Maisons-Alfort, Wednesday, November 23

The Director General

OPINION

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

on the revision of maximum content for cadmium in foodstuffs intended for human consumption

ANSES undertakes independent and pluralistic scientific expert assessments.
ANSES primarily ensures environmental, occupational and food safety and assesses potential health risks in these areas.
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 the necessary information concerning these risks as well as the requisite expertise 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 made public.

On Tuesday 21 July 2011, the French Agency for Food, Environmental and Occupational Health & Safety received a request from the Directorate General for Food (DGAl) to undertake the following expert appraisal: the revision of maximum content for cadmium in foodstuffs.

1. BACKGROUND AND PURPOSE OF THE REQUEST

Cadmium (Cd) is a widespread metallic trace element, naturally present in the environment but also found in high concentrations at certain sites as a result of human activities (metalworking, mines and other industries) and is of potential concern as a contaminant in the food chain.

As a result, the European Union has passed and amended a series of Regulations on cadmium: these are based on setting maximum levels (MLs) of cadmium in food, accompanied by a general provision banning the sale of any food with a concentration of cadmium in excess of the ML set for it[1]. However, since EFSA lowered the toxicological threshold by a factor of almost three in 2009 (EFSA 2009), and since new data became available concerning food contamination and the exposure and body burden of different population groups, the European Commission and the Member States have put in motion a revision of the MLs for cadmium in foodstuffs.

[1] Regulation (EC) 194/97, followed by Regulation (EC) 466/2001 and finally Regulation (EC) no. 1881/2006 setting certain maximum levels for contaminants in foodstuffs and amended several times for the parts concerning cadmium.

In this context, on 21 July 2011 the French Directorate General for Food (DGAl) asked ANSES to thoroughly investigate the revision of MLs for cadmium, taking into account their effect on consumer exposure. It asked the Agency to answer the following questions:

1. What are the specific characteristics of individuals identified as being overexposed in the 2nd French Total Diet Study (TDS2)[2]? Are the foods that most contribute to exposure the same for the general population as for those belonging to the group of 0.6% who are overexposed?

2. Are the conclusions of TDS2 more conservative than the assessments using biological markers for cadmium in the French population?

3. Which foods should be regulated with a view to lowering the exposure of consumers to cadmium and, primarily, to reducing the proportion of consumers for whom exposure exceeds the Toxicological Reference Value (TRV)? It is important that ANSES define the food groups most in need of regulation and that it explain its choices. Should these groups be defined for the general population or for consumers whose have the highest exposure?

4. Is there any benefit to public health if only groups of highly contributing foods are regulated, or should highly *contaminated* foods also be regulated?

5. If the agency also recommends regulating highly contaminated but low contributing foods, this will protect certain population groups who do not have a standard dietary pattern: are these groups the same as those identified by TDS2 as being overexposed?

6. Can ANSES confirm that *in fine* the toxicological reference value is based on an “end point” of little relevance to children and that therefore, in reality, the fact that this value is exceeded for 15% of them is not a matter of concern?

7. Would MLs specifically for chosen contributing foods reduce exposure for overexposed children?

8. With the available data from both national monitoring programs and TDS2, can ANSES determine, for the main groups of contributing food, mean and median contaminations as well as the 90th and 95th percentiles (P90 and P95)[3] for contamination?

9. With the help of scenarios concerning the contamination of foodstuffs on the market, can ANSES estimate whether MLs based on the P90 or P95 values of Question 8 above would have a protective effect, i.e. whether they would mitigate exposure, on the one hand in the general population and on the other in those who are overexposed?

10. Can ANSES indicate whether the MLs listed in the annex to the Request (based on the ALARA principle[4]) will have a protective effect and lead to modification of exposure, on the one hand in the general population and on the other in those who are overexposed?

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[2] Undertaken at the national level, Total Diet Studies (TDSs) have for primary objective to monitor the population's exposure to substances present in food (prepared as consumed) and of concern in terms of public health. The first TDS was undertaken between 2000 and 2004 and the second was published in 2011.

[3] 90th and 95th percentiles of the distribution of levels of contamination for a foodstuff.

11. For the particular case of fish, can ANSES estimate which of two regulatory options would provide potentially greater protection for consumers: (i) MLs as suggested by the European Commission in the attached document or (ii) a situation in there would only be a single ML for all fish, which could be set at 0.1, 0.2 or 0.3 mg/kg? Can this be verified specifically for a given species of fish, in this case the sardine (*Sardina pilchardus*): can ANSES quantify the gain in protection given by an ML set at 0.1, 0.2 or 0.3 mg/kg for this species?

2. ORGANISATION OF THE EXPERT APPRAISAL

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

The collective expert appraisal was carried out by the Expert Committee (CES) for "Physical and chemical contaminants and residues" (RCCP) which met on 13 September, 10 October and 14 November 2011 on the basis of initial reports written by experts appointed from among the members of the CES, with scientific and technical support from the Agency's "Unit for methods development & support in chemical risk" (UAERS).

The expert assessment was based on the following data:

<u>Body burden data:</u>

- The environmental section of the French National Nutrition and Health Study (ENNS) regarding biological surveillance of exposure of the French population to chemical substances in the environment (Fréry et al. 2011). In this study, cadmium levels in urine were determined for a population of 1930 participating adults (aged from 18 to 74 years old).
- The CALIPSO study on high French consumers of seafood (at least twice a week) (AFSSA 2006). In this study, urinary levels of cadmium were found in 380 adults out of 1011 adults tested.

<u>Consumption data</u>: The consumption data used in this opinion are taken from the French individual and national study on food consumption (INCA2) (AFSSA 2009). National representativeness was ensured by stratification (age, gender, socio-professional category and size of household). In all, more than 4079 people were surveyed between 2005 and 2007 taking seasonal effects into account; the sample population included 1444[5] children and adolescents from 3 to 17 years, and 1918[5] adults (18 years and over). To ensure national representativeness, each subject studied was assigned a weighting coefficient and the calculations performed for this opinion take these coefficients into account.

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[4] "As Low As Reasonably Achievable". The ALARA principle is designed first to protect consumers by excluding the most contaminated batches of foodstuffs and secondly to limit the percentage of batches excluded to a financially tolerable level. The exclusion threshold is therefore generally placed at the 95th percentile of the distribution of contamination levels.

[5] after removal of those who under-report

Contamination data (details in Annex 8):

- the most recent data from national monitoring programs were used to simulate the impact of different maximum levels (MLs) on population exposure;
- data from the French Institute for Agro-Food Research on Cereals (IRTAC), France Agrimer, Coop de France and Arvalis were used to simulate the impact of maximum levels on ingredients and foods made from soft wheat and durum wheat;
- in addition, contamination data from the latest French Total Diet Study (TDS2) were used to calculate exposure for individuals on the basis of their total dietary intake[6] (ANSES 2011).

3. ANALYSIS AND CONCLUSION OF THE CES *RCCP*

3.1. Toxicological Reference Values

Several studies indicate that the kidneys and bone tissue are the main target organs for chronic oral exposure to cadmium.

Cadmium that accumulates in the kidneys' proximal tubules leads to their degeneration and atrophy and consequently a shedding of proteins with low molecular weight (beta-2-microglobulin, retinol-binding protein (RBP), alpha-1-microglobulin, etc.). This condition may be associated with other disorders of the proximal tubules: enzymuria, aminoaciduria, glycosuria, hypercalciuria, hyperphosphaturia. Loss of phosphate and calcium can lead to kidney stones. At a more advanced stage, lesions can extend to the distal tubule, leading to disorders involving the acidification and concentration of urine. In the skeleton, cadmium can cause a decline in bone mineral density (Åkesson et al. 2006). Lastly, cadmium is listed by the IARC[7] as a Category 1 carcinogen.

The half-life for elimination of cadmium from the blood is approximately 100 days, and the half-life for biological elimination is between 10 and 30 years (with a mean of 12 years). Chronic exposure in individuals is estimated from the load of cadmium in the renal cortex, which is itself calculated from the subject’s cadmium level. This is possible because there is a close relationship between urinary cadmium levels and the concentration of cadmium in the renal cortex. This relationship is relevant as long as renal function is normal and storage sites in the body are not saturated. The level of cadmium found must be corrected by the level of creatinine in the urine to provide a weighting coefficient for eliminations related to muscle mass and meat consumption.

In 2009, EFSA lowered the Provisional Tolerable Weekly Intake (PTWI) of 7 µg Cd/kg body weight (bw)/week to a Tolerable Weekly Intake (TWI) of 2.5 µg Cd/kg b.w. per week (EFSA 2009). These two toxicological reference values are based on the observation of renal effects following chronic exposure to low doses of cadmium. EFSA’s opinion, confirmed in 2011, is based on a meta-analysis of 35 studies showing a relationship between urinary excretion of cadmium and beta-2-microglobulin, which is a good marker for renal tubular dysfunction[8]. Modelling all these data leads to the choice of a target value for human urinary cadmium levels

[6] Approximately 90% of the diet of the French population is covered in this study
[7] International Agency for Research on Cancer
[8] The choice of beta-2-microglobulin as a cadmium effect biomarker is questionable, considering that it is not necessarily specific to cadmium and is highly unstable when the pH is acidic.

of 4 µg Cd/g creatinine($BMDL_5$)[9], which corresponds to a concentration of urine beta-2-microglobulin that is below the threshold above which tubular disorders become a cause for concern (in the region of 300 µg beta-2-microglobulin/g creatinine). A correction factor of 3.9 chosen to take individual variability into account (which is not the case when a model is developed from mean values alone) leads to a critical threshold of 1 µg Cd/g creatinine. For urine cadmium concentration to remain below this value, EFSA considers, by modelling, that dietary intake of cadmium should not exceed 0.36 µg Cd/kg b.w. per day, for the 95th percentile of non smoking women from 56 to 70 years old, or 2.5 µg/kg b.w. per week.

CES RCCP considers that the TWI proposed by EFSA is relevant in the context of a risk assessment for the adult population related to the ingestion of cadmium.

It suggests that the adult body burden be interpreted with regard to two threshold indicators:

- A threshold of toxicological concern which, if exceeded, requires implementation of complementary studies to refine the risk assessment and determine the most effective preventive measures for reducing population exposure.

- An action threshold which, if exceeded at the scale of the general population, must lead to the immediate implementation of preventive measures to significantly reduce population exposure levels.

CES RCCP considers that the critical body burden value of 1 µg Cd/g creatinine calculated by EFSA may be considered as the threshold of toxicological concern. Studies should be initiated to define the action threshold value[10].

Specific case of children (in partial answer to Question 6):

Children are considered to be more exposed to dietary cadmium exposure than adults (NTP, 2005 reported by ATSDR, 2008), largely as a result of their dietary patterns (food and water consumption plus respiration, all expressed per kilogram of body weight, which are greater than for adults) (ATSDR 2008). Certain findings suggest that digestive absorption is greater in young organisms (Kostial 1984; Sasser & Jarboe 1977, 1980). Moreover, the immaturity of developing organisms could be the reason why children are more prone to exposure than adults. In experiments with rats and mice, cadmium was shown to be reprotoxic (delayed ossification, skeletal malformations, neuro-behavioural modification in the young) after long-term treatment of the parent generation or of gestating females. There is a lack of experimental data for determining, qualitatively or quantitatively, the toxicity of cadmium administered directly to young animals by the oral route and at low doses (WHO 1992). The current state of knowledge does not warrant the defining of a specific cadmium Toxicological Reference Value for children.

The current TWI was determined on the basis of epidemiological studies that mostly concerned population groups aged over 40 years old. These groups may have been exposed to cadmium of environmental origin since childhood. Furthermore, the level of atmospheric contamination is currently lower than before the 1970s, with the result that the thresholds based on a study of population groups that are now middle-aged or beyond can be considered as relevant for protecting population groups that are currently less exposed.

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9 The Benchmark Dose (BMD) is an alternative, quantitative approach particularly used to assess the dose-effect relationship based on various experiments in animals or epidemiological and observational studies. It corresponds to the dose leading to an excess risk level fixed at 5 or 10% of the chosen critical effect. The Benchmark Dose lower confidence Limit (BMDL) is the lower limit of the confidence interval at 95% of the BMD.

10 For information, the German Human Biomonitoring Commission has set this threshold at 5 µg/g creatinine.

Since it is based on effects observed after close to half a century of exposure, this TWI cannot be used to calculate the hazard to children. However, it seems reasonable to consider that the TWI for cadmium, determined on the basis of epidemiological studies of population groups exposed via the environment, is relevant insofar as it takes into account the effects in adults resulting from exposure since childhood.

3.2. Exposure of the general population

3.2.1. Adults

Body burden of the French population with cadmium (in answer to Question 2):

In the adult population (between 18 and 74 years old) studied in the ENNS (Fréry et al. 2011), the mean and median concentrations of urine cadmium were both equal to 0.29 µg Cd/g creatinine, and the 95th percentile to 0.91 µg Cd/g creatinine.

These mean levels are in agreement with those found in France during previous investigations carried out by InVS in 1997, 2000 and 2005 (about 0.3 µg Cd/g creatinine at Salsigne and its surrounding area (RNSP & INSERM 1997) as well as in Marseille (ORS PACA-InVS 2001), and 0.27 µg Cd/g creatinine in the national study on incineration plants (AFSSA & INVS 2006).

Mean human urinary cadmium levels found in the ENNS study were similar to those observed in the NHANES[11] study carried out in 2003-2004 (CDC 2009) on a representative sample of the population of the United States, in the CHMS[12] in 2007-2009 (Health Canada 2010) and in the population of the Czech Republic in 2005 (NIPH 2006, 2010). On the other hand, the levels observed in Germany in the adult population ten years ago were slightly lower (Becker et al. 2003), 1.5 times lower than the mean in the adult French population and 1.25 times lower at the 95th percentile.

Recent data for body burden (ENNS, 2011) suggest that 3.6% of French adults exceed the 1 µg Cd/g creatinine threshold of toxicological concern. Note that none of the subjects in the study exceeded the action threshold proposed by the German Human Biomonitoring Commission (5 µg Cd/g creatinine).

In the CALIPSO study (2006), high consumers of seafood (fish, molluscs and crustaceans) had a higher body burden than the national average, with mean cadmium levels of 0.65 µg Cd/g creatinine and 1.19 µg Cd/g creatinine at P95[13]. In this study, subjects over the age of 64 years had mean body burden of 0.95 µg Cd/g creatinine and 1.94 µg Cd/g creatinine at P95. Fifteen percent[7] of subjects in the study had body burden exceeding the threshold of concern. On the other hand, none exceeded the level of 5 µg Cd/g creatinine.

The difference between the proportion of subjects exceeding the threshold of concern (3.6%) and that found in TDS2 (0.6%) can be explained, leaving aside methodological differences, by the fact that diet accounts for 90% of exposure of non-smokers (UNEP 2008) and that part of the general population's body burden can be attributed to other contamination vectors (e.g.

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11 National Health and Nutrition Examination Survey

12 Canadian Health Measures Survey

13 These values apply to a sample which included smokers. However, a detailed examination of these levels of impregnation when smoking/non-smoking is taken into account show that impregnation is greater in non-smokers, because the non-smokers in the study sample were older on average than the smokers.

tobacco). Moreover, dietary exposure data (TDS2) suggest that 1.4% of adults are exposed to more than 90% of the TWI. For these individuals the exposure margin is low if other potential sources of cadmium are taken into account.

These two approaches converge, emphasising that a small part of the adult population is over-exposed to cadmium, largely through dietary intake, and that high consumers of seafood appear to be more exposed than the general population. The level of overexposure remains moderate, and it would be prudent to compare it to a future action threshold to help decide on the most appropriate reduction measures to be taken.

Description of consumption profiles for those individuals most exposed to cadmium via food (in answer to Questions 1 and 5):

Exposure was assessed on the basis of consumption data from the INCA2 survey and contamination data from the TDS2 survey (Annex 3).

The INCA2 survey was carried out using the consumption notebook method. Each participant keeps a dietary consumption "diary" for seven days, from which his/her annual dietary intake is deduced. It is possible to extrapolate these individual consumption data to the level of the entire population because of the large size of the cohort (individual variability) and the variety of dates used throughout the year (temporal variability). In addition, since the data for EAT2 and INCA2 were collected independently, there is no reason to suppose that foods consumed by participants in the consumption survey were contaminated in the ways suggested by the contamination survey. The 0.6% of the adult population exceeding the tolerable daily intake TWI are consequently only theoretical. The data for individual consumption cannot, under any circumstances, be interpreted on an individual basis and with such a small sample.

A statistically more robust solution would seem to be to investigate a more highly exposed population group such as the 5% most exposed to cadmium (95^{th} percentile of exposure, or P95). These 5% of individuals have a consumption profile similar to that of the 0.6% exceeding the TWI. (a detailed description of the 0.6% of subjects whose levels exceed the TWI is given in Annex 1).

The 5% of most exposed subjects make up a sample of 90 adults including 55 women, aged from 18 to 78 years old. Their mean exposure was 2.24 ± 0.05 µg/kg b.w. per week. Their mean body weight (63 ± 11 kg) and mean body mass index (BMI) (22.2 ± 3.5 kg/m^2) were significantly lower than those for the general population (70 ± 14 kg and 24.6 ± 4.5 kg/m^2). This can be explained by the fact that the number of women in the group was disproportionately high.

A table comparing the contributions of foods for this population group and for the general population is given in Annex 2.

The major contributors to exposure, in adults whose exposure exceeds the 95^{th} percentile, are essentially the same as the contributors identified for the general population. Molluscs and crustaceans alone contribute 5% of exposure in the general population compared with 21% in adults exceeding P95, with an important contribution from scallops, as a result of their high level of contamination when compared with other foods (0.36 mg/kg of fresh weight on average). The second main contributor is the "bread and dried bread products[14]" group (22% in both cases), followed by "vegetables" (9% compared to 10% for the population as a whole) and "potatoes"

[14] Typical range of French bakery products: breads (*baguette*, white loaf, *pain de mie*, *pain de campagne*, etc.), *biscottes*, *pain grillé*, etc.

(10% compared to 12% for the population as a whole). The four main contributors identified account for 62% of exposure in the most exposed subjects, compared with 49% for the general population.

Although the groups encompassing “offal”, “sweet and savoury biscuits and bars” and “chocolate” are among the groups with the highest levels in TDS2, they do not appear to be major contributors to exposure.

It should be noted that the “fish” group contributes very little to exposure in both cases (1%).

Mean overall consumption[15] by adults exceeding the 95th percentile of exposure (3.3 ± 0.9 kg) is significantly higher than for the rest of the population (2.7 ± 0.8 kg).

Compared to the rest of the population, adults exceeding the 95th percentile of exposure consume significantly more:

- crustaceans and molluscs (133 g/w) than the rest of the population (28 g/w). In comparison, the mean consumption of crustaceans and molluscs in high consumers of seafood in the CALIPSO study was 198 g/w. In this study, the consumption of crustaceans/molluscs was found to be a preponderant factor for high levels of individual exposure;
- bread and dried bread products (201 g/d on average, compared to 111 g/d). The other cereal products do not appear to be over-consumed;
- potatoes and potato products than the rest of the population (87 g/d versus 57 g/d).

Furthermore, there appears to be no significant difference between the P95 group and the general population regarding consumption of the other contributors and the foods most highly contaminated with cadmium (with the exception of crustaceans and molluscs). The consumption data are laid out in Annex 4.

It should nonetheless be emphasised that although no vegetarians[16] in this study were found to be overexposed to cadmium (P95), EFSA identifies this group as being potentially at risk as a result of its very particular diet.

This analysis shows that the principal factors explaining the high levels of exposure (expressed in µg/kg b.w. per week) in adults are:

- **generally high consumption and particularly high consumption of the principal contributors (five times more crustaceans/molluscs, twice as much bread and 1.5 times more potatoes);**
- **low body weight.**

[15] Including beverages
[16] Vegetarians made up 2% of the INCA2 cohort

3.2.2. Children (information in answer to Questions 6 and 7)

In TDS2, 15% of children exceeded the TWI of 2.5 µg Cd/kg b.w. per week, based on their dietary intake. This represents a sample of 157 children (65 girls and 92 boys) aged from 3 to 16, broken down as follows:

Table 1: Children whose exposure exceeds the TWI, distributed by age and body weight

Age	Number	Mean body weight (kg)
3	16	14.6
4	19	16.1
5	29	17.3
6	21	19.6
7	16	21.6
8	15	24.9
9	17	26.3
10	7	32.1
11	6	31.7
12	5	32.0
14	3	44.3
15	2	53.5
16	1	53.0

Children exceeding the TWI are significantly younger (6.5 ± 3.1 years versus 11.0 ± 3.9 years) and have lower body weight (21 ± 9 kg versus 41 ± 17 kg) than children not exceeding the TWI. After the age of five, the number of children exceeding the TWI decreases as their body weight increases.

The major contributors (>5%) to exposure in children exceeding the TWI are the same as for the entire child population, with fairly similar contributions for potatoes and potato products, bread and dried bread products, vegetables excluding potatoes, pasta, mixed dishes, and sweet and savoury biscuits and bars. As in adults, the offal and chocolate groups do not appear to be major contributors to exposure (Annex 5).

There appears to be no significant difference in the consumption of foods contributing the most to cadmium exposure between children whose exposure to cadmium exceeds the TWI and the entire population of children (Annex 6). The dietary profiles of the two groups are therefore very similar.

Unlike for adults, children whose exposure to cadmium (relative to body weight) exceeds the TWI differ from other children only by their body weight and lower ages. One may therefore suppose that the majority of cases exceeding the TWI are transient and will disappear as the children grow older.

Although there are no data available concerning urinary biomarkers for exposure to cadmium in French children, data from other countries can be used to assess the body burden of these children. The most complete set of data, and the closest to conditions in France, are those reported in the German GerES[17] III study for adults (Becker et al. 2003) and GerES IV study for children (Schulz et al. 2009), and also in the American CDC study (CDC 2009). The data are listed in Table 2.

Table 2: Comparative data on urinary cadmium levels (µg/g creatinine) measured in the populations of France, Germany and the USA

Studies	Type of population	Ages	Number	P50	P90	P95
France						
ENNS (2011)	General population	>18	1939	0.29	0.68	0.91
CALIPSO (2006)	High consumers of seafood	>18	387	0.50	1.19	1.46
Germany						
GerES IV (2003-2006)	General population	3-14	1734	0.07	0.17	0.28
GerES III (1998)		>18	3061	0.28	0.62	0.78
USA CDC		6-11	287	0.09	0.20	0.31
(2009)	General population	>20	1532	0.27	0.77	1.02

It would appear that for the general population, impregnation levels and their distributions are comparable for the different studies and population groups (adults and children). It should be noted that impregnation in children in the German and American data is approximately one third that in adults (for all percentiles). For information, in all cases, the 95th percentile is well below the threshold of concern of 1 µg Cd/g creatinine established by the German Human Biomonitoring Commission for children.

CES RCCP considers that the French values should be similar to these and that no child should be at risk. Nevertheless, body burden data for children in France are needed to confirm this hypothesis.

To conclude, the CES RCCP considers that, in view of renal toxicity observed after prolonged exposure (40 to 50 years or more), the 15% of cases of children with excess levels should disappear once the children reach adulthood, as they are more the result of the children's low bodyweight than of any particular dietary pattern. Furthermore, it is unlikely that they correspond to critical renal overload as the available body burden data suggest that, on average, children are subject to only one-third of the body burden of adults. In consequence, the CES considers that although 15% of children exceed the TWI in TDS2, this does not suggest that these children will be at risk on reaching the age of 50.

3.3. Management tools for reducing exposure of the general population

A small fraction of the French population is overexposed to cadmium. Since foods are the main source of contamination (excluding smoking and occupational exposure), dietary regulations would be an effective way of reducing exposure. Since cadmium is a ubiquitous metal found in a large number of foods, it is important to identify the food groups to be regulated. The health

[17] German Environmental Survey

impact of statutory levels on the general population and the overexposed population was assessed on the basis of the chosen food groups.

This section therefore presents the results of the simulations carried out to estimate the impact of statutory measures on the cadmium exposure of the French population. These measures only concerned the application of maximum levels (MLs). An ML is the maximum level of cadmium contamination beyond which it is forbidden to market a foodstuff. By taking into account the reduction in mean levels for each regulated food brought about by the introduction of an ML, together with the levels of consumption from INCA2, it was possible to simulate the impact of an ML on exposure levels for the population in comparison to the currently known reference situation (TDS2). The details of the method used are given in Annex 7.

3.3.1. Choice of food groups to be regulated

This section provides information in answer to Questions 3, 4 and 11.

It would be possible to propose statutory limits concerning foods contributing the most to exposure in the general population (bread and dried bread products, potatoes and potato products, vegetables), and also molluscs and crustaceans, the most contaminated foods, which contribute little to the exposure of the general population but considerably to that of the most exposed adults.

There is little to be gained by regulating foods that make only a small contribution to exposure. Indeed, reducing the exposure related to consumption of foods contributing 1% to overall exposure by 10% would reduce total exposure by only 0.1%. For example, there seems little point in reducing cadmium levels in offal, chocolate or biscuits, even though these are among the foods with the highest levels of cadmium, considering that they contribute less than 1% to total exposure, as these foods are consumed in only small quantities. Reducing exposure via consumption of these foods would therefore have very little impact. In the same way, the impact of reduced exposure via the consumption of fish would consequently be slight (contribution in the region of 1%, including in the most exposed individuals) as these foods are only slightly contaminated.

3.3.2. Application of maximum levels defined as the P90 and P95 of contamination levels (the ALARA[18] principle)

This section provides answers to Questions 8 and 9.

The simulations concerned the main contributors to the exposure of the general population and of overexposed individuals to cadmium, i.e. products based on wheat flour; molluscs and crustaceans; and potatoes. For these foodstuffs, the distribution of contamination data detected by national monitoring programs (Annex 9) and monitoring programs by the main operators in the cereals industry determined a P90 and a P95[19] (Table 3). Although vegetables also figured among the main contributors to cadmium exposure, it was not possible to assess the effect of an ML on their levels of contamination because of insufficient data. For all these foods, except

[18] "As Low As Reasonably Achievable". The ALARA principle is designed first to protect consumers by en excluding the most contaminated batches of foodstuffs and secondly to limit the percentage of batches excluded to a financially tolerable level. The exclusion threshold is therefore generally placed at the 95th percentile of the distribution of contamination levels.

[19] 90th and 95th percentiles of the distribution of levels of contamination for a foodstuff.

for soft wheat, the results obtained are similar, irrespective of the censorship hypothesis (low or high bounds). For soft wheat flour, only the results obtained using the upper bound hypothesis are presented (conservative hypothesis). The characteristics of the data used in these calculations and the way they were used are described in detail in Annex 9.

Based on these data, Table 3 sets out the distribution of the levels of contamination in those foodstuffs contributing most to cadmium exposure.

Table 3: Distribution of contamination of the main contributors to cadmium exposure (in mg/kg)

Foodstuff	**n**	**Levels of contamination (mg/kg)**								
		min	**P5**	**P25**	**P50**	**mean**	**P75**	**P90**	**P95**	**max**
Bivalve molluscs	242	0.032	0.043	0.065	*0.118*	0.165	0.203	**0.340**	**0.431**	0.787
Oysters	*57*	*0.048*	*0.068*	*0.123*	*0.160*	*0.182*	*0.227*	*0.316*	*0.334*	*0.414*
Mussels	*138*	*0.001*	*0.037*	*0.058*	*0.071*	*0.149*	*0.134*	*0.400*	*0.633*	*0.787*
Scallops	*47*	*0.040*	*0.047*	*0.118*	*0.157*	*0.184*	*0.257*	*0.366*	*0.376*	*0.390*
Potatoes	89	0.001	0.001	0.008	0.017	0.023	0.031	**0.049**	**0.062**	0.080
Soft wheat bran	478	0.005	0.010	0.053	0.078	0.074	0.090	**0.110**	**0.120**	0.300
Soft wheat flour	2861	0.005	0.010	0.020	0.025	0.031	0.031	**0.050**	**0.050**	3.020
Soft wheat grains	1644	0.003	0.010	0.025	0.030	0.036	0.044	**0.050**	**0.060**	0.320
Durum wheat	486	0.005	0.030	0.050	0.080	0.085	0.110	**0.130**	**0.151**	0.240

The P90 and P95 values for these foodstuffs have been chosen as maximum levels (MLs) for the following impact simulations.

<u>Results of impact simulations:</u>

Table 4: Impact of MLs set at P90 and P95 on levels for the main contributors and on the exposure level of the adult population

Regulated foodstuffs	Reduction observed following application of Maximum Levels (MLs)							
	P90				P95			
	Mean level[a]	Mean exp.[b]	Exp. at P95[c]	%>TWI[d]	Mean level	Mean exp	Exp. at P95	%>TWI
Bivalve molluscs		2.6% (1.09)	4.2% (1.81)	25.0% (0.5%)		1.8% (1.10)	1.6% (1.86)	0% (0.6%)
Oysters	*4.0%*				*0%*			
Mussels	*33.0%*				*30%*			
Scallops	*20.0%*				*0%*			
Potatoes	17.0%	3.5% (1.08)	3.2% (1.83)	0% (0.6%)	13.0%	3.5% (1.08)	3.2% (1.83)	0% (0.6%)
Wheat bran	8.0%	6.2% (1.05)	7.4% (1.75)	0% (0.6%)	5.0%	6.2% (1.05)	7.4% (1.75)	0% (0.6%)
Wheat flour	23.0%[e]				13.0%			
Wheat grains	10.0%				6.0%			
Durum wheat	10.0%	6.2% (1.05)	3.7% (1.82)	0% (0.6%)	6.0%	0% (1.12)	3.7% (1.82)	0% (0.6%)
Bivalve molluscs and potatoes	-	5.3% (1.06)	6.8% (1.76)	25.0% (0.5%)	-	3.5% (1.08)	3.2% (1.83)	0% (0.6%)

Bivalve molluscs, potatoes, soft wheat and durum wheat	-	6.2% (1.05)	7.4% (1.75)	25.0% (0.5%)	Not calculated. as impact less than for an ML set at P90

[a] reduction in mean level
[b]: percentage reduction compared to reference exposure of 1.12 µg/kg b.w. per week (mean exposure of the general population in µg/kg b.w. per week after application of the ML)
[c]: percentage reduction compared to reference exposure of 1.89 µg/kg b.w. per week (exposure of 95th percentile of the general population in µg/kg b.w. per week after application of the ML)
[d]: percentage reduction compared to the reference situation (0.6%) (percentage of individuals whose weekly exposure exceeds the TWI
[e]: 13% below the lower bound hypothesis

Impact on mean levels in foodstuffs:

On the basis of the available data, setting MLs at P90 would have a significant impact on mean levels in the chosen foods. Setting an ML at P90 for all bivalve molluscs (i.e. 0.34 mg/kg, see Table 3) would bring about a reduction in the mean level in scallops, mussels and oysters of 20%, 33% and 4% respectively. Similarly, the mean level in potatoes would drop by 17%. An ML set at P90 for contamination of soft wheat grains would reduce contamination levels in grain, flour and bran by 10%, 23% and 8% respectively. Lastly, the mean level in durum wheat would be reduced by 10% if the ML was set at P90.

If MLs were set at P95 of the distribution of contamination levels, reductions would be less. For some foods such as oysters and scallops, applying such a threshold would not lead to any reduction in their mean level of contamination.

Impact on individual exposure:

In terms of health effect, applying these MLs would lead to a considerable reduction in mean exposure levels for the general population. By reducing mean levels in products produced from soft wheat, including bread and dried bread products, through application of an ML set at P90 or P95, mean exposure levels would be reduced by 6.2%. For bivalve molluscs, potatoes and durum wheat, which are minor contributors, mean exposure of the general population would be lowered by 2.6%, 3.5% and 3.5% respectively, for an ML set at P90. The combined effect of applying MLs to these four contributors, which together represent food groups accounting for 62% of exposure, would lead to a reduction of 6.2% of mean exposure for the general population.

The impact is greater if we take the 95th percentile of the general population (i.e. the 5% of individuals most exposed to cadmium) consuming more of these contributors than the general population. The combined effect of the four MLs (set at P90 of cadmium levels) decreases the exposure by 7.4% for the 95th percentile of the population. In this case, the percentage of individuals overexposed would be 0.5% instead of 0.6% in the reference case.

Although cases of children exceeding recommended levels can be considered to be transient, the impact of MLs applied to soft wheat (indirectly a principal contributor) and durum wheat was assessed for children. With an ML set at P90 for the contamination of soft wheat grains, total mean exposure for children would be 1.61 µg/kg b.w. per week (a reduction of 4.1%) and the 95th percentile would be at 3.01 µg/kg b.w. per week (a reduction of 4.4%). The percentage of children exceeding the TWI would be 12% (compared with 15% at the moment). For durum wheat, an ML set at P90 would not lead to any reduction in mean exposure of children and a negligible reduction (2.2%) of exposure at the 95th percentile.

<u>Conclusions:</u>

Applying MLs set at P90 and P95 of the levels of the main contributors of cadmium exposure for the French population (adults and children) would not reduce exposure levels significantly. The impact would be greater in the most exposed individuals (beyond the 95th percentile), but none of the MLs simulated brought intake down to the TWI.

The modest efficacy in terms of health effect of MLs established at P90 and P95 of contamination levels can be explained by the following facts:

- Cadmium is a ubiquitous contaminant found in many foods. For the general population, the greatest contributing food group contributes no more than 22%, which means that it would be necessary to act on several food groups to lead to a significant impact.
- Since regulations imposing MLs have been applied since 1997[20], none of the levels of contamination are excessively high, which explains why eliminating the highest levels of cadmium (P90 and P95) would not lead to a significant reduction in mean levels of the foods affected.
- The consumption profiles of the overexposed population are too heterogeneous.

<u>Supplementary elements in answer to Questions 3, 4 and 5</u>

For information, a soft wheat ML set at P50 of contamination levels for wheat grains would lead to a reduction of 13.3% in mean exposure of adults (0.97 µg/kg b.w. per week). The percentage of adults exceeding the TWI would be 0.4% compared to 0.6% at the moment.

In the same way, an ML set at P50 for bivalve molluscs would lead to a reduction of 5.3% of mean exposure for adults, with 0.2% of adults exceeding the TWI, corresponding to non-statistically significant overexposure. At the 95th percentile of exposure, this ML would lead to a reduction of exposure levels of 10.6%.

Based on these simulations, the CES RCCP considers that reinforcing current regulations for the main contributing foods would not have any significant effect on exposure of the population and that only action on environmental sources of exposure would significantly reduce cadmium levels in food.

Regarding overexposed individuals following specific dietary regimes (high consumers of molluscs), consumption recommendations seem to be a more effective management measure than setting lower MLs than those currently in place.

3.3.3. Impact of the European Commission's proposed MLs

Question 10 asked whether the MLs proposed by the European Commission (proposal attached to the request) would have a protective effect and lead to a modification of the exposure of the general population and of overexposed individuals.

In the EC's proposal, three different cases can be distinguished:

1. Foods for which MLs remain unchanged regarding Regulation 1881/2006;

[20] Regulation (EC) 194/97, followed by Regulation (EC) 466/2001 and finally Regulation (EC) no. 1881/2006 setting certain maximum thresholds for contaminants in foodstuffs and amended several as concerns cadmium

2. Foods that are currently regulated (MLs set out in Regulation 1881/2006), for which reduced MLs have been proposed;

3. Foods not currently regulated (no MLs under Regulation 1881/2006), for which MLs have been proposed.

In the first case, the proposal would have no impact on exposure related to consumption of the foods concerned. In the second case, the new MLs can be compared to the available contamination data in order to estimate an impact on the market (by excluding the most highly contaminated foods) and on potential exposure (if enough data are available and if significant amounts of the food are consumed by the general population). In the third case, as no data are available from monitoring or control programs, it is not possible to estimate any impact.

Table 5 lists the suggested changes to the MLs for foodstuffs, together with the estimated impact on the market, compared with data from 2009-2010 monitoring and control programs and data from professional organisations on durum wheat (grain) and soft wheat (grain and bran). The foods for which MLs remain to be defined are not listed (e.g. seaweed). With the exception of crustaceans and molluscs, foods for which the MLs are unchanged are not listed in the table. For foods that are currently unregulated, mean levels from foods investigated in TDS2 are given for information.

Table 5: Proposed modification of MLs in foods and the estimated impact on the market (on the basis of data from 2009-2010 monitoring and control programs)

Food	**Current ML (mg/kg FM*)**	**Proposed ML (mg/kg FM)**	**Impact**	**Mean level in TDS2 (mg/kg FM)**
Bonito, Common two-banded seabream, Eel, Grey Mullet, Trachurus, Louvar, Pilchard, *Dicologlossa cuneata*	0.10	0.05	None or impossible to assess (for separate species)	
Bonito	0.20	0.15	Impossible to assess	
Swordfish	0.30	0.25	None	
Bivalve molluscs	1.0	1.0	None	From 0.135 (mussels) to 0.364 (scallops)
Cephalopods (without viscera)	1.0	1.0	None	
Crustaceans: muscle flesh of appendices and the abdomen. In the case of crabs and crab-type crustaceans (*Brachyura* and *Anomura*), muscle flesh of appendices	0.50	0.50	None	0.021 (shrimps)
Cereals (excluding wheat and rice)	0.20	0.075	None	
Wheat (excluding durum wheat), rice	0.20	0.10	Soft wheat: 0.7% of market withdrawals	
Durum wheat	0.20	0.15	5% of market withdrawals	
Wheat bran, wheat germ	0.20	0.15	Wheat bran: 1% of market	

			withdrawals	
Cereal-based products and children's foods	-	0.01-0.05	Impossible to assess	From 0.005 (breakfast cereals) to 0.0299 (biscuits)
Soybeans	0.20	0.10	Impossible to assess	
Raw milk, UHT milk and milk for dairy products	-	0.005	Impossible to assess	Milk: 0.001
Stem vegetables, root and tuber vegetables (excluding celery)	0.10	0.075	None except for leeks (2 non-compliant samples out of 17)	
Leaf vegetables (excluding spinach), cabbage	0.20	0.15	None	
Oil seeds (excluding poppy: 1.0; soybeans: 0.1 and grains for oil production)	-	0.50	Impossible to assess	Dried fruits, nuts and seeds: 0.017
Pine nuts	-	0.50	Impossible to assess	Dried fruits, nuts and seeds: 0.017
Chocolate and derived products	-	0.30-0.50	Impossible to assess	Chocolate: 0.029

*FM: fresh matter

These comparisons mainly show that the new MLs would have an impact on wheat, with 5% being withdrawn from the market for durum wheat, 1% for wheat bran and 0.7% for soft wheat. The impact on mean levels in foods and therefore on population exposure of the MLs proposed by the European Commission would be less than that obtained by the simulation mentioned previously with an ML set at P90.

For foods that are currently regulated and monitored by surveillance and control plans, leeks would be the only vegetable affected by the new regulations. Considering the contribution of leek to total exposure[21], the impact on population exposure would be negligible

3.4. Conclusions

Concerning adults:

The French body burden data suggest that only a small proportion of the adult population are overexposed to cadmium, considering the threshold of toxicological concern set at 1 µg Cd/ g creatinine by the CES RCCP. With the exception of smoking and occupational exposure, food is the main route for exposure to cadmium for the general population (90%). Calculations of exposure via food intake also indicate a situation of overexposure, but with the toxic threshold (TWI) being exceeded more moderately. This overexposure can be partially explained by lower body weight and a variety of particular dietary patterns resulting in high food consumption with significant levels of consumption of bread and dried bread products, of bivalve molluscs and potatoes. With the exception of molluscs, these foods are also the main contributors identified for the general population.

[21] 0.09% in adults beyond the 95th percentile of exposure and 0.12% in the rest of the adult population

Concerning children:

The current state of knowledge does not warrant defining a toxicological reference value for cadmium specific to children. The TWI currently proposed by EFSA is established on the basis of effects observed after half a century of exposure. This is insufficient to characterise the hazard to children reliably, but nevertheless remains relevant in that it takes into account effects in adults resulting from exposure since childhood. The CES RCCP considers that, in view of renal toxicity observed after prolonged exposure (40 to 50 years or more), the 15% of cases of children with excess levels should disappear once the children reach adulthood, as they are more the result of the children's low body weight than of any particular dietary pattern. Furthermore, it is unlikely that they correspond to critical renal overload as the available body burden data suggest that, on average, children are subject to only one third the body burden of adults. In consequence, the CES considers that although 15% of children exceed the TWI in TDS2, this does not suggest that these children will be at risk on reaching the age of 50.

Recommendations :

The CES RCCP considers that the MLs under discussion at European level would not have a significant impact on mean levels in foods, nor on consumer exposure. Similarly, tightening the regulations by applying MLs established according to the ALARA principle for the main contributors would not lower exposure levels significantly, either for the general population or for overexposed groups.

To make a real impact on population exposure levels, the CES RCCP recommends:

- acting on the level of contamination in environmental sources, especially on intrants (contaminated fertilizers, spreading sludge from sewage treatment plants, etc.) that are at the origin of contamination of soil and foods. Identifying at-risk farming practices would be a first step towards reducing the cadmium that currently finds its way into the soil;

- assessing the efficacy of management measures based on consumption recommendations to reduce the exposure levels of individuals overexposed as a result of their specific diet.

Furthermore, the CES reiterates that other routes of exposure to cadmium should also be taken into account for the purpose of reducing population exposure, primarily via specific management measures.

4. THE AGENCY'S CONCLUSION AND RECOMMENDATIONS

The French National Agency for Food, Environmental and Occupational Health & Safety endorses the conclusions of the CES RCCP.

The Director General

Marc Mortureux

KEYWORDS

Cadmium, foods, exposure, maximal levels

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ANNEXES

ANNEX 1: Detailed description of the 16 individuals in the INCA2 study whose exposure levels exceeded the TWI

An analysis of the TDS2 data shows more clearly which of the adults (18 and older) in the INCA2 population study have a weekly exposure greater than the TWI. The 16 individuals had an average age of 51 (31 to 77) and included 11 women. They exceeded the TWI only slightly (102% to 163%). Their mean body weight (61 ± 8 kg) and mean body mass index (BMI) (22.2 ± 2.5 kg/m^2) were significantly lower than those for the general population (70 ± 14 kg and 24.6 ± 4.5 kg/m^2). This can be explained by the fact that the number of women in the group was disproportionately high.

A table comparing the contributions of foods for the adult population exceeding the TWI and for the general population is given in Annex 2.

The major contributors to exposure, in adults exceeding the TWI, are essentially the same as the contributors identified for the general population. The chief difference is that molluscs and crustaceans contribute only 5% of exposure in the general population compared with 37% in adults exceeding the TWI. The second main contributor is the “bread and dried bread products[22]” group (20% compared with 22% in the general population), followed by “vegetables” (9% compared to 10%) and “potatoes” (7% compared to 12%). Amongst vegetables, spinach is the highest contributor (5% compared to 3%). The four main contributors identified account for 73% of exposure in overexposed subjects, compared with 49% for the general population. Although the groups encompassing “offal”, “sweet and savoury biscuits and bars” and “chocolate” are among the groups with the highest levels in TDS2, they do not appear to be major contributors to exposure. It should be noted that the “fish” group contributes very little to exposure in both cases (1%).

A more detailed analysis of the consumption profiles of adults exceeding the TWI shows that:

- these adults had fairly diverse consumption profiles but almost always with higher than average consumption of one of the foods contributing more than 10% of their exposure;
- a majority (8 out of 16) were high consumers of molluscs and crustaceans, with mean levels of consumption higher than 182 g per week, which is close to the mean consumption (198 g per week) of high consumers of seafood in the CALIPSO study;
- the absence of any vegetarians[23];
- mean overall consumption (3.6 ± 0.8 kg per day) significantly higher than for the rest of the population (2.7 ± 0.8 kg per day).

Among these 16 individuals, three “atypical” consumption profiles were identified. For these individuals, the possibility cannot be ruled out that they had consumed an unusual quantity of some food contributing to their exposure during the week of the survey, and that the resulting values should not be extrapolated for the entire year.

[22] Typical range of French bakery products: breads (*baguette*, white loaf, *pain de mie*, *pain de campagne*, etc.), *biscottes*, *pain grillé*, etc.
[23] The population surveyed for the INCA2 study included 2% of vegetarians.

ANNEX 2: Contribution to cadmium exposure of 40 food groups in adults exceeding the TWI and in the total population (%)

Food groups	Adults exceeding the TWI (n=16)	Adults beyond the P95 for exposure (n=90)	Total (n=1918)
Bread and dried bread products	**20**	**22**	**22**
Breakfast cereals	0	0	0
Pasta	**2**	**4**	**6**
Rice and durum or cracked wheat	0	1	2
Croissant-like pastries	0	1	1
Sweet and savoury biscuits and bars	0	1	2
Pastries and cakes	1	1	2
Milk	0	0	1
Ultra-fresh dairy products	1	1	1
Cheeses	0	0	1
Eggs and egg products	0	0	0
Butter	0	0	0
Oil	0	0	0
Margarine	0	0	0
Meat	0	0	0
Poultry and game	0	0	0
Offal	1	1	1
Delicatessen meats	1	1	1
Fish	1	1	1
Crustaceans and molluscs	**37**	**21**	**5**
Vegetables (excluding potatoes)	**9**	**9**	**10**
Potatoes and potato products	**7**	**10**	**12**
Vegetables	0	1	1
Fruits	2	2	2
Dried fruits, nuts and seeds	0	1	1
Ice creams and frozen desserts	0	0	1
Chocolate	1	1	1
Sugars and sugar derivatives	4	4	3
Water	2	2	3
Non-alcoholic beverages	0	1	1
Alcoholic beverages	0	0	1
Coffee	1	1	2
Other hot beverages	1	1	1
Pizzas, quiches and savoury pastries	1	2	2
Sandwiches and snacks	0	1	1
Soups and broths	2	3	3
Mixed dishes	2	3	5
Dairy-based desserts	2	3	2
Compotes and cooked fruit	0	1	1
Seasonings and sauces	1	1	1
Dietetic foods	0	0	0
TOTAL	**100**	**100**	**100**

In bold: Major contributors (>5%) for at least one of the 2 population groups

ANNEX 3: Estimated mean cadmium levels in foods according to TDS2 data (µg/kg fresh matter)

Food groups	**DM (%)**	**Mean**
Bread and dried bread products	**76**	**19.3**
Breakfast cereals	30	5.3
Pasta	33	11.4
Rice and durum or cracked wheat	36	8.3
Croissant-like pastries	79	13.7
Sweet and savoury biscuits and bars	**98**	**29.9**
Pastries and cakes	71	8.5
Milk	11	1.1
Ultra-fresh dairy products	17	1.8
Cheeses	44	2.4
Eggs and egg products	27	1.1
Butter	65	0.8
Oil	100	0.5
Margarine	60	1.0
Meat	41	1.2
Poultry and game	41	1.1
Offal	**33**	**52.6**
Delicatessen meats	48	9.4
Fish	37	7.3
Crustaceans and molluscs	**23**	**166.6**
Vegetables (excluding potatoes)	12	12.2
Potatoes and potato products	**29**	**21.5**
Vegetables	30	8.8
Fruits	11	2.1
Dried fruits, nuts and seeds	82	17.0
Ice creams & frozen desserts	50	7.5
Chocolate	**98**	**28.6**
Sugars and sugar derivatives	84	10.9
Water	-	0.5
Non-alcoholic beverages	15	1.7
Alcoholic beverages	3	0.9
Coffee	-	0.8
Other hot beverages	9	3.1
Pizzas, quiches and savoury pastries	52	10.1
Sandwiches and snacks	51	10.1
Soups and broths	8	5.9
Mixed dishes	32	13.3
Dairy-based desserts	29	11.3
Compotes and cooked fruit	20	5.9
Seasonings and sauces	40	16.9
Dietetic foods	**25**	**22.9**

FM: dry matter, ML: statutory maximum level (*modified by Regulation EU No.420/2011 of 29 April 2011), **in bold**: food groups with the highest levels

ANNEX 4: Mean consumption and 95th percentile of INCA2 food groups by adults beyond the 95th percentile of exposure and the rest of the population (g/day)

Food groups	>P95 (n=90)	Total (n=1828)		*P*
	Mean	Mean	P95	
Bread and dried bread products	**201.4**	**110.8**	**262.1**	**<0.0001**
Breakfast cereals	3.3	4.9	32.1	0.3121
Pasta	53.0	37.1	107.1	0.0461
Rice and durum or cracked wheat	25.0	24.6	85.7	0.9312
Other cereals	0.2	0.6	0.0	0.1695
Croissant-like pastries	15.2	11.6	51.4	0.3997
Sweet and savoury biscuits and bars	10.9	8.9	42.7	0.3575
Pastries and cakes	42.0	37.2	119.3	0.2976
Milk	73.2	86.3	350.0	0.3592
Ultra-fresh dairy products	83.0	81.9	232.1	0.9227
Cheeses	39.5	33.2	88.0	0.1121
Eggs and egg products	15.9	15.2	49.8	0.7852
Butter	15.9	10.8	32.9	0.0316
Oil	9.7	10.7	30.3	0.4661
Margarine	4.0	4.5	20.6	0.5084
Other fats	0.2	0.1	0.0	0.4989
Meat	47.6	49.8	121.8	0.6764
Poultry and game	45.6	31.2	93.1	0.0129
Offal	3.7	2.9	18.6	0.417
Delicatessen meats	38.9	34.1	87.9	0.4036
Fish	29.5	26.4	73.1	0.3562
Crustaceans and molluscs	**18.5**	**3.8**	**21.3**	**<0.0001**
Vegetables (excluding potatoes)	173.3	137.7	294.1	0.0125
Potatoes and potato products	**87.4**	**56.9**	**150.0**	**0.0006**
Vegetables	14.8	9.4	50.0	0.1565
Fruits	214.8	141.0	398.3	0.0287
Dried fruits, nuts and seeds	4.9	2.6	14.3	0.1438
Ice creams and frozen desserts	6.1	8.8	45.7	0.093
Chocolate	9.1	5.5	26.4	0.0893
Sugars and sugar derivatives	**36.2**	**19.8**	**60.0**	**0.0004**
Water	864.5	784.9	1885.7	0.4216
Non-alcoholic beverages	143.6	139.7	525.7	0.9106
Alcoholic beverages	136.8	155.7	640.0	0.386
Coffee	255.3	253.1	768.6	0.951
Other hot beverages	199.8	126.1	639.3	0.0258
Pizzas, quiches and savoury pastries	26.9	23.0	82.9	0.6354
Sandwiches and snacks	15.8	16.5	82.9	0.8672
Soups and broths	132.8	83.9	342.9	0.0679
Mixed dishes	71.1	69.0	194.3	0.808
Dairy-based desserts	40.5	24.5	100.7	0.0636
Compotes and cooked fruit	17.5	13.1	64.3	0.3757
Seasonings and sauces	24.2	19.1	49.8	0.068
Dietetic foods	0.0	2.9	0.4	0.0096

*Result of the Student test, **in bold**: significant test. The risk of a Type I error is 0.001 (0.05/43 food groups, adjusted to mitigate errors related to multiple testing).

ANNEX 5: Contribution to cadmium exposure for the 40 food groups in children exceeding the TWI and the entire child population (%)

Food groups	**Children exceeding the TWI (n=157)**	**Entire child population (n=1444)**
Bread and dried bread products	**12**	**13**
Breakfast cereals	1	1
Pasta	**7**	**8**
Rice and durum or cracked wheat	2	2
Croissant-like pastries	2	3
Sweet and savoury biscuits and bars	**5**	**5**
Pastries and cakes	3	3
Milk	3	3
Ultra-fresh dairy products	2	2
Cheeses	1	1
Eggs and egg products	0	0
Butter	0	0
Oil	0	0
Margarine	0	0
Meat	0	1
Poultry and game	0	0
Offal	0	0
Delicatessen meats	1	1
Fish	1	1
Crustaceans and molluscs	3	2
Vegetables (excluding potatoes)	**10**	**8**
Potatoes and potato products	**13**	**14**
Vegetables	1	1
Fruits	2	2
Dried fruits, nuts and seeds	0	0
Ice creams and frozen desserts	1	1
Chocolate	2	2
Sugars and sugar derivatives	2	2
Water	2	2
Non-alcoholic beverages	1	1
Alcoholic beverages	0	0
Coffee	0	0
Other hot beverages	1	1
Pizzas, quiches and savoury pastries	2	2
Sandwiches and snacks	1	1
Soups and broths	3	3
Mixed dishes	**7**	**7**
Dairy-based desserts	3	3
Compotes and cooked fruit	3	2
Seasonings and sauces	2	2
Dietetic foods	0	0
TOTAL	**100**	**100**

In bold: Major contributors (>5%) for at least one of the 2 population groups

ANNEX 6: Mean consumption and 95th percentile of INCA2 food groups for children exceeding the TWI and general child population (g/day)

Food groups	Children exceeding TWI (n=157)		General child population (n=1287)		*P**
	Mean	P95	Mean	P95	
Bread and dried bread products	58.9	150.0	55.2	149.3	0.43
Breakfast cereals	15.1	51.4	14.1	53.6	0.57
Pasta	41.0	94.3	42.2	114.3	0.68
Rice and durum or cracked wheat	21.0	64.3	23.3	78.6	0.24
Other cereals	0.2	0.0	0.4	0.0	0.08
Croissant-like pastries	15.4	47.1	18.2	65.0	0.08
Sweet and savoury biscuits and bars	22.0	72.6	15.4	50.0	0.004
Pastries and cakes	35.3	98.0	37.8	112.1	0.40
Milk	215.6	500.0	170.5	427.1	0.0015
Ultra-fresh dairy products	85.2	187.9	74.4	201.4	0.07
Cheeses	19.5	58.9	18.7	51.9	0.69
Eggs and egg products	10.6	36.0	10.4	36.3	0.88
Butter	9.2	22.6	7.4	21.3	0.006
Oil	8.5	21.7	6.6	20.9	0.07
Margarine	2.1	10.7	2.5	12.6	0.21
Other fats	0.1	0.0	0.1	0.0	0.87
Meat	33.4	79.3	38.9	96.6	0.04
Poultry and game	16.8	49.3	20.8	62.7	0.01
Offal	0.7	5.7	0.9	7.1	0.32
Delicatessen meats	24.4	62.3	25.2	68.6	0.72
Fish	20.3	52.4	17.9	51.8	0.08
Crustaceans and molluscs	2.5	10.3	1.3	8.6	0.06
Vegetables (excluding potatoes)	88.5	187.4	76.3	183.3	0.02
Potatoes and potato products	53.1	114.3	52.0	125.0	0.72
Vegetables	9.4	40.0	7.8	42.9	0.21
Fruits	76.5	174.6	67.2	199.5	0.12
Dried fruits, nuts and seeds	0.6	4.3	1.2	6.7	0.02
Ice creams and frozen desserts	11.1	47.3	10.6	46.1	0.77
Chocolate	10.7	42.9	12.0	41.7	0.41
Sugars and sugar derivatives	11.5	36.8	9.2	31.4	0.05
Water	456.9	942.9	489.2	1144.3	0.23
Non-alcoholic beverages	165.5	430.0	200.4	568.6	0.02
Alcoholic beverages	2.3	1.7	3.8	14.3	0.33
Coffee	3.1	0.0	10.7	51.4	0.003
Other hot beverages	15.3	51.4	24.9	142.9	0.009
Pizzas, quiches and savoury	**13.7**	**62.9**	**21.3**	**71.4**	**<0.0001**
Sandwiches and snacks	**8.4**	**34.0**	**14.9**	**65.7**	**<0.0001**
Soups and broths	52.1	200.0	39.1	185.7	0.13
Mixed dishes	56.6	146.6	58.7	159.9	0.59
Dairy-based desserts	38.6	121.4	28.2	100.0	0.01
Compotes and cooked fruit	**29.1**	**100.0**	**14.7**	**68.6**	**<0.0001**
Seasonings and sauces	14.4	48.0	12.4	37.1	0.19
Dietetic foods	1.0	0.0	0.4	0.0	0.44

*Result of the Student test, **in bold**: significant test. The risk of Type I error is 0.001 (0.05/43 food groups, adjusted to mitigate errors related to multiple testing).

ANNEX 7: Method chosen for simulating the impacts of MLs on levels of exposure for the French population

Concerning bivalve molluscs and potatoes, since surveys are designed to consider either all or part of the samples, these data are not necessarily representative of foods consumed in France. It is therefore not possible to estimate the real exposure of consumers and therefore the precise impact of simulations on these data. It was therefore assumed that the impact of maximum levels on future mean levels in foods was identical whether based on data taken from surveys or data used in TDS2 to calculate exposure. Exposure of individuals via intake of the foods affected is therefore reduced in the same proportion.

Concerning soft wheat, mainly used as an ingredient (flour, bran, etc.), contamination data were supplied to the Agency by the principal operators in the cereal sector. It was generally found that there was no change in cadmium level in the three types of matrix (flour, bran and grain) between 2000 and 2010. The mean level of cadmium in flour is 73% to 82% of the level in wheat grains, depending on the censorship hypothesis. It may therefore be assumed that the impact on the mean level in flours is equivalent to the impact on the mean level in wheat grains.

Contamination data for durum wheat were also supplied to the Agency by the principal operators in the cereal sector. As for soft wheat, cadmium levels did not change significantly between 2000 and 2010.

For simulation purposes, when applying the effect of changes in ML to TDS2 contamination data, it is necessary to consider the proportions of soft wheat and durum wheat in the different foods sampled and analysed. The composition table drawn up by the Agency[24] was therefore combined with the consumption table used in TDS2, in order to determine the percentage of ingredients based on soft wheat[25] and durum wheat[26] in all the foods taken into account to calculate exposure. It was assumed that the reduction (%) of the mean level in ingredients based on durum wheat was equivalent to the reduction in the mean level of durum wheat following application of a new ML. Equally, for ingredients based on soft wheat, the mean level was reduced by the same factor as that obtained in the mean level in soft wheat after application of a new ML[27].

24 AFSSA. The INCA 2 recipe database –AFSSA Activity Report 2009.
25 The available ingredients (n=16) were as follows: whole wheatflakes, wheat, semi-whole (t110) wheat flour, baked t45 wheat flour, wheat starch, whole wheat, partially germinated (diastase) wheat flour, malted wheat flour, wholemeal flour, wheat flakes, wheat germ, wheat germ oil, wheat glucose syrup, wheat glucose-fructose syrup, wheat plant proteins, wheat bran. Nevertheless, the following ingredients were not considered because of the lack of contamination data or knowledge of how the cadmium is transferred to them from grain: malted wheat flour, wheat germ, wheat germ oil, wheat glucose syrup, wheat glucose-fructose syrup, wheat plant proteins.
26 There were four ingredients available: whole grains of precooked durum wheat, raw semolina, couscous (the grains alone), precooked semolina and precooked pasta. It was assumed that pasta was made up of 100% durum wheat (with no conversion factor from the wheat to flour). Lastly, insofar as these ingredients are consumed cooked, it was considered that the mass of the foods and ingredients consumed cooked (i.e. rehydrated) represented one third of the mass of the dish actually consumed.
27 Except for soft wheat bran, for which the reduction of the level in bran was applied directly.

ANNEX 8: Details of contamination data and conditions of use of these data

Official monitoring programs:

To simulate the impact of different maximum levels (MLs) on population exposure, the most recent data from official monitoring programs were used:

- Data from PSPC DGCCRF 2009 and 2010 (vegetables)
- Data from the DGAI's seafood and molluscs monitoring programs for 2009 and 2010
- Data from the DGAI's monitoring programs under Directive 96/23 (eggs, butcher's meat, game, honey, milk, poultry, farmed fish, rabbit) for 2009 and 2010

In all, 6256 elements of data were available. Few cases of non-compliance were observed. The overall level of censorship of 69% showed the need to perform calculations according to two hypotheses:

- Lower-bound hypothesis which "underestimates" the levels and therefore the exposure: non-detected results are replaced by zero and non-quantified results are replaced by the limit of detection (LOD);
- Upper-bound hypothesis which "overestimates" the levels and therefore the exposure ("conservative" hypothesis): non-detected results are replaced by the LOD and non-quantified results are replaced by the limit of quantification (LOQ).

As some data were lacking (the LODs for 1654 results, the LOQs for 1472 results), protective hypotheses were formulated to use as much of the censored data as possible:

- when the LOD was necessary but unknown, it was considered to be the LOQ/2;
- when no boundaries were known, results "<x" were considered by default to mean "detected but not quantified" with x as the LOQ. The LOD was considered as being equal to LOQ/2.

Surveys by the operators of the cereals sector

Soft wheat:

Data from the *Institut de Recherches Technologiques Agroalimentaires des Céréales* (IRTAC), from France Agrimer and from Arvalis were used to simulate the impact of maximum levels on ingredients and foods based on soft wheat. The data provided by IRTAC include results for 2000 to 2010 on soft wheat in the form of grain (n=1118), flour (n=2861) and bran (n=478). The data provided by France Agrimer and Arvalis include results for 2009 and 2010 on soft wheat grain (n=526).

As for the monitoring programs, some information was missing. For the censored data, if the result is lower than the LOD, only the LOD is given, and if the result is lower than the LOQ, only the LOQ is given. For results lower than the LOQ under the lower-bound hypothesis, LOQ/2 was therefore considered

Durum wheat:

The data from Coop de France and Arvalis were used for durum wheat. The data from Coop de France included 89 results from 2000 to 2009. The data from Arvalis included 397 results from 2009 and 2010.

As for the monitoring programs, some information was lacking. Only four elements of data were censored. For these data, half of the analytical limit supplied was taken into consideration (insofar as it is not specified whether this limit is the LOD or the LOQ).

ANNEX 9: Mean levels (mg/kg) and number of cases of non-compliance (under the lower-bound [LB] and upper-bound [UB] hypotheses) for foods in the following groups, according to data from government surveys: bread and dried products, potatoes and potato products, vegetables, molluscs and crustaceans

Regulated food group	Food	ML	n	Non comp. LB	Non comp UB	LB			UB			TDS2
						Mean	SD	Max	Mean	SD	Max	
3.2.15	aubergine	0.05	7	0	0	0.004	0.003	0.010	0.004	0.003	0.010	-
	cucumber	0.05	3	0	0	0.002	0.002	0.004	0.003	0.001	0.004	0.001
	courgette	0.05	20	0	0	0.002	0.002	0.006	0.003	0.001	0.006	0.001
	bean	0.05	7	0	0	0.002	0.002	0.005	0.003	0.002	0.005	0.004
	dried bean	0.05	10	0	0	0.004	0.003	0.011	0.006	0.004	0.011	0.006
	lentil	0.05	10	0	0	0.004	0.004	0.011	0.008	0.006	0.020	0.012
	maize	0.05	4	0	0	0.005	0.004	0.011	0.006	0.004	0.011	0.002
	pea	0.05	2	0	0	0.001	0.000	0.002	0.003	0.000	0.003	0.005
	sweet pepper	0.05	2	0	0	0.008	0.010	0.015	0.009	0.009	0.015	0.007
	tomato	0.05	10	0	0	0.007	0.009	0.030	0.008	0.008	0.030	0.005
3.2.16	artichoke	0.10	4	0	0	0.016	0.015	0.037	0.016	0.015	0.037	0.006
	asparagus	0.10	1	0	0	0.001	-	0.001	0.002	-	0.002	-
	beetroot	0.10	2	0	0	0.025	0.008	0.031	0.025	0.008	0.031	-
	carrot	0.10	32	0	0	0.018	0.017	0.070	0.018	0.017	0.070	0.014
	celery	0.10	3	0	0	0.013	0.016	0.031	0.014	0.015	0.031	0.028
	turnip	0.10	15	0	0	0.009	0.008	0.024	0.009	0.007	0.024	0.015
	onion	0.10	23	0	0	0.012	0.012	0.050	0.012	0.012	0.050	0.012
	potato	0.10	23	0	0	0.022	0.017	0.069	0.022	0.017	0.069	0.022
	leek	0.10	17	0	0	0.018	0.025	0.082	0.018	0.025	0.082	0.009
	radish	0.10	5	0	0	0.009	0.009	0.023	0.009	0.009	0.023	0.006
3.2.17	broccoli	0.20	4	0	0	0.016	0.022	0.048	0.016	0.022	0.048	-
	button mushroom*	**0.20**	**31**	**1**	**1**	**0.025**	**0.043**	**0.211**	**0.025**	**0.043**	**0.211**	**-**
	cabbage	0.20	17	0	0	0.003	0.004	0.010	0.004	0.003	0.010	0.005
	endive	0.20	1	0	0	0.008	-	0.008	0.008	-	0.008	0.007
	spinach	0.20	3	0	0	0.100	0.063	0.168	0.100	0.063	0.168	0.073
	celeriac	0.20	2	0	0	0.010	0.002	0.011	0.010	0.002	0.011	0.021
	lettuce*	**0.20**	**21**	**2**	**2**	**0.069**	**0.080**	**0.337**	**0.070**	**0.080**	**0.337**	**0.018**
3.2.18	other mushrooms	.	12	.	.	0.172	0.218	0.717	0.172	0.218	0.717	-
bivalves	oyster	1.00	57	0	0	0.182	0.089	0.414	0.182	0.089	0.414	0.146
bivalves	mussel	1.00	138	0	0	0.149	0.171	0.787	0.151	0.170	0.787	0.135
bivalves	scallop	1.00	47	0	0	0.184	0.104	0.390	0.184	0.104	0.390	0.364
wheat	**durum wheat**	**0.20**	**7**	**1**	**1**	**0.082**	**0.062**	**0.210**	**0.082**	**0.062**	**0.210**	**-**
wheat	soft wheat	0.20	14	0	0	0.028	0.010	0.053	0.028	0.010	0.053	-
cephalopods	squid	1.00	11	0	0	0.169	0.203	0.537	0.169	0.203	0.537	-
cephalopods	octopus	1.00	3	0	0	0.005	0.004	0.010	0.010	0.000	0.010	-
cephalopods	cuttlefish	1.00	8	0	0	0.083	0.142	0.420	0.085	0.141	0.420	-
crustaceans	spider crab	0.50	13	0	0	0.121	0.098	0.310	0.121	0.098	0.310	-
crustaceans	**crab**	**0.50**	**29**	**1**	**1**	**0.086**	**0.201**	**0.852**	**0.087**	**0.201**	**0.852**	**-**
crustaceans	**shrimp**	**0.50**	**14**	**1**	**1**	**0.062**	**0.164**	**0.610**	**0.065**	**0.163**	**0.610**	**0.021**
crustaceans	spiny lobster	0.50	10	0	0	0.038	0.026	0.079	0.038	0.025	0.079	-

In bold: food with one or two non-compliant samples
ML: maximum limit (Regulation EC No.1881/2006 of 29 April 2011)
*The food names as given here include several foods (see Regulation EC No.1881/2006)
3.2.15: Fruit and vegetables, excluding leaf vegetables and fresh herbs, leafy brassica, mushrooms, stem vegetables, root and tuber vegetables, and sea weeds

3.2.16: Stem vegetables, root and tuber vegetables, excluding celeriac

3.2.17: Leaf vegetables and fresh herbs, leafy brassica, celeriac and the following mushrooms: *Agaricus bisporus* (button mushroom), *Pleurotus ostreatus* (oyster mushroom), *Lentinula edodes* (Shiitake)

3.2.18: Mushrooms, excluding those listed in Point 3.2.17