuffs and dietary supplements.

The generic term "seaweed" will be used repeatedly in this paper. It refers to species identified by the general public as living in a marine biotope (Le Bras *et al.* 2014) but it includes more precisely microalgae, macroalgae and halophytes. Freshwater, terrestrial and marine microalgae are unicellular organisms belonging to the groups of cyanobacteria and microscopic algae. Spirulina is the microalgae most commonly used as a food ingredient or supplement due to its consumption history in third countries and its nutritional potential (Cornillier, Korsia-Meffre, and Senart 2008). Marine macroalgae are multicellular plant-like organisms: they can cover large spaces forming fields or forests, often compared to those of the terrestrial system (Kornprobst 2005). Marine macroalgae vary greatly in colour and are divided into three groups (phyla) based on their pigmentation: green seaweed, brown seaweed and red seaweed. Halophytes are higher plants that grow in salty environments such as coastal soils and saline inland soils. Three halophytes are likely to be consumed: sea kale, sea fennel and glasswort. Seaweed are also a bioindicator of marine environmental quality (Almela *et al.* 2006; NIFES 2016), especially regarding metal contamination. Indeed, despite the fact that fresh seaweed contains 70-90% water (Arne Jensen 1993; Stévant *et al.* 2017; Qing Chen *et al.* 2018; Roleda *et al.* 2019), their structural components are characterised by high levels of specific polysaccharides, which have a propensity to bind metals (including cadmium). This binding can affect both levels and the availability of these metals bound to the seaweed. For example, marine macroalgae are known for their ability to concentrate heavy metals (Besada *et al.* 2009). However, the types of polysaccharides differ between brown, red and green macroalgae with

various degrees of binding affinity to metals ranked as: alginates (brown algae) > carrageenans (red algae) > agar (red algae) (Roleda *et al.* 2019). Other factors such as the surface area of the seaweed in contact with water (NIFES 2016) or environmental factors (location, temperature, salinity, light, etc.) can also influence the level of seaweed contamination (NIFES, 2016, Roleda *et al.* 2019; Banach *et al.* 2020).

The emergence of potential risks associated to the use of seaweed in food, especially related to metals such as cadmium, was pointed out by EFSA (2016).

Except USA, Australia and New Zealand, in Europe, only France has recommended maximum levels of heavy metals for seaweed as issued by the French High Council for Public Health (CSHPF) (1997) (CEVA 2014). A maximum cadmium level of 0.5 mg kg⁻¹ dry matter (DM) in edible seaweed authorized for human consumption is recommended by the CSHPF. Nevertheless, European regulations do not currently establish maximum limits for cadmium and other heavy metals in seaweed (macro / microalgae and halophytes), except for food supplements containing seaweed. Regulation (EC) n° 1881/2006 provides only regulatory maximum cadmium levels of 3.0 mg kg⁻¹ in commercial food supplements, consisting exclusively or mainly of dried seaweed or products derived from seaweed.

Since 2009, seaweeds are included as part of the French annual monitoring and control plan for contamination of certain foodstuffs by trace elements. According to ANSES, 38% of samples of seaweed (excluding food supplements, agar-agar, beverages and seaweed powder) analysed between 2010 and 2018 exceeded the value of 0.5 mg Cd kg⁻¹ DM recommended by the CSHPF, mainly in samples including red and brown macroalgae (ANSES 2020).

Due to (i) the emergence of the seaweed consumption as a new foodstuff, (ii) the absence of European regulatory maximum limits for cadmium in seaweed, and (iii) the observation of higher levels of cadmium concentration in seaweed, it is difficult to manage the risk posed by cadmium and seaweed consumption in a population already overexposed through its usual diet. The objective of this work was to derive a low and protective cadmium concentration in edible seaweeds to limit cadmium overexposure in consumers. To do so, we applied a probabilistic approach to data collected on French seaweed consumers, taking other sources of exposure for cadmium into account. Results were used to calculate a protective maximum concentration that reduced the risk of exceedance of the HBGV, considering the current consumer exposure level. The proposed method is generic and could be applied to other relevant food / substance pairs to revise the fixation of maximum limit in the regulatory system, based on the ALARA principle taking the various sources of exposure into account.

Materials and methods

Cadmium seaweed contamination data

The dataset included data from French Annual Monitoring and Control Plan (FAMCP database), the Centre for Study and Promotion of Algae (CEVA) in France and the scientific literature.

One hundred and thirty-one samples of seaweed (macroalgae, microalgae e.g spirulina, and halophytes e.g glasswort) were collected through the French Annual Monitoring and Control Plan between 2009 and 2017 (FAMCP database), including seaweed harvested in France and imported seaweed often of unknown origin. Samples were composed by seaweeds used as such (fresh, dried or roasted), as a food ingredient (agar-agar, beverages) and as a food supplement ingredient. Samples were analysed between 2009 and 2018 by four COFRAC-accredited laboratories of the Directorate General for Competition, Consumer Affairs and Fraud Control DGCCRF's Joint Laboratory Service (SCL), mainly by electrothermal atomic absorption spectrometry (ETAAS) or by inductively coupled plasma mass spectrometry - (ICP-MS) and ICP-optical emission spectrometry (ICP-OES).

The Centre for Study and Promotion of Algae (CEVA) also measured the cadmium levels in one-hundred and seventy-two samples of seaweed collected in France. These samples were analysed in dried form between 1996 and 2016 by the ICP-MS method (contamination data provided by CEVA to ANSES; unreferenced).

In addition, an optimized and validated ICP-MS method was employed by Rodenas de la Rocha *et al.* (2009) and thus cadmium contamination data from eight seaweeds in this study were also retained. Results came from analysis of samples of seaweeds from France, Spain, Korea, and Japan.

From these three sources of information, we were able to produce a dataset including a total of three hundred and eleven contamination data of cadmium in seaweeds. Contaminations originally expressed as wet weight were converted in dry matter using a conversion factor defined from the literature (Arne Jensen 1993; Stévant *et al.* 2017; Qing Chen *et al.* 2018; Roleda *et al.* 2019). An average dry matter content of 20% in fresh seaweed was calculated. To adopt a protective approach, the cadmium data have been treated using the upper bound (UB) hypothesis. The upper bound assumption corresponds to a scenario in which non-detected values are estimated to be equal to the limit of detection and the values detected but not quantified are estimated to be equal to the limit of quantification. It represents the maximum possible value.

French seaweed consumption data

Our study covered several types of edible seaweeds, such as (i) intended for direct human consumption as food (condiment or vegetable); (ii) used as an ingredient in foodstuffs; and (iii) used in food supplements.

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

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 24-h recall method for individuals aged from 15 to 79 years, and the 24-h record method for individuals aged from 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 (2698 children from birth to age 17 and 3157 adults between the ages of 18 and 79) participating in the study, 4114 (1993 children and 2121 adults) validated the consumption part by taking part in at least two food interviews.

The data on food supplement consumption collected in the INCA 3 study 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 possible. 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 consumption study as it is mostly used as an ingredient for its phycocolloids features. Seaweed as ingredients could only be identified in home-made recipes (against industrial), for the ingredient list was only available for them. Thus, recipes mentioned, at least once, as having been home-made and including seaweed were identified, such as "dairy-based desserts and cooked desserts", "fruit jams" (unsweetened or with reduced sugar content), "jellied flans", "makis" and "California rolls", the last two systematically comprising 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, regardless of their production method (home-made, industrial, restaurant, etc.).

Food supplements containing at least one edible seaweed were retained for the study. Number of consumption occasions, consumer rates (with a 95% confidence interval), number

of consumers and the quantities of seaweed consumed as a food, ingredient or food supplement (being estimated at the individual level) were derived separately for adults and children.

Estimation of cadmium dietary exposure for French edible seaweed consumers

Dietary cadmium exposure for seaweed consumers were obtained using the combination of the consumption and individual weight data from INCA 3 (ANSES 2017) with seaweeds cadmium contamination data (CEVA (1996-2016), Rodenas de la Rocha *et al.* (2009), French Annual Monitoring and Control Plan - FAMCP database (2009-2017).

Dietary exposure to cadmium in seaweed consumers was estimated on the basis of the following four consumption scenarios, considering: (i) Seaweed consumed directly as a food as such without processing (vegetable or condiment), (ii) Seaweed consumed as an ingredient in foodstuffs (maki, California roll), (iii) Seaweed consumed as a food supplement ingredient and (iv) Seaweed consumed in all its forms (food, ingredient, food supplement).

A probabilistic approach was used to estimate cadmium dietary exposure to seaweed consumers for each scenario in order to generate a probability distribution of possible exposure values. It consisted in randomly selecting a large number of possible contamination and consumption values according to a probability distribution assigned to them from the available data. This approach made it possible to take the various factors influencing exposure (contamination, consumption, body weight) into account. Specifically, 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. This procedure yielded 100,000 exposure values (contamination \times consumption) describing an exposure distribution from which conventional such as the mean, median and percentiles of the distribution, were calculated. This approach was applied for each sub-population (children aged 3 to 17, adults), and each scenario (seaweed as food, ingredients, food supplements, all sources combined). Simulations were performed using @Risk 7.5 and R software (R fitdistrplus package).

Estimation of maximum cadmium level in seaweed intended for human consumption taking into account the total diet exposure of French consumers

The maximum cadmium concentration in edible seaweed was calculated so as not to increase the initial dietary cadmium exposure of seaweed consumers compared to the oral health-based guidance value (HBGV) for cadmium. ANSES (2019) has established a tolerable daily intake (TDI) of $0.35 \mu\text{g Cd kg bw}^{-1} \text{d}^{-1}$ resulting in a urinary cadmium concentration of $0.5 \mu\text{g g}^{-1}$ creatinine, in a 60-year-old adult, assuming that ingestion is the sole source of cadmium exposure (Leconte *et al.* 2021). Data from TDS2 (ANSES 2011a) provided a distribution of cadmium exposure of the French general population. These data reflected the baseline exposure of the population, also known as "background exposure", i.e. cadmium exposure from the total diet. Importantly, these data did not take into account the cadmium dietary exposure resulting from the consumption of edible seaweeds. Without consumption of edible seaweed, mean cadmium total diet exposure equal to $0.15 \mu\text{g kg bw}^{-1} \text{d}^{-1}$ and a percentile 95% (P95) equal to $0.27 \mu\text{g kg bw}^{-1} \text{d}^{-1}$ were estimated for adult consumers from TDS2 (ANSES 2011a). Among child consumers, the mean and P95 exposure were estimated at $0.24 \mu\text{g kg bw}^{-1} \text{d}^{-1}$ and $0.45 \mu\text{g kg bw}^{-1} \text{d}^{-1}$, respectively, from TDS2 (ANSES 2011a).

The maximum limit (ML) of cadmium in unprocessed seaweed intended for human consumption was calculated as:

$$ML = \frac{(TDI - Background) \times Bodyweight}{Consumption} \quad (1)$$

where Background is the background exposure defined above, Body weight is the body weight of the consumer, and Consumption is the consumption of unprocessed seaweed. The use of ML (1) ensures that the TDI was not exceeded when unprocessed seaweeds are consumed taking background exposure into account. All the seaweed consumption in (1) vary across consumers. In order to deal with this variability, a distribution of 100,000 values of ML was generated by a random sampling, at each of the 100,000 iterations, in the distributions of Background exposure, Body weight, and seaweed Consumption. The resulting distribution of these 100,000 values of ML was summarized by its mean and 95% probability interval (percentiles 2.5 and 97.5%) comparing to the TDI.

The distribution of ML described plausible upper limit values of cadmium content of unprocessed seaweed used as a vegetable or condiment that would ensure that the TDI is not exceeded, considering the entire consumer diet. By selecting a low percentile (e.g., 10%) of this distribution, we could ensure that a high proportion of the French population (e.g., 90%) is protected. Here, we used the ML distribution to define a range of ML values protecting from 75 to 95% of the French population.

Results

Description of the cadmium levels in seaweed

Out of 131 samples analysed from FAMCP database, the levels measured in 26 samples were less than the quantification/LOQ ($n = 17$) or detection limit/LOD ($n = 9$) (the LOD/LOQ were between 0.001 and 0.090 mg kg⁻¹ of dry matter (DM)). Out of these 131 analysed samples, 39 analytical results concerned macroalgae (brown, red, green) used as such, while 11 and 3 analytical results concerned microalgae (spirulina only) and halophytes (glasswort only) respectively. The seaweed genus was unspecified or unknown for 20 of the analysed samples. Fifty-three analytical results were linked to food supplements containing seaweed. Two samples of seaweed mixtures, one sample of seaweed powder, one sample of agar-agar and one sample of seaweed-based beverage analysed for cadmium were present in the FAMCP database. The groups of seaweed, or food containing seaweed, 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)). The mean and median cadmium contamination levels of all seaweed combined from FAMCP database, 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 DM). Red, brown macroalgae and unknown seaweed were the most contaminated with cadmium, with mean values above 1.14 mg kg⁻¹ DM. A maximum cadmium level of 9.4 mg kg⁻¹ DM was observed in a sample of red macroalgae (nori) from Argentina. Table A1 in the appendices describes the distribution of cadmium contamination in seaweed from the FAMCP database.

Data from CEVA reported 35 out of 172 values as less than the quantification limit/LOQ of 0.15 ($n = 32$) or LOQ of 0.06 mg kg⁻¹ DM ($n = 3$). Cadmium was quantified in the eight samples of seaweed analysed by Rodenas de la Rocha *et al.* (2009). Table A2 in the appendices describes the distribution of cadmium contamination in seaweed resulting of CEVA and

Rodenas de la Rocha *et al.* (2009). These data 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%). A maximum concentration of 3.18 mg Cd kg⁻¹ DM was measured in a sample of red macroalgae (nori) from Japan. Red and brown macroalgae were the most contaminated with cadmium, with mean values above 0.39 mg kg⁻¹ DM compared to mean values below 0.20 mg kg⁻¹ DM for the green macroalgae and halophytes.

Combining all data sources (FAMPC database, CEVA and Rodenas de la Rocha *et al.* (2009)) and excluding 3 samples of seaweed powder, agar-agar and seaweed-based beverage, a total of 308 cadmium contamination data (255 samples of unprocessed seaweed, all species combined, and 53 samples of food supplements containing dried seaweed) were considered. In this dataset, the mean cadmium contamination level over all seaweed species combined, unprocessed, was 0.60 mg kg⁻¹ DM (min-max 0.001-9.4 mg Cd kg⁻¹ DM). Mean cadmium concentration in food supplements containing dried seaweed (0.112 mg kg⁻¹ DM) was lower than unprocessed seaweed (Table 1).

Overview of French seaweed consumption data

Table 2 describes the average amounts of seaweed consumed in France. Consumption occasions and consumption rates of edible seaweed as food were very low among French adults (0.3% of consumers), and even lower among French children (0.07% of consumers). Between the two foodstuffs related to seaweed used by consumers as such in the consumption study, the "seaweed" item was the main representative of edible seaweed consumed, with the consumption of "glasswort" seeming minor. Edible seaweed was more frequently consumed in the form of ingredients, although consumption occasions and consumer rates remained low. The consumption frequency of 30 food supplements identified as containing at least one edible seaweed, was also relatively low, close to 1% in French adults and less than 0.1% in French children (Table 2).

In the INCA 3 study, 2.5% of French adults and 0.5% of French children reported at least one consumption occasion of seaweed-based food or food supplement (Table A3 in appendices).

Estimated cadmium dietary exposure of French edible seaweed consumers

Data used to estimate dietary cadmium exposure for French edible seaweed consumers according to several scenarios are presented in **Table 3**. Due to the small consumption dataset

available for seaweed, individual consumption occasions are taken into account, not consumers as such.

For adults consumers, the consumption occasions of seaweed as a food, as an ingredient and as a food supplement were considered for estimating the associated cadmium exposures whereas for children, due to the lack of consumption data, only their eating occasions of seaweed as an ingredient were taken into account. Probability distribution of cadmium dietary exposure to seaweed consumers for each scenario are generated with probability distributions defined in Table A4 in appendices.

Table 4 presents the exposure results for each scenario for French adults seaweed consumers and only for the "Ingredient" scenario for French children, based on the combination of the distributions of cadmium contamination observed in seaweed and the acts of seaweed consumption available in INCA 3 (ANSES 2017). Dietary exposure to cadmium in seaweed was then compared to the TDI of $0.35 \mu\text{g Cd kg bw}^{-1} \text{d}^{-1}$ (ANSES 2019).

For French adult seaweed consumers, exposure to cadmium by seaweed consumed as a food (condiment or vegetable) represented on average about 16% of the TDI. When seaweed was consumed as a food ingredient or food supplement, it represented between 1.6 and 1.7% of the TDI. Cadmium intake by all seaweed sources (food, ingredient, food supplement) represented on average around 19% of the TDI (Table 4).

For French children consuming seaweed, the mean cadmium intake from seaweed as a food ingredient was less than 2% of the TDI.

Estimated maximum cadmium concentration in seaweed for the seaweed-consuming population

Figure 1 represents the distribution of the maximum cadmium concentration in unprocessed seaweed used as a vegetable or condiment and its confidence interval derived from eq.(1), as a function of the percentile of the French 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 eq. (1) 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. Considering the 5% of the population exceeding TDI, the estimated value of ML is equal to 0.35 mg Cd kg⁻¹ DM of seaweed as an unprocessed food with a 95% confidence interval of [0.18,1.09] (Figure 1).

Comparison of cadmium dietary exposures to cadmium for French edible seaweed consumers

Contribution to the cadmium TDI of cadmium dietary exposure in French seaweed consumers per report was compared according to situations based on observed cadmium concentration in seaweed or cadmium limits applied for edible seaweed (Table 5). Considering the application of a limit value of 0.5 mg Cd kg⁻¹ DM recommended by CSHPF (1997), the estimates of mean dietary exposure to cadmium in seaweed consumers showed a contribution of 15.4% of the TDI when seaweed is consumed in all its forms (food, ingredient, food supplement). Mean exposure to cadmium when seaweed was consumed as a food ingredient or food supplement was 1.3% of the TDI. For children consuming seaweed, the mean cadmium intake from seaweed as a food ingredient was 1.4% of the TDI. Considering the application of a proposed reduced cadmium concentration of 0.35 mg kg⁻¹ dry matter of seaweed as an unprocessed food, dietary exposure of consumers of seaweed in all its forms (food, ingredient, food supplement) would contribute on average to 11.5% of the TDI for cadmium. Under this assumption, the mean cadmium intake from seaweed as a food ingredient for children consuming seaweed represented 1 % of the TDI.

Discussion

Limitation of the overexposure of French consumers to cadmium due to the emergence of seaweed consumption

To limit the high exposure of the general population to cadmium, establishing or strengthening management measures is necessary. The case of cadmium and emerging seaweed consumption in the French population due to fashion and possibly to sustainability claims raises the issue of risk management.

In our study, almost a quarter of our dataset of 255 cadmium contamination data in unprocessed seaweed (26%) exceeded 0.5 mg Cd kg⁻¹ DM as recommended by CSHPF in France (68 samples including 29 samples of seaweed from FAMCP database). Higher cadmium levels were found for brown and red macroalgae (Table A1 and A2 in appendices). Cadmium levels higher than 0.5 mg Cd kg⁻¹ DM are also highlighted in the literature linked to the strong

affinity to metals by the structural components of brown and red macroalgae (Almela *et al.* 2006; Superior Health Council 2015; NIFES 2016; Paz *et al.* 2018; Roleda *et al.* 2019; Banach *et al.* 2020). Lower range cadmium contamination was observed in microalgae compared to macroalgae in the dataset, probably due in part to production by phyco-culture or seaweed farming through controlled conditions. It highlighted the recommendation to have set water quality standards for the harvesting of seaweed intended for feed and food production from fresh and coastal waters.

Otherwise, the levels of cadmium contamination measured in the food supplements samples (n=53) did not exceed the regulatory maximum cadmium levels of 3.0 mg kg⁻¹ (EC Regulation n°1881/2006); these samples mainly consisted of dried seaweed or products derived from seaweed. Additionally, the cadmium levels in the food supplements containing dried seaweed were lower than those in the unprocessed seaweed in our dataset. This may be explained by the lower fraction of seaweed in the composition of food supplements compared to the unprocessed seaweed samples.

Our estimation of cadmium dietary exposure in French adult seaweed consumers highlighted that seaweed consumed as such as a vegetable or condiment accounted for the majority of this intake (Table 4). Whereas contribution of food supplements containing seaweed was always minor among adult consumers. 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. Thus, seaweeds consumed as such are identified as a major contributor. Subgroups of the population such as vegetarians are already overexposed to cadmium (EFSA 2012) and may be further at risk by an additional major intake through the introduction of seaweed in their diet. The emergence of potential risk to cadmium by the introduction of a growing consumption of edible seaweed is thus underlined. Banach *et al.* (2020) corroborated that cadmium in seaweed as a prioritized major hazard that may pose a risk to human health. It can be seen especially in France where the consumption of edible seaweed is an emerging and growing phenomenon (Le Bras *et al.* 2014).

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. The development of an approach giving a maximum level of chemical contaminant as low as

possible to limit the overexposure of consumers during the emerging and increasing consumption of a new food as seaweed for cadmium is relevant.

Interest of developing an approach proposing a maximum level of chemical contaminant as low as possible to limit the overexposure of consumers in the case of cadmium and the emerging consumption of edible seaweed in the French population

Our work enabled development of a probabilistic approach allowing to best account for the sources of variability in cadmium exposure (both for basic and added consumption). This approach, highlighted by a back-calculation method (eq. (1)), led to identify a cadmium concentration should ensure that the seaweed-consuming population does not exceed the TDI of cadmium according to a probability of cases, when simultaneously exposed to other dietary sources of cadmium. Considering that the seaweed-consuming population did not exceed the TDI of cadmium in 95% of cases, when simultaneously exposed to other dietary sources of cadmium, a cadmium concentration of $0.35 \text{ mg kg}^{-1} \text{ DM}$ of unprocessed seaweed consumed as condiment or vegetable (confidence interval: [0.18,1.09]) was derived to ensure it.

The application of this concentration reduced cadmium dietary exposure in French seaweed consumers. The contribution of seaweed to consumers in all its forms (food, ingredient, food supplement) relative to the TDI has been decreased by a factor of 1.63 compared to the situation based on cadmium concentrations observed in our dataset and by a factor of 1.34 compared to the situation based on the application of a maximum concentration in seaweed of $0.5 \text{ mg Cd kg}^{-1} \text{ DM}$ recommended in France by the CSHPF (1997) (Table 5).

However, as the confidence interval of our estimation included the maximum concentration of $0.5 \text{ mg Cd kg}^{-1} \text{ DM}$ of seaweed, it is likely that this concentration would prevent 95% of the population from exceeding the TDI for cadmium. Precisely, from our probabilistic back-calculation taking into account the background exposure from the rest of the diet, it appeared that the cadmium exposure of the seaweed-consuming population would not exceed the TDI in 93% of cases with a maximum cadmium concentration in edible unprocessed seaweed of $0.5 \text{ mg kg}^{-1} \text{ DM}$ recommended by the CSHPF. Thus, the derived probabilistic method makes it possible to give decision-support elements to risk managers according to the choice of the decision threshold to protect the population (Figure 1). This approach would be in line with the request of the European Union by its Commission Recommendation (EU) 2018/464 on the monitoring of metals and iodine in seaweed, halophytes and products based on seaweed, which

is likely to be followed by proposals for maximum levels established in Europe and in France in the framework of relevant regulations.

Limitations of the study

Our probabilistic approach could be improved with more detailed seaweed consumption data. The information about the consumption of seaweed as ingredients from industrial products was missing in our study as the access to their composition was difficult to obtain. In addition, only eating occasions were included in our estimation. Given the small dataset, our work failed to include children's consumption data of unprocessed seaweed and food supplements containing seaweed for exposure estimates. To investigate the frequency in adult and child specifically, the mode of consumption and quantity of seaweed consumed by species of seaweed according to the food product would provide a more accurate qualitative and quantitative data. These data would help to refine the estimate of exposure associated with the various types of seaweed consumption for the populations concerned and, where appropriate, of cadmium concentration limits in edible seaweed and recommendations for its consumption.

Ficheux *et al.* (2022) published a study dealing with seaweed consumption in the city of Brest (Brittany region, France) focusing on 780 consumers living near the coast. Despite the quality of this study, it was not representative of the French population consuming seaweed foodstuffs. The authors highlighted the interest in performing a higher scale study with a representative sample of the consuming population and to refine the proportion of consumers in the general population. In our work, data from the INCA3 study (ANSES 2017) were used because the French 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.

Moreover, the back-calculation carried out in our study can be improved by avoiding the incorporation of two different population samples related to seaweed consumers: a first one based on the consumption data from the INCA3 study, and another one based on the previous consumption study (INCA2) linked to the TDS2 to background levels of exposure to cadmium through the total diet of the general population (ANSES 2011a). The changes in the eating habits of French consumers over the time were not included.

Perspectives

Our probabilistic approach could be applied for other trace elements arsenic, mercury and lead which are also of potential concern due to their presence in seaweed (ANSES 2011a, 2020; Superior Health Council 2015; NIFES 2016; Banach *et al.* 2020). In contrast to the case of cadmium, the maximum concentration of inorganic arsenic, methylmercury and lead in edible seaweeds recommended by the CSHPF did not frequently exceed in French Annual Monitoring and Control Plan (2009-2017) (ANSES 2020). Nevertheless, according to TDS2 (ANSES 2011a), a health risk to French consumers associated with exposure to inorganic arsenic and lead through total diet, and methylmercury through fish and seafood consumption, cannot be ruled out. However, regarding all contaminants taken together, situations where HBGV are exceeded for a fraction of the population are emphasised to be up to the competent authority to identify and define the appropriate management levers for foods that are new entrants to the existing supply. This may consist of: (i) implementation of maximum levels based on control statistics in an ALARA approach (e.g. by setting a P95 type value), (ii) use of existing limit levels in other food categories (e.g. vegetables) or (iii) specific provisions for different categories that make a greater contribution (specific recommendations or maximum levels based on a back-calculation).

In the context of population overexposed to cadmium compared to HBGV, the emergence of consumption of a new food could lead to a low possibility of toxicological credit when there was already an unexplored risk for the consumer. In a way of valorisation of seaweed as food, the consumption of seaweed as the last foodstuff entering the diet is thus impacted in an already overexposed population to cadmium by other previous food. This situation should be observed too in the case of arsenic, mercury, and lead when seaweed had binding affinity. In the future, our approach could be improved by adjusting the distribution of the toxicological credit across the diet for cadmium so that HBGV is not exceeded without penalising the last food to entering. Our approach could be applicable to other relevant food/contaminant pairs to recommend appropriate maximum contaminants levels in food. The implementation of our approach could be a support for food safety in order to setting health maximum levels for contaminants as cadmium in foodstuffs. This improvement should lead to the final implementation of the revision of regulatory maximum limits by managers (initially based on the ALARA principle) if they have approved the approach in their perspectives. This refinement should contribute to overall consumer health protection.

Finally, seaweed are also used as fertiliser in agriculture or for bio-fuel production which may be the source of contamination in the environment. Taking actions to diminish its source by controlling processes or releases such as limits in fertilizers, reducing contamination of agricultural soils and food, can be also an efficient complementary perspective to reduce the dietary exposure to cadmium (ANSES 2011b, 2016, 2019; Carne *et al.* 2021).

Conclusions

Considering the background exposure to cadmium and several sources of information on consumptions and cadmium levels, a stricter maximum limit has been established for cadmium in seaweed in order to offer a better protection of seaweed consumers. The proposed cadmium limit in seaweed of $0.35 \text{ mg kg}^{-1} \text{ DM}$ (confidence interval: [0.18,1.09]) was estimated to ensure that 95% of seaweed-consuming consumers would not exceed the TDI of cadmium, while also taking the other dietary sources of exposure to cadmium into account. This approach developed in our work evolved the fixing of a regulatory maximum limit generally based on the ALARA principle. Based on our approach, the set-up of maximum limit for relevant food/contaminant pairs could be improved by the possibility to assign differently the maximum concentrations of the total food groups considering a last foodstuff entering the diet or new consumption habits. This developed approach allows to ensure better health consumer protection by the derivation of health maximum levels for contaminants in foodstuffs in support of food safety. This approach would be at first glance support assessment of the need to establish maximum limits of cadmium and other toxic trace elements (arsenic, mercury and lead) after assessment of their contribution from seaweed and halophytes to the total exposure of these substances in line with Commission Recommendation (EU) 2018/464.

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1 Géraldine CARNE
2 Risk Assessment Department,
3 French Agency for Food, Environmental and Occupational Health & Safety,
4 14 rue Pierre et Marie Curie, 94701 Maisons-Alfort Cedex
5 FRANCE
6
7

8 Title of the manuscript: *“Probabilistic determination of a maximum level of contaminant to reduce the*
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10 *the French population”*

11 Authors: G. Carne*, D. Makowski, S. Carrillo, T. Guérin, P. Jitaru, J-C Reninger, G. Rivière, N. Bemrah
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26 a function of concentrations in seaweeds.

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Tables

30

31 **Table 1. Cadmium concentrations in unprocessed seaweed and food supplements**
 32 **containing dried seaweed observed in the dataset, following the Upper Bound hypothesis**

		Cadmium concentrations (mg.kg ⁻¹ dry matter (DM))			
		Min	Mean	95th percentile	Max
Unprocessed seaweed	N = 255	0.001	0.604	2.700	9.400
<i>Source: CEVA (1996-2016), Rodenas de la Rocha et al. (2009) and FAMCP (2009-2017) dataset</i>					
Food supplements containing dried seaweed	N = 53	0.004	0.112	0.500	0.588
<i>Source: FAMCP (2009-2017) dataset</i>					

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35

36 **Table 2. Number of consumption occasions, consumer rates and mean consumption of**
 37 **edible seaweed as a food, food ingredient and food supplement ingredient in French adults**
 38 **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

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42 **Table 3. Input data for estimating dietary cadmium exposure for French edible seaweed**
 43 **consumers**

	Contamination input data		Consumption input data	
	Source	N	Source	N*
Scenario for seaweed consumed as a food	CEVA (1996-2016), Rodenas de la Rocha <i>et al.</i> (2009) and FAMCP (2009-2017) 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), Rodenas de la Rocha <i>et al.</i> (2009) and FAMCP (2009-2017) 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	FAMCP dataset (2009-2017)	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), Rodenas de la Rocha <i>et al.</i> (2009) and FAMCP (2009-2017) dataset	N = 308 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

44 * Consumption occasions

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

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50 **Table 4. Estimated dietary exposure to cadmium of French seaweed consumers by scenario**
 51 **and contribution of mean exposure to the Tolerable Daily Intake (TDI) of cadmium.**

	Adults			Children		
	Mean	P95	% TDI	Mean	P95	% TDI
Exposure to seaweed as a food in $\mu\text{g.kg}^{-1}$ bw.d⁻¹	0.05	0.20	15.5%			
Exposure to seaweed as a food ingredient in $\mu\text{g.kg}^{-1}$ bw.d⁻¹	0.006	0.023	1.6%	0.006	0.024	1.7%
Exposure to seaweed as a food supplement ingredient in $\mu\text{g.kg}^{-1}$ bw.d⁻¹	0.006	0.005	1.7%			
Exposure to seaweed in all forms combined (food + ingredients + food supplement) in $\mu\text{g.kg}^{-1}$ bw.d⁻¹	0.07	0.22	18.8%	0.006	0.024	1.7%

52

54 **Table 5. Estimated dietary exposure to cadmium (Cd) of French edible seaweed consumers**
 55 **by scenario considering a maximum concentration in seaweed of 0.35 mg Cd.kg⁻¹ dry**
 56 **matter. The contribution of mean exposure to the Tolerable Daily Intake (TDI) of cadmium**
 57 **was computed as a function of concentrations in seaweeds.**

	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	P95	% TDI	% TDI	% TDI
Exposure to seaweed as a food in µg.kg ⁻¹ bw.d ⁻¹	0.03	0.13	8.9%	12.7%	15.5%					
Exposure to seaweed as a food ingredient in µg.kg ⁻¹ bw.d ⁻¹	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 food supplement ingredient in µg.kg ⁻¹ bw.d ⁻¹	0.006	0.005	1.6%	1.3%	1.7%					
Exposure to seaweed in all forms combined (food + ingredients + food supplement) in µg.kg ⁻¹ bw.d ⁻¹	0.04	0.15	11.5%	15.4%	18.8%	0.003	0.007	1.0%	1.4%	1.7%

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1 Géraldine CARNE
2 Risk Assessment Department,
3 French Agency for Food, Environmental and Occupational Health & Safety,
4 14 rue Pierre et Marie Curie, 94701 Maisons-Alfort Cedex
5 FRANCE
6
7

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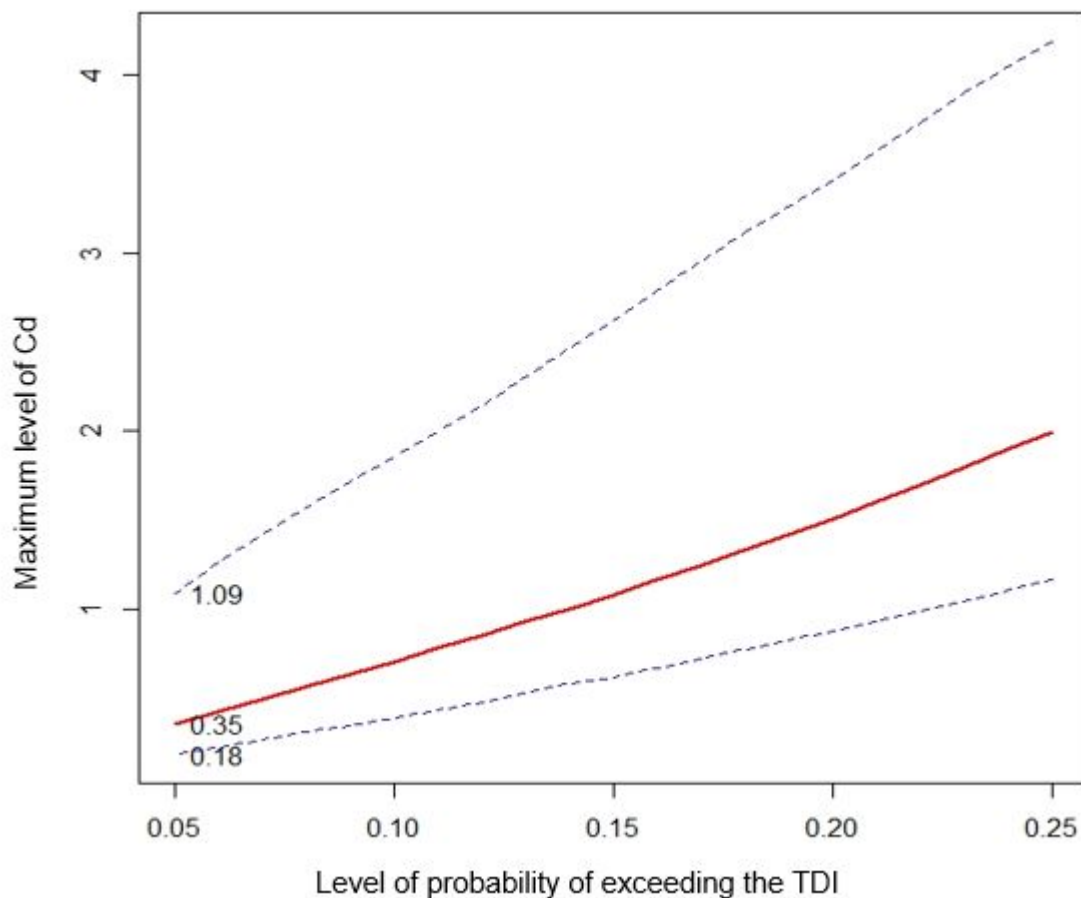
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- 14 - **Figure 1.** Distribution of the maximum cadmium (Cd) concentration in unprocessed seaweed
15 used as a vegetable or condiment (mg.kg⁻¹ dry matter DM) and its confidence interval, as a
16 function of the percentile of the French population for which exposure is not expected to
17 exceed the Tolerable Daily Intake (TDI) for cadmium when considering the entire diet.

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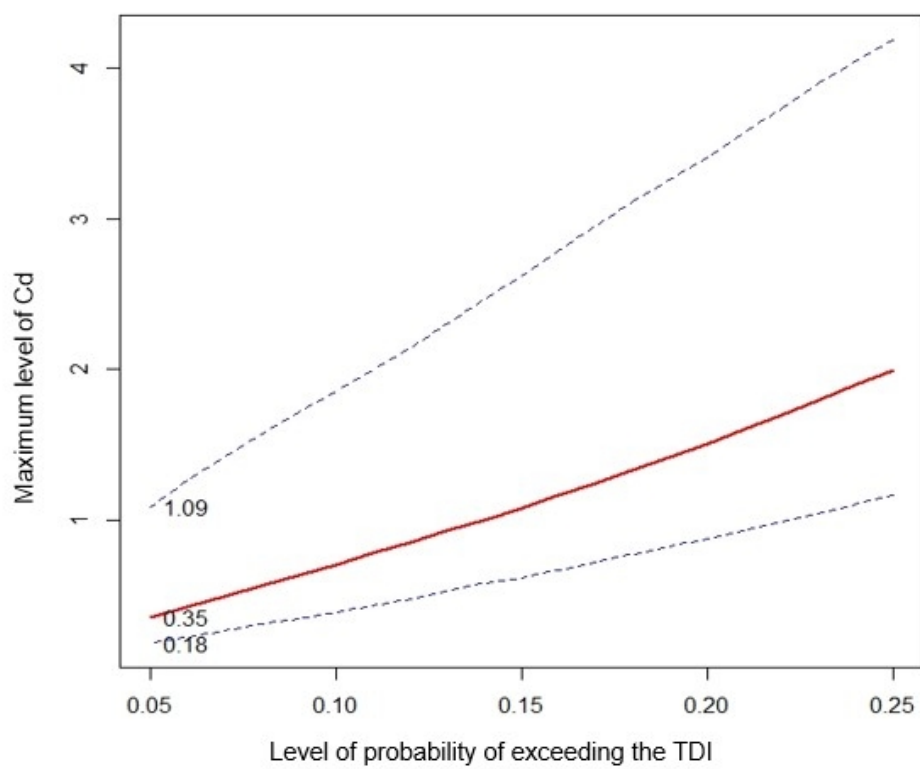
20

FIGURE.

21

22 **Figure 1. Distribution of the maximum cadmium (Cd) concentration in unprocessed**
 23 **seaweed used as a vegetable or condiment (mg.kg^{-1} dry matter DM) and its confidence**
 24 **interval, as a function of the percentile of the French population for which exposure is not**
 25 **expected to exceed the Tolerable Daily Intake (TDI) for cadmium when considering the**
 26 **entire diet.**

27



156x123mm (96 x 96 DPI)

1 **APPENDICES**
2 **TO**

3
4 **Probabilistic determination of a maximum level of contaminant to reduce the risk of**
5 **overexposure for an emerging consumption of food: the case of cadmium in edible**
6 **seaweed in the French population**
7

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9 G. Carne¹, D. Makowski², S. Carrillo¹, T. Guérin³, P. Jitaru⁴, J-C Réninger¹, G. Rivière¹, N.
10 Bemrah¹
11

12 ¹ ANSES, Risk Assessment Department, 14 rue Pierre et Marie Curie, F-94701 Maisons-Alfort Cedex, France

13 ² INRAE AgroParisTech University Paris-Saclay, UMR MIA, 16 rue Claude Bernard, 75231 Paris, France

14 ³ ANSES, Strategy and Programmes Department, F-94701 Maisons-Alfort Cedex, France

15 ⁴ ANSES, Laboratory for Food Safety, 14 rue Pierre et Marie Curie, F-94701 Maisons-Alfort Cedex, France
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19 **1. Supplementary data concerning the materials and methods**
20 **1.1 Cadmium seaweed contamination data**
21

22 **Table A1. Cadmium concentrations (mg.kg⁻¹ dry matter (DM)) measured in different samples of seaweed of the French Annual Monitoring**
 23 **and Control Plan between 2009 and 2017 (FAMCP database), following the Upper Bound hypothesis**
 24

	Total ^a	Unknown ^b	Brown macroalgae ^{c*}	Red macroalgae ^{d*}	Green macroalgae ^{e*}	Microalgae ^{f*}	Halophytes ^{g*}	Mixtures ^{h*}	FS ⁱ
<i>n</i>	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

25 ^aTotal: all seaweed categories combined (Brown, red and green macroalgae, microalgae, halophytes), except food supplements, agar-agar, beverages and seaweed powder;

26 ^bUnknown: seaweed whose parent group is not specified;

27 ^cBrown macroalgae: seaweed belonging to the group of brown macroalgae;

28 ^dRed macroalgae: seaweed belonging to the group of red macroalgae;

29 ^eGreen macroalgae: seaweed belonging to the group of green macroalgae;

30 ^fMicroalgae: specie related to spirulina;

31 ^gHalophytes: specie related to glasswort;

32 ^hMixtures: mixtures of dried seaweed;

33 iFS: food supplements containing dried seaweed.
34 *Due to the small number of samples, the 95th percentile was not calculated.
35
36

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Table A2. Cadmium concentrations (mg.kg⁻¹ dry matter (DM)) measured in different samples of seaweed of the Centre for Study and Promotion of Algae (CEVA) between 1996 and 2016 and 8 results obtained from Rodenas de la Rocha *et al.* (2009), following the Upper Bound hypothesis

	Total ^a	Brown macroalgae ^b	Red macroalgae ^c	Green Macroalgae ^{d*}	Halophytes ^{e*}
<i>n</i>	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
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

^aTotal: all seaweed categories combined (Brown, red and green macroalgae, halophytes);

^bBrown macroalgae: seaweed belonging to the brown macroalgae;

^cRed macroalgae: seaweed belonging to the red macroalgae ;

^dGreen macroalgae: seaweed belonging to the green macroalgae ;

^eHalophytes: specie related to glasswort.

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

1.2 French seaweed consumption data

Table A3. Number of consumption occasions and consumer rates of edible seaweeds in all forms combined (food, recipe ingredients and food supplement ingredients) for French 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%)

2. Supplementary data concerning the results

2.1 Estimated cadmium dietary exposure of French edible seaweed consumers

Table A4. Selected probability distributions for each type of data

Type of data	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 food supplement containing seaweed	Log-normal (0.15225;0.58499)
Consumption of food supplement 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 (μ , λ); ^b Log-normal distribution (mean, standard deviation), ^c Log-logistic distribution (γ , β , α)