Infant Total Diet Study (iTDS)

Report 1

ANSES Opinion
Summary and conclusions

anses

French agency for food, environmental
and occupational health & safety

Investigate, evaluate, protect

Infant Total Diet Study (iTDS)

Report 1

ANSES Opinion
Summary and conclusions

The Director General

Maisons-Alfort, 16 September 2016

OPINION[1]
of the French Agency for Food, Environmental and Occupational Health & Safety

on the dietary exposure of children under three years of age to certain substances

---

ANSES undertakes independent and pluralistic scientific expert assessments.

ANSES's public health mission involves ensuring environmental, occupational and food safety as well as assessing the potential health risks they may entail.

It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with 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.

This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 16 September 2016 shall prevail.

On 17 September 2010, the French Agency for Food, Environmental and Occupational Health & Safety issued an internal request for an opinion on the total diet study concerning dietary exposure of children under three years of age to certain substances.

In addition to the present opinion, the full study report and a summary are also available on the Agency's website.

1. BACKGROUND AND PURPOSE OF THE REQUEST

The foods that are consumed provide many nutrients, but are also a vector for a number of chemical substances (contaminants, food additives, phyto-oestrogens, sex steroids of animal origin, pesticide residues, etc.).

Exposure of the population to these substances through food can raise questions about consumer health: it therefore seems necessary to assess this everyday exposure. In the case of nutrients, it is important to assess the health consequences associated with both insufficient and excessive intakes. For the other substances, the issue mainly concerns assessment of the health risks associated with exposure levels considered to be too high.

Knowledge of the levels of nutrients and these other substances in food therefore constitutes a major tool for protecting health. It helps with documenting dietary exposure to this group of substances. This knowledge on exposure is then used to assess the risks and benefits for the population and to inform decision-making in risk management (control and regulation), at the national, European and international levels.

In France, monitoring of food contamination by substances regularly takes place within a regulatory framework through control and surveillance plans, led by the competent ministries. However, the resulting

---

[1] Cancels and replaces the Opinion of 30 August 2016. The changes made to the previous version are listed in the annex at the end of this opinion.

contamination data are not suited for accurately estimating the exposure or intake levels of the French population (restricted sampling, agricultural foodstuffs and raw products not prepared, limited coverage of the total diet, no measurement of nutrients, etc.).

"Total Diet Studies" (TDSs) are cross-cutting national surveys designed to estimate the exposure to chemical compounds by ingestion, in order to respond to the needs for knowledge mentioned previously. They include in particular the analysis of a large number of substances in food samples that reflect the diet of the population under study. To achieve this, they rely on national food consumption surveys. TDSs make it possible to identify the substances for which there is a risk of inadequate intake (for minerals) and/or excessive exposure (for minerals and contaminants) in the population, as well as the foods contributing most to this intake or exposure. In France, two total diet studies have been conducted (TDS1[2] and TDS2[3]), targeting adults and children over three years of age.

This Opinion relates to the infant total diet study (iTDS), which is one of the first studies anywhere in the world to estimate the dietary exposure of children under three years of age (non-breastfed) to 670 substances (mainly environmental contaminants, minerals and plant protection products), in mainland France. Indeed, the population of children under three years of age has two specific characteristics that justify this study: they are more vulnerable individuals (possible impact of certain substances on the stages of development, more unfavourable "consumption/body weight" ratio than for adults), and they consume specific food products (foods intended for infants and young children) for which there are very few contamination data available (in particular on contaminants).

2. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French Standard NF X 50-110 "Quality in Expert Appraisals – General Requirements of Competence for Expert Appraisals (May 2003)". Implementation of the study (methodology, sampling and analysis) was coordinated in-house by the Methodology and Studies Unit (MSU) and the Phytopharmacovigilance and Observatory of Pesticide Residues Unit (POU) of the Risk Assessment Department. These units also generated the exposure data on the basis of data on concentrations in foods and food consumption.

The collective expert appraisal was carried out using analyses conducted in-house by the Expert Committees (CESs) on "Assessment of the risks associated with human nutrition", "Water", "Assessment of plant protection products" and "Assessment of the physical and chemical risks in foods" (CES ERCA) in their respective spheres of competence, and by the Working Groups (WGs) on "Assessment of substances and processes subject to authorisation in human food", "Analytical methods in food" and "iTDS total diet study", on the basis of the work carried out by rapporteurs from all of these expert groups.

The various elements of this opinion were validated by the CES ERCA at several meetings between 29 November 2012 and 25 March 2016, the date of validation of the final version of the Opinion.

ANSES analyses the links of interest declared by the experts prior to their appointment and throughout the work, in order to avoid potential conflicts of interest with regard to the matters dealt with as part of the expert appraisal.

The experts' declarations of interests are made public via the ANSES website (www.anses.fr).

3. ANALYSIS AND CONCLUSIONS OF THE EXPERT COMMITTEES

3.1. Methodology of the study

3.1.1. Selection of the substances

The infant total diet study (iTDS) was established to follow on from the second total diet study (TDS2), and therefore all the groups of substances considered in the TDS2 were analysed here: metal and mineral trace elements, polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/Fs), polychlorinated biphenyls (PCBs), perfluoroalkyl acids (PFAAs), brominated flame retardants, mycotoxins, phyto-oestrogens, heat-induced compounds, pesticide residues and food additives.

---

[2] Leblanc JC, coordinator (2004). French Total Diet Study - Mycotoxins, minerals and trace elements.

[3] ANSES (2011). Second French Total Diet Study (TDS2) - Volume 1: Inorganic contaminants, minerals, persistent organic pollutants, mycotoxins and phyto-oestrogens. Expert appraisal report: Scientific Editions. Maisons-Alfort, ANSES: 305
ANSES (2011). Second French Total Diet Study (TDS2) - Volume 2: Pesticide residues, additives, acrylamide, polycyclic aromatic hydrocarbons. Expert appraisal report. Scientific Editions. Maisons-Alfort, ANSES: 405

Other substances that were not screened for in the TDS2 were included because of questions (by the authorities or ANSES, for example), of a general nature or specific to the population considered, being raised about the health risk in a context where there are few French data on food contamination for these substances. This concerns in particular furan, sex steroids of animal origin or substances migrating from food contact materials (FCMs) such as certain bisphenols (bisphenol A - BPA and bisphenol A diglycidyl ether - BADGE), phthalates, ink photoinitiators and alkylphenols.

In total, concentration data were obtained for 670 substances, and dietary exposure was assessed for 500 of them. The complete list of substances is available in the study report.

3.1.2. Consumption data

The latest French food consumption data for children under three years of age available at the time of implementation of the sampling plan were used. These were data from the "BEBE-SFAE" 2005 study, carried out by TNS-Sofres-CHU Dijon for the French Association for Children's Food (SFAE) (Fantino and Gourmet 2008). This cross-sectional survey was conducted between January and March 2005, with a representative national sample of infants and young children in mainland France, non-breastfed (even partially) at the time of the study.

For each child, the care-givers (most often the mother and/or the nanny, with the participation of the father) were asked to note all food consumption using a food diary over three consecutive days, including a weekend day. The portion sizes of each food consumed were noted as well as the body weight of each child.

A total of 705 children took part in the study. In order to take into account the possible differences in diet between 1 and 36 months, the study population was divided into four age groups. These groups were defined on the basis of the stages of food diversification (Table 1).

Table 1: Breakdown by age group corresponding to the different stages of food diversification

Age groups	Introduction of foods*
1-4 months	First infant formulas[4]
5-6 months	Follow-on formulas
7-12 months	+ dairy products, fruits, vegetables, potatoes, meat, fish, hard-boiled eggs, added fat
13-36 months	+ growing-up milk, fruit and vegetables in pieces, pulses, salt

*Extract from the companion booklet to the Nutrition Guide for children and teenagers intended for health professionals (PNNS 2004).

3.1.3. Choice, collection and preparation of the foods studied

In order to better reflect reality, the selection of foods to be sampled and their preparation were based on data on consumption, purchase and preparation practices. The foods consumed most often (in terms of quantity and/or percentage of consumers) or identified as major contributors (known or assumed) for at least one of the targeted substances, were selected. Given the study population, brand loyalty for infant foods and water was taken into account when setting up the sampling plan. The products purchased were prepared "as consumed" in order to reflect practices in homes: preparation (removal of the non-edible part, washing of foods, etc.) and cooking (duration and power, addition or not of salt, fat, etc.). The infant formulas were diluted and heated most of the time, prepared baby dishes were reheated, vegetables (excluding raw vegetables), meat and fish were cooked according to the practices reported in the survey set up in 2011 to determine the preparation methods for normal foods employed by parents of children under three years of age (Hulin et al. 2014).

In total, the sampling plan was made up of 457 composite food samples, each made up of 12 sub-samples purchased and prepared every month for one year (one sub-sample per month). This corresponds to 5,484 food products (sub-samples).

---

[4] This name commonly refers to industrial formulas intended specifically for young children. Their regulatory designation is "formula" and not "milk". Indeed, while the majority of these foods are manufactured from constituents of cow milk, certain formulas are made from other products (for example, soy). But regardless of their designation, they are all foods specifically designed for a healthy full-term child, from birth to the age of three years (Source: INPES, Nutrition Guide from birth to three years).

The sampling phase took place between July 2011 and July 2012 in one region of France (the Centre region). The sampling plan (and the use of other sources of data) was able to cover more than 97% of the diet of children under 36 months of age.

3.1.4. Analysis of samples and assessment of intake and exposure

The analyses were carried out by around ten accredited laboratories (mainly national reference laboratories and including ANSES's Laboratory for Food Safety and Nancy Hydrology Laboratory) employing validated methods. For each of the substances, the laboratories were asked to achieve analytical limits that were as low as possible, in order to conduct a risk assessment. In particular, for pesticide residues, the analytical performances were increased: the limits of detection were two to 10 times lower than those used in the TDS2, or in the most recent surveillance programmes. These improvements helped reduce the uncertainty associated with the exposure assessment and obtain more realistic results.

Exposure to substances (relative to body weight) was calculated individually for each of the children in the consumption study, taking into consideration the food packaging type and, for the water, the regional concentrations and the type (and brand) if bottled water was used to reconstitute the products to be diluted.

The share (%) of intake or exposure attributable to each category of food was then calculated in order to identify the major contributors[5] to this intake or exposure.

3.1.5. Assessment of the toxicological risks

In order to characterise the risks to the infant population, the calculated exposures were compared with reference values (referred to as "TRVs" in this study).

As the infant population was specifically targeted in this study, the experts determined whether the selected TRVs could be applied to this population, mainly by confirming that toxicological data specific to the infant population (perinatal and postnatal toxicity studies, developmental toxicity studies, reproduction studies over several generations, etc.) had been taken into account when establishing each of these TRVs.

Thus, depending on the substance considered, four groups of TRVs were defined, and the health risk assessment (HRA) was conducted bearing in mind the limitations to the applicability to the infant population of the selected TRVs (Table 2).

Table 2: Toxicological risk assessment approach according to the relevance of the selected values

Categories of TRV according to their robustness	HRA process
Absence of a TRV or TRV not deemed to be robust for the adult population	No HRA
Robust TRV for the adult population but no evidence relating to its applicability to the infant population	HRA, but uncertainty taken into account in the interpretation of the results*
TRV applied to the infant population because reprotoxicity/ developmental or multigenerational studies had been taken into account, but in the absence of a comprehensive expert appraisal of the toxicological data, following a specific analysis by the rapporteurs	HRA
Protective TRV for the infant population	

* If no excessive exposure was observed for the population under three years of age but the estimated exposure was close to the selected TRV, it was considered that the health risk could not be ruled out with certainty. Exposure is considered to be close to a reference value when the ratio between the two is less than a factor of 10.

For substances with a "threshold" TRV (acceptable or tolerable daily intake - ADI or TDI, (provisional) tolerable weekly intake - (P)TWI, or (provisional) tolerable monthly intake - (P)TMI, etc.), individual exposures were compared directly to the TRVs. For each age group, the percentage of individuals in the

---

[5] In the present study, the major contributors are those contributing more than 10% to total exposure.

study whose exposure was above the TRV was calculated, accompanied by its confidence interval at 95%. When this excessive exposure concerned fewer than five children, it was indicated that the limits had been exceeded, but that it was difficult to estimate the proportion in light of limitations related to the sampling or to the measurement of exposure (excessive exposure regarded as "not representative").

In the case of substances characterised by a "benchmark dose limit" or BMDL ("threshold" or "non-threshold" substance), the risk was characterised by calculating respectively a margin of safety (MOS) or a margin of exposure (MOE).

On the basis of these results, and therefore depending on the robustness of the TRV and its applicability to the infant population, characterisation of the risk for all the substances studied was summarised into four categories (Table 3).

Table 3: Conclusions reached according to characterisation of the toxicological risk

Results	Status in light of the risk
TRV exceeded significantly or low margin of exposure	**Situation identified as a concern**
Limits not exceeded significantly or robustly or TRV exceeded significantly and robustly under the high assumption (UB) only, i.e. the scenario that overestimates levels and therefore exposure or Limits not exceeded with a robust TRV only for the adult population but exposure close	**Risk cannot be ruled out**
TRV not exceeded or margin of exposure sufficiently high (proposed for each substance)	**Risk considered tolerable* or acceptable***
Conditions make it impossible to conduct a relevant HRA: for example, toxicological point of departure not established due to a lack of data or not considered sufficiently robust	**Impossible to reach a conclusion as to the risk**

* The term "tolerable" is used for substances found unintentionally in foods (for example, persistent organic pollutants or mycotoxins). A TRV such as a tolerable daily/weekly/monthly intake (TDI, TWI, TMI, etc.) is then used. The term "acceptable" is used to characterise the risk in the case of substances whose use is subject to a prior assessment (for example, additives or pesticide residues). A TRV such as an acceptable daily intake (ADI) is then used.

3.1.6. Assessment of the nutritional risks

The nutritional references for minerals for children under three years of age were updated for this study on the basis of data and nutritional references from different European (European Food Safety Authority - EFSA), North American (Institute of Medicine - IOM) and international (World Health Organisation - WHO) organisations.

Concerning the population of infants under six months of age, the adequate intakes (AIs) presented by EFSA in 2013 (EFSA 2013b) and regarded by ANSES as adequate intakes (AS - *apports satisfaisants*) or, where they were lacking, other intakes regarded by EFSA as adequate, were used. The AS corresponds to the mean intake level observed or estimated for a group of individuals in apparent good health and regarded as satisfactory.

Concerning children over six months of age, the nutritional reference selected was the AS or the average requirement (AR) updated by EFSA from 2013. The AR corresponds to the average daily nutritional intake able to cover the needs of the mean of the healthy individuals in a population group of a given age and sex (Touvier et al. 2006).

Regarding the tolerable upper intake levels (ULs) for minerals, the values proposed by EFSA in 2006 were used. When EFSA was unable to establish ULs, due to a lack of data, the values proposed by the IOM (IOM 2001, 2011) were taken into consideration. All these ULs were either established from studies on the infant

population, or determined by extrapolation of the ULs established for the adult population, on the basis of body weight, when relevant.

Concerning the assessment of the risk of excessive intake for minerals, the percentage of children whose intakes were higher than the selected UL was calculated, as well as its confidence interval at 95%.

Concerning the assessment of the risk of insufficient intake, for minerals for which the AR had been determined, inadequate intake was calculated on the basis of the AR cut-off point method (de Lauzon, Volatier, and Martin 2004) by calculating the proportion of children whose intakes were lower than the AR[6] with its confidence interval at 95%. The approach described by EFSA in 2010 was followed (EFSA 2010) for minerals for which only an AS (adequate intake, or other intakes regarded as adequate) had been established. In these cases, the mean intakes were compared directly to the AS in order to appraise the situation (Table 4).

On the basis of the results, and according to the nutritional references adopted, the degree to which intakes meet needs was summarised into four categories (Table 4).

Table 4: Conclusions reached according to characterisation of the risk of insufficient nutrient intake in minerals

Results	Risk phrase
Mean intake of the population above the AS or intake above the AR for the whole of the population considered	**Intakes meet needs at a generally satisfactory level**
Intake below the AR for a significant number of individuals	**Risk of insufficient intake for some groups of consumers**
Mean intake of the population below the AS	**Impossible to know whether needs are met and to what extent**
No nutritional reference selected for the age group considered, or nutritional reference deemed not to be robust	**No conclusion possible regarding inadequate intake**

3.1.7. Study limitations and uncertainties

Study limitations

The study's limitations are above all inherent to its scope.

As the population of breastfed children was excluded from the consumption study, it was not taken into account for the exposure calculations. Similarly, preterm children and children living outside mainland France (Corsica, the overseas territories) were not included in the consumption study.

The iTDS did not set out to assess acute exposure to a substance at a given time, nor exposure resulting from specific situations such as contamination of food by the local environment (polluted sites, for example), the occasional consumption of food supplements, specific and systematic cooking/preparation methods or practices for a given individual (use of a kettle to heat the water for baby bottles, heating of jars of baby food in stainless-steel or non-stick pans, etc.) or specific diets (exclusively "organic" food, for example). The study does however generally reflect the diversity of food preparation practices as indicated in 3.1.3.

This study mainly targeted substances for which earlier work (toxicological and/or health risk assessments) had suggested a potential risk. However, there are other contaminants for which the hazard has only been poorly characterised, or not at all.

This study does not include routes of exposure other than food.

For certain substances that can accumulate in the body (persistent organic pollutants - POPs, etc.), exposure during foetal life, via maternal exposure, can lead to a non-negligible body burden for the child at birth. This prenatal exposure was not taken into account in the present study.

Lastly, "cocktail" effects or the potential cumulative effects of different substances were only taken into account for certain mixtures of substances belonging to the same chemical class and for which TRVs were selected by the expert committees (this is the case with dioxins and furans, for example).

---

[6] This proportion, usually called "prevalence of inadequate intake", will be referred to in this document as "prevalence of insufficient intake", in order to clearly distinguish cases of excess and insufficient intake.

Study uncertainties

The uncertainties listed in Table 5[7] below may be present at the different steps of the risk assessment and have an impact on the result of the risk assessments conducted in this study. They may lead to the risks being overestimated or underestimated, without it always being possible to correct this impact. Where applicable, methodological tools have been used to limit the impact of these uncertainties, always with a view to improving protection.

Table 5: Sources of uncertainty noted in the iTDS

Sources of uncertainty
Reference values and risk assessment
Validity of the reference value and the available data
Applicability over the period 0-3 years: - From the point of view of the hazard   - From the point of view of the comparison with the exposure data (versus lifelong)
Assessment of the hazard associated with several substances ("cocktail" effect), congeners or metabolites
Consumption data and sampling plan
Information not collected in the consumption study
Representativeness of the consumption data
Only taking into account major practices or consumer profiles
Collection of samples and composition and contamination data
Representativeness of the composition and contamination data
Robustness of the data
Use of contamination data for exposure calculations

The sources of uncertainty were identified and analysed using a qualitative approach, to determine the direction of the impact of each source of uncertainty on the risk estimate. However, it was not possible to reach a conclusion as to the overall impact of these uncertainties on the risk estimate. In most cases, it may underestimate or overestimate the risk. In light of this analysis, the uncertainties that may have a major impact in terms of underestimating the risk are probably those related to the nutritional and toxicity reference values and specifically in connection with the period examined in this study (applicability of values to children aged 0-3 years in terms of susceptibility and exposure) and the failure to take into account the potential cumulative effects of different substances in the health risk assessment. To obtain a more precise estimate of the impact of these uncertainties, their amplitude should be analysed and characterised for each of the substances considered.

Concerning the question of the applicability of the reference values to the population under three years of age, two uncertainties remain:

1. The infant population may have particular susceptibility to certain substances. A specific process was therefore set up to decide on the relevance of the reference values, usually defined for the general population, in light of the specificities of the infant population (see the toxicological HRA process).
   For some substances, it was not possible to demonstrate the applicability of the selected TRV to the infant population. In this case and where the TRV was not exceeded, the risk may be underestimated. Accordingly:
   - the health risk was not ruled out when exposure was considered to be too close to this value[8];
   - an additional literature review is needed to determine the extent to which a new reference value should be defined for the infant population and a new risk assessment conducted.

2. There may also be uncertainties according to the mechanism of action (particularly for substances that accumulate in the body) due to the comparison of TRVs, which are normally established for "lifelong" exposure, with a duration of exposure that is limited in time (here, less than three years).

---

[7] Details of the uncertainties are presented in the study report.
[8] Exposure is considered to be close to a reference value when the ratio between the two is less than a factor of 10.

Despite this uncertainty, it was considered that cases where the TRV was exceeded nonetheless made it possible to identify substances that could present a potential risk.

Regarding the cumulative effects, certain substances share the same mechanism of action and can have a synergistic or additive action. It was possible to take this into account for certain classes of substances, such as the class of PCBs, or for a parent substance and its metabolites (in the case of certain pesticides, for example). Thus, within the same class of substances, toxic equivalency factors were taken into account to express the toxic potential of the congeners or metabolites compared to the reference substance, according to the principle of additivity of effects. These phenomena may also exist for other substances, but were not taken into account because of the lack of scientific data. The risk calculated substance by substance may therefore underestimate the actual risk of cumulative effects.

3.2. General observations on the contaminants

3.2.1. Change in exposure levels by age groups from 0 to 3 years

The analysis of the exposure data shows differences in exposure between the age groups. Thus, depending on the substances considered, there was an increase (in the case of PCBs, for example) or a decline (in the case of PBDEs, for example) in the exposure levels observed between 1 and 36 months. Two phenomena can explain the differences in exposure observed:
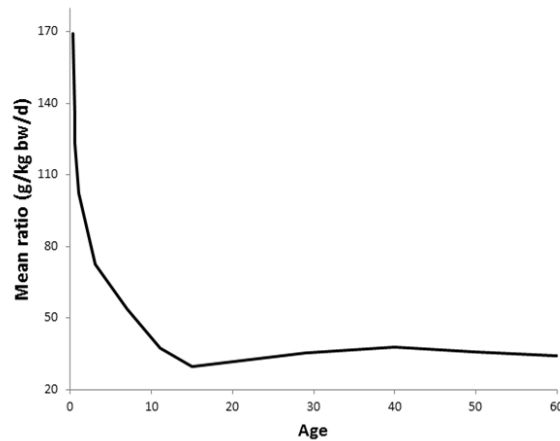
- The change in the "total quantity of food consumed to body weight of individuals" ratio, which seems to be the main parameter explaining the decline in the exposure levels of children aged 1 to 36 months.
- Food diversification, whose effects on exposure levels could on the other hand explain the increase in the levels of exposure of children aged 1 to 36 months.

The "total quantity of food consumed to body weight of children" ratio decreased sharply between the age of 1 and 36 months (Figure 1). This can be explained by a larger increase in the body weight of individuals with age in relation to the quantity of food consumed. It should be noted that the share of water in the quantity of food consumed fell from 80% in children aged 1-4 months to 20% in those aged 13-36 months.
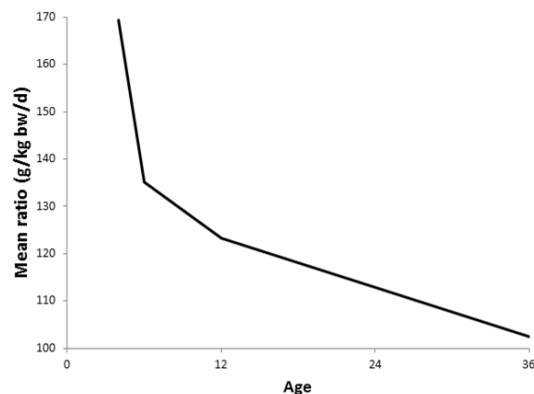
Figure 1: Change in the "total quantity of food consumed to body weight" ratio from birth to 36 months (from BEBE-SFAE data)

In general, the "total quantity of food consumed to body weight" ratio is higher in children under six years of age (between 60 and 170) than in adults (between 20 and 40, Figure 2). In adulthood, this ratio remains relatively stable. In short, children consume greater quantities of food in proportion to their body weight. This largely explains why, in the framework of the TDS2, the exposure levels calculated in children aged 3 to 17 years were higher than those of adults.

Figure 2: Change in the "total quantity of food consumed to body weight" ratio from birth to 60 years (from INCA2 and BEBE-SFAE data)

However, for the majority of substances, despite the decrease in the "total quantity of food consumed to body weight" ratio, the exposure levels increased between 1 and 36 months. The gradual introduction of a food or food group that is more contaminated than the infant formulas largely explains this upward trend. For example, the introduction of normal milk and ultra-fresh dairy products in the diet is reflected by higher levels of exposure to PCDD/Fs in children aged 13-36 months than in children under one year of age, for whom the majority contributors are infant formulas.

The National Health and Nutrition Programme (PNNS 2004) recommends beginning food diversification ideally from the age of six months and never before four months of age. Thus, between the age of 4 and 6 months, the vast majority of children begin to receive a varied diet. Accordingly, the number of categories of foods consumed by individuals increases until the age of six years (Figure 3). The consequence of this diversification of the diet is to expose individuals to different sources of contaminants while they are growing.
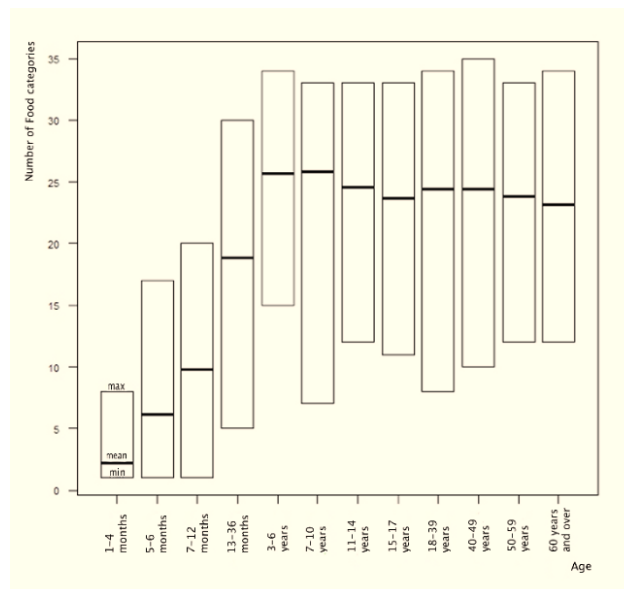
Figure 3: Change in the number of food categories consumed from birth to the age of 60 years and over

In general, it appears that food diversification largely explains the increases in exposure observed between the various age groups of the iTDS. On the other hand, the "total quantity of food consumed to body weight"

ratio appears as the main factor explaining the decline in exposure levels observed between children over three years of age and adults.

3.2.2. Changes in exposure between the iTDS and the TDS2

For each substance, the exposure of individuals aged 13 to 36 months (from the iTDS) was compared to that of children aged 3 to 6 years (from the TDS2) in order to verify the coherence between the results of these two contiguous age groups. As a general rule, this coherence was verified, even though the exposure of children aged 3 to 6 years was, overall, considerably higher on average than that of children aged 13 to 36 months. This can be explained by the methodological differences between the iTDS and the TDS2 (performance of the analytical methods, number of normal foods analysed, period of the sampling campaigns, different food consumption survey methods, etc.). In some more unusual cases, the differences were very marked; explanations have been proposed, on a case-by-case basis, in the corresponding sheets of the report (this was the case with deoxynivalenol – DON, and its derivatives, for example).

3.2.3. General observations relating to food containers

Although the protocol of the iTDS was not designed specifically with this in mind, an effort was made, to the extent possible, to determine whether differences could be found in contamination by substances derived from migration from FCMs, according to the type of packaging in which the foods were contained.

For alkylphenols (nonylphenols and *4-tert*-octylphenol) and ink photoinitiators, no specific difference in contamination was observed according to the type of packaging.

On the other hand, for BPA, as previously observed (Bemrah et al. 2014), the highest concentrations were measured in normal foods, especially canned foods. At the date of the study, these canned foods were the main contributors to dietary exposure to BPA.

Lastly, for phthalates, because of the low detection rates, it was difficult to highlight a significant difference in concentration according to the type of packaging. Higher detection rates were however observed for prepared baby dishes (dishes of vegetables, or dishes of vegetables with meat or vegetables with fish) packaged in plastic plates or bowls, compared to those packaged in glass jars (for BBP), as well as for infant cereals presented in individual packaging (sachets) compared to those in cardboard packaging (for BBP and DEHP). For DEHP, significantly higher concentrations were found in dishes of vegetables with meat or vegetables with fish packaged in plastic plates or bowls, compared to those packaged in glass jars. Higher concentrations were also observed in cereals presented in individual packaging (sachets) compared to those in cardboard packaging, although this difference was not statistically significant.

3.3. Summarised results of the risk assessments

The summarised results of the risk assessments are shown in Tables 6 and 7. The detailed results are available in the study report as well as in the summary of this report.

3.3.1. Results regarding the toxicological risk

The results of the toxicological risk assessment are shown in Table 6.

Table 6: Summarised results of the HRAs for contaminants, food additives and pesticide residues

	Situation identified as a concern	Risk cannot be ruled out	Risk considered tolerable or acceptable	Impossible to reach a conclusion as to the risk
Metal and mineral trace elements	Lead**, inorganic arsenic**, nickel	Aluminium, methylmercury**, strontium, chromium VI, selenium (> 1 year), cobalt, barium, cadmium**, copper (> 1 year)	Chromium III, inorganic mercury, antimony	Germanium, copper (< 1 year), selenium (< 1 year), silver, organic arsenic, tin**, gallium, tellurium, vanadium
Persistent organic	Dioxins and furans**, polychlorinated		Polybrominated diphenyl ethers (7 congeners), PBDE-	Perfluoroalkyl acids (other than PFOS and

	Situation identified as a concern	Risk cannot be ruled out	Risk considered tolerable or acceptable	Impossible to reach a conclusion as to the risk
pollutants	biphenyls**		209, polybrominated biphenyls, hexabromocyclododecane, perfluorooctanesulfonic acid, perfluorooctanoic acid, tetrabromobisphenol A	PFOA)
Heat-induced compounds	Acrylamide, furan		Polycyclic aromatic hydrocarbons**	
Mycotoxins	T-2/HT-2 toxins**, deoxynivalenol** and its derivatives	Ochratoxin A**, aflatoxins**	Nivalenol, patulin**, fumonisins**, zearalenone**	*Alternaria* toxins
Substances derived from migration from food contact materials		Bisphenol A	Benzophenone, 4-methylbenzophenone (4-MBP), nonylphenols, BADGE and hydrolysis products, DEHP, DnBP, DIDP & DiNP, BBP	*4-tert*-octylphenol, 4-hydroxybenzophenone (4-BPH), 4-benzoylbiphenyl (PBZ), 2-isopropylthioxanthone (ITX), chlorohydrin derivatives of BADGE, DiBP, DEP, DCHP, DnOP
Phyto-oestrogens and sex steroids of animal origin		Genistein (in consumers of soy-based products)	Genistein (in non-consumers of soy-based products)	17β-testosterone & 5α-dihydrotestosterone, 17α & 17β-oestradiol, oestrone, progesterone and other sex steroids of animal origin. Other isoflavones (daidzein and related compounds, and glycitein), enterolignans (secoisolariciresinol, matairesinol and enterodiol), coumestrol
Additives		Phosphoric acid (E338) & orthophosphate**, ascorbyl palmitate (E304)**		Tartaric acid (E334) and its salts**
Pesticide residues		Dieldrin (including aldrin)*, Lindane (HCH-gamma)*, Propylene thiourea (a metabolite of propineb, a fungicide approved under Regulation (EC) No 1107/2009)	278 pesticide residues**	Among the pesticides that are a priority from a toxicological point of view and/or were detected at least once in the iTDS: Biphenyl (NA), Chlorantraniliprole (A), Chlorpropham (A), Chlorothalonil (A), Dodine (A), Fenpropimorph (A), Fenuron (NA), Flucythrinate (NA), Flusilazole (A), Metolcarb (NA), Oxyfluorfen (A), Propargite (NA), Pyridaben (A), Tepraloxidim (A), Tolfenpyrad (NA), Tricyclazole (ongoing), Triflumizole (A)

	Situation identified as a concern	Risk cannot be ruled out	Risk considered tolerable or acceptable	Impossible to reach a conclusion as to the risk

Status according to Regulation (EC) No 1107/2009[9]: A (approved), NA (not approved) or assessment ongoing
*: POP listed in the Stockholm Convention (environmental contaminant)
**: Substances (or specific congener of a class of substances) that are subject to regulation (excluding water).

3.3.2. Results regarding the nutritional risk

Twelve minerals were analysed in the context of the iTDS. The results of this study show that intakes meet needs to a satisfactory level overall for children under three years of age.
This is the case for iron and zinc in children under six months, for magnesium, calcium and copper in those under one year, and lastly for manganese, selenium, molybdenum and potassium in children under three years of age.
However, there were insufficient intakes of zinc (37% for children aged from 7 months to 3 years), calcium (14%) in children aged 13-36 months, and iron in children aged 7-36 months (48% in those aged 7-12 months and 81% in those aged 13-36 months). For magnesium and copper in children aged 13-36 months, intakes were below the adequate intake, i.e. the observed mean intake for a group of individuals in apparent good health. Given the nature of this nutritional reference, the health risk associated with an insufficient intake cannot be assessed.
As no nutritional reference has been adopted for chromium, lithium or sodium, the prevalence of inadequate intake could not be calculated. The experts deemed that the health risk associated with an insufficient intake of these elements could not be assessed for children under three years of age.

Concerning excessive intakes, the tolerable upper intake levels (UL) set for molybdenum in children aged 1-3 years and for calcium in children aged 7-36 months were not exceeded. The risk associated with excessive intake can therefore be ruled out for these age groups.

On the other hand, the ULs were observed to have been exceeded for calcium in children under six months of age, and for manganese, selenium and copper in children aged one to three years. It is, however, difficult to estimate the proportion of the population exposed to these excessive limits given the limitations related to the sampling or the measurement of exposure. Concerning calcium, all the children in whom the UL was exceeded had consumed semi-skimmed milk during the three days of the survey, and in greater quantities than the mean consumption. Moreover, milk is higher in calcium than infant formulas; this consumption therefore explains these excessive levels. Lastly, for zinc, the limits were observed to have been exceeded in all age groups (up to 75% of children under the age of six months). A risk related to the excessive intake of these minerals cannot therefore be ruled out for certain groups of consumers.

For iron, potassium, sodium, lithium and magnesium, in the absence of any ULs, it is impossible to reach a conclusion as to a possible excessive intake for children under three years of age. Similarly, for manganese, molybdenum, selenium and copper, in the absence of any ULs for children under one year of age, it is impossible to reach a conclusion as to a possible excessive intake.

---

[9] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC.

Table 7: Summarised results of the nutritional risk assessments

Conclusions relating to coverage of nutritional needs		
Intakes meet needs	Intakes insufficient	Impossible to conclude
Iron (< 6 months), zinc (< 6 months), magnesium (< 1 year), calcium (< 1 year), copper (< 1 year), manganese, selenium, molybdenum, potassium	Zinc (between 7 months and 3 years), calcium (between 1 and 3 years), iron (between 7 months and 3 years)	Magnesium (between 1 and 3 years)[a], copper (between 1 and 3 years)[a], chromium[b], lithium[b], sodium[b]
Conclusions relating to the tolerable upper intake levels		
Limits not exceeded	Limits exceeded	Impossible to conclude[c]
Molybdenum (between 1 and 3 years), calcium (between 7 months and 3 years)	Calcium (< 6 months), manganese (between 1 and 3 years), selenium (between 1 and 3 years), copper (between 1 and 3 years), zinc	Iron, potassium, sodium, lithium, magnesium, manganese (< 1 year), molybdenum (< 1 year), selenium (< 1 year), copper (< 1 year)

[a]: Intakes in these minerals lower than the adequate intake
[b]: Lack of nutritional reference for these minerals
[c]: Lack of tolerable upper intake level for these minerals

3.4. Risk associated with the consumption of normal milk before the age of 1 year

In this study, 14% of children under one year of age consumed normal milk[10], with almost half of them consuming it exclusively. This is contrary to the recommendations of the National Health and Nutrition Programme (PNNS 2004), which particularly advises against the consumption of cow's milk before the age of one year because it is unsuited to nutritional needs and may cause digestive disorders.

Apart from the nutritional considerations, this exclusive consumption of normal milk instead of infant formulas[11] led to the observation of significantly higher exposure levels, in particular for contaminants vectored by dairy products. For example, in children consuming exclusively normal milk, total exposure to PCDD/Fs was two to three times higher than that of children only consuming infant formulas (see Table 8). Similarly, for PCBs, a marked difference in total exposure was also observed. Children consuming exclusively normal milk had exposure levels two to six times higher than those only consuming infant formulas.

---

[10] In the present study, the milk referred to as "normal" is considered to be cow's milk.
[11] These are first infant formulas, follow-on formula and growing-up milk.

Table 8: Total exposure of children under one year to PCDD/Fs and PCBs depending on the type of "milk" consumed

Age group	Type of "milk" consumed	N (%)	Total exposure to PCDD/Fs ($pg_{TEQ\ WHO05}$.kg bw^{-1}.d^{-1})	Total exposure to PCBs (ng.kg bw^{-1}.d^{-1})
1-4 months	Normal milk	3 (2.4%)	0.74	6.16
	Infant formulas	121 (97.6%)	0.20	0.72
5-6 months	Normal milk	11 (8.7%)	0.43*	3.45*
	Normal milk and infant formulas	9 (7.1%)	0.29*	1.77*
	Infant formulas	107 (84.2%)	0.21	1.14
7 to 12 months	Normal milk	22 (11.3%)	0.46*	3.87*
	Normal milk and infant formulas	17 (8.7%)	0.31*	2.37
	Infant formulas	156 (80%)	0.25	1.98

*: $p < 0.05$ Mean comparison between exposure via infant formulas and the other two types of milk consumed (Student's t test). Given the small number of individuals, no statistical comparison was performed between infant formulas and normal milk for the 1-4 month age group.

Following the recommendations made in the framework of the PNNS, which consist in not consuming normal milk (exclusively or partly) before the age of one year, would significantly limit the exposure of children to PCDD/Fs and PCBs.

3.5. Recommendations

The iTDS made it possible to adequately assess the levels of dietary exposure of children under three years of age to 500 substances (including 314 pesticide residues). The risk was characterised for 400 of them[12] (including 281 pesticide residues) and, where appropriate, recommendations were made. Three possible levels of intervention seem possible.

3.5.1. Need to reduce exposure

The risk assessments led to substances being identified for which the exposure levels of a significant number of children exceed the reference values adopted.

- For nine substances or classes of substances (inorganic arsenic, lead, nickel, PCDD/Fs, PCBs, DON, T-2 & HT-2, acrylamide and furan), the degree to which the limits were exceeded were quantified, without there being any major source of uncertainty. This situation was therefore identified as a concern for these nine substances or classes of substances. It should be recalled that for six of these substances, in the framework of the TDS2, the risk for the general public could not be ruled out: inorganic arsenic, lead, PCDD/Fs, PCBs, DON and acrylamide.

- For seven other substances (aluminium, cobalt, strontium, methylmercury, cadmium, genistein and selenium) it was not possible to precisely estimate the proportion of individuals in a risk situation, due to limitations of the study associated with the measurement of exposure. It was therefore not possible to rule out the risk. It should be recalled that for three of these substances, in the framework of the TDS2, the risk for the general population could not be ruled out: methylmercury, cadmium and aluminium.

---

[12] Corresponding to 330 substances or classes of substances.

These situations are not systematically synonymous with the occurrence of adverse effects, but do indicate a health concern. The establishment or strengthening of management measures aimed at limiting levels of exposure to these substances are therefore both desirable and necessary.

In order to decrease the levels of consumer exposure, in most cases the levels of contamination of the main contributing foods should be lowered (policy to control releases into the environment, control of processes, establishment or reduction of regulatory thresholds). When it is difficult to reduce the contamination levels, reducing consumer exposure by other management measures should be considered, for example specific consumption recommendations (Table 9).

Priority reductions of exposure

The CES considers that the management measures aiming to reduce exposure levels to the substances or classes of substances for which the situation was identified as a concern (inorganic arsenic, lead, nickel, PCDD/Fs, PCBs, DON, T-2 & HT-2, acrylamide and furan) should each be considered with the same level of priority.

High co-exposure to substances of concern

A preliminary study conducted only on the substances identified as a concern and with a TRV (acrylamide, DON, T-2 & HT-2, dioxins, PCBs and nickel) indicated that 1 to 46% of children under three years of age, according to the age groups, had exposure levels identified as a concern for at least two substances simultaneously. This proportion increases steadily with age. The proportion of children subject to an alarming level of exposure to a single substance varied between 32 and 43%. Lastly, 21 to 67% of children under three years of age did not exhibit any problematic exposure levels as regards the substances identified as a concern for a share of the population. Figure 4 below details, by age category, the proportion of children concerned by these co-exposures.
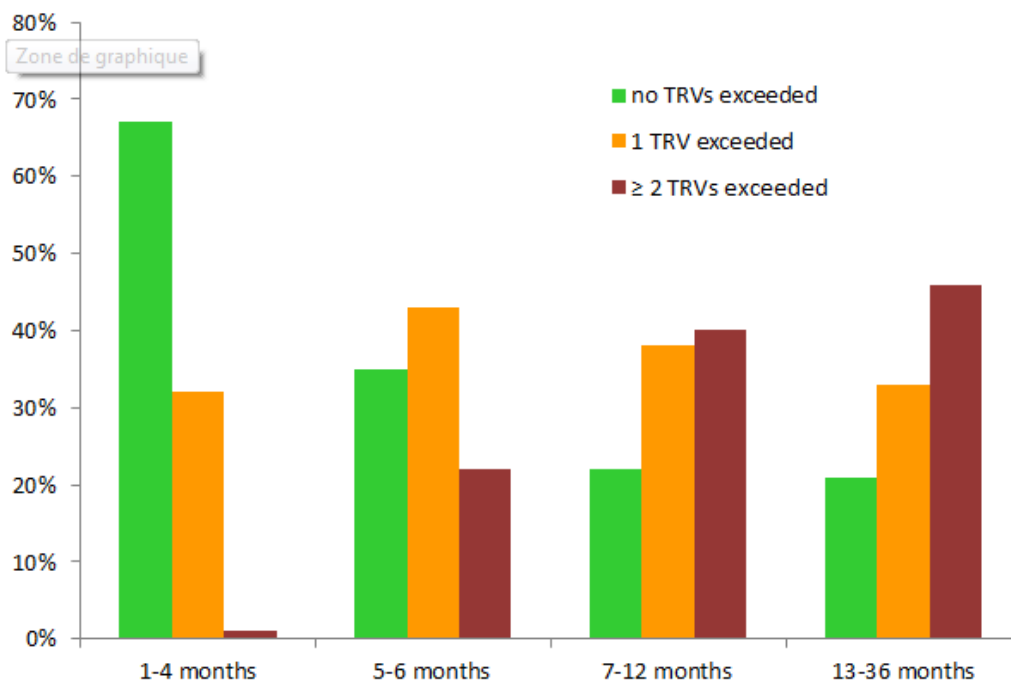
Figure 4: Percentage of children not concerned by any exceeded TRVs, or concerned by the TRV being exceeded for one or more substances identified as a concern (DON, T-2 & HT-2, dioxins, PCBs, nickel and acrylamide for its neurotoxic effects) according to the age groups

Between 13 and 36 months, the situations of co-exposure to substances identified as a concern affected almost half of the children. Co-exposure to acrylamide and nickel was the most frequent among children aged 5 to 12 months. In children aged 13 to 36 months, it was co-exposure to acrylamide, nickel and DON.

The number of children in whom the TRV was not exceeded for these substances decreased with age, contrary to that of children concerned by multiple exposure. This is due to the fact that, as a general rule, the infant diet seems less contaminated than a diet comprised of normal foods.

In addition, the effect of diversification on exposure levels was not examined in the framework of this study due to the fact that the nutritional components need to be considered as a whole in order to cover the needs of children.

Contributing foods

The foods making a major contribution to the exposure of the most exposed children were identified. Thus,

- in children under 4 months, mainly because of their almost exclusive consumption, first infant formulas and childhood cereals made a major contribution to exposure to inorganic arsenic, lead, nickel, furan and T-2 & HT-2 mycotoxins. In addition, the unusual consumption of normal milk by some children in this age group largely explains their high exposure to PCDD/Fs and PCBs.

- in children under one year of age, jars of vegetable-based baby food, alone or with meat or fish, represented important contributors, in particular for furan, acrylamide, nickel, inorganic arsenic and DON. They remain the main contributors to furan exposure in children over one year of age.

- in children over 7 months of age, some normal foods were identified as high contributors to exposure, such as fish (PCBs, PCDD/Fs and inorganic arsenic), normal milk (PCDD/Fs and PCBs), potatoes (acrylamide), biscuits (acrylamide, nickel, DON), vegetables (lead) and chocolate-based products (nickel).

The recommendations

For DON, the main contributors were cereal-based milk drinks, jars of fruit and jars of vegetable-based baby food (with or without meat), sweet/savoury biscuits and bread. Efforts must be concentrated on these foods.

For lead, vegetables and water appear as major contributors to exposure. Since 2013, the regulations have reduced the quality limit of lead in water intended for human consumption, but it was not possible to assess the impact of these regulations in this study given that the water samples analysed were collected before 2013. As regards vegetables, it seems difficult to reduce the lead levels given the ubiquitous nature of lead. The CES ERCA therefore recommends providing all children with a varied diet to ensure that they are not systematically consuming the most contaminated foods.

For inorganic arsenic, Regulation (EU) No 2015/1006[13], which has been in force since 1 January 2016, amends Regulation (EC) No 1881/2006[14] by laying down maximum levels of inorganic arsenic for rice and rice-based foods, including those intended for infants or young children. Infant rice and cereals (mainly rice-based ones) indeed appear to be major contributors in children under three years of age. Analytical speciation data on these foods and on jars of vegetable- and fish-based baby food are however needed, to confirm that these are indeed contributors on which efforts should be focused to reduce the levels.

For PCBs, the concentrations reached are very low. In order to allow optimal coverage of nutrient needs while limiting the risk of overexposure to chemical contaminants, ANSES recommends *"consuming two portions of fish per week, including one with a high docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) content (salmon, sardines, mackerel, herring, smoked trout). ANSES also reiterates the need to vary the fish species and sources of supply (wild, farmed, fishing sites, etc.) […], in the framework of a varied diet"* (ANSES 2013b). These recommendations should be supplemented by those established in light of the risk associated with methylmercury.

For PCDD/Fs, the levels are also very low, however efforts should be pursued to limit the exposure of children under three years of age, in particular via milk and fish.

For furan, similar to what was done to limit the population's exposure to acrylamide (creation of a "toolbox" for the introduction of process management measures), ANSES recommends seeking to reduce the levels in industrial products through the optimisation of manufacturing processes, in particular for jars of baby food based on vegetables (alone or with meat or fish).

---

[13] Commission Regulation (EC) No 2015/1006 of 25 June 2015 amending Regulation (EC) No 1881/2006 as regards maximum levels of inorganic arsenic in foodstuffs.
[14] Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs.

For nickel, chocolate-based products appear to be the major contributors for children over one year of age. Efforts to reduce nickel levels must prioritise these products. Furthermore, given the existence of a nickel-sensitised population, a study could be conducted to characterise acute exposure in order to assess the risk in these individuals.

For T-2 & HT-2 mycotoxins and acrylamide, the European Commission recommends that Member States implement monitoring, with the support of industrial operators, to detect their presence in the main contributors and, in the event that the indicative values are exceeded, calls for surveys to better understand the origin of the contamination. Nevertheless, efforts to limit contamination levels should continue in the case of:

- acrylamide in jars of vegetable-based baby food with or without meat, potatoes and biscuits.
- T-2 & HT-2 mycotoxins in infant formulas in particular.

Acquisition of knowledge to guide management measures

Additional data need to be acquired to better guide the efforts to be implemented for some substances for which, despite everything, the situation is identified as a concern. Thus:

- additional toxicological data are needed to confirm the existence of a specific sensitivity in young children that may not have been taken into account in the establishment of the TRVs used in this study for acrylamide, DON and inorganic arsenic.
- additional analytical improvements are needed in order to refine the measurement of contamination levels in foods identified as high contributors for T-2 & HT-2 mycotoxins, DON, nickel and inorganic arsenic.
- given furan's volatility, it would be interesting to study reheating practices in the home for infant foods prepared industrially in order to limit the exposure.

Reduction in exposure as a precaution

For aluminium, cobalt, cadmium, strontium, methylmercury, selenium and genistein, the risk could not be ruled out due to a major uncertainty in precisely estimating the proportion of individuals at risk. Nevertheless and as a precaution, recommendations aimed at reducing the exposure levels to these substances were formulated with, in some cases, the identification of a specific sub-population. Thus:

- for aluminium, it is recommended to limit exposure by varying the vegetables consumed.
- for cobalt, efforts to reduce dietary exposure should be continued.
- for strontium, the excessive values observed were associated with the use of a natural mineral water with a high strontium concentration used for therapeutic purposes to reconstitute baby formula. It should be reiterated that highly mineralised natural mineral water must only be used in infants under medical advice and for a limited time.
- for selenium, the cases where the safety limit was exceeded in children aged 13-36 months were mainly linked to high fish consumption. It is worth recalling the recommendations formulated by ANSES for children under three years of age (ANSES 2013b), i.e. two portions of fish per week, including one with a high EPA-DHA content (salmon, sardines, mackerel, herring, smoked trout), and varying the species and sources of supply (wild, farmed, fishing sites, etc.), in the framework of a varied diet.
- for methylmercury, the risk is associated with high consumption of fish. As a reminder, in addition to the general recommendations relating to fish consumption mentioned earlier, it is recommended "[…] for children under three years of age, limiting the consumption of wild predator fish[15] (monkfish or angler fish, bass, bonito, eel, orange roughy, grenadier, halibut, pike, sea bream, skate, cutlassfish, tuna, etc.), and avoiding, as a precaution, consumption of swordfish, marlin, deepwater spiny dogfish, shark and sea lamprey, due to the risk associated with methylmercury" (ANSES 2013b).
- for cadmium, the cases in which the TWI were exceeded should be put into perspective (see study report and summary), but because the TWI was observed to have been exceeded in the adult population (0.6%) (ANSES 2011) and because of the existence of cognitive effects associated with low exposure levels, the exposure to cadmium is not regarded as tolerable. It is therefore recommended that efforts be continued to reduce exposure from a very young age, by

---

[15] Predator fish as defined by Regulation (EC) No 1881/2006.

acting on the same contributors as those identified for the adult population (potatoes and vegetables).

- for genistein, the risk cannot be ruled out for children consuming soy-based products, which contain large quantities of isoflavones. The consumption of soy-based products by children under three years of age should therefore be limited.

Table 9: Summary of the recommendations relating to the substances for which a reduction in exposure levels should be considered

Substances	Conclusions	Recommendations for management measures	Research recommendations
Reduction in exposure to consider as a priority			
Lead	MOE < 10 $BMDL_{10}$: 0.63 µg.kg bw^{-1}.d^{-1}	Reduce exposure by providing all children with a varied diet	
Inorganic arsenic	Very low MOEs (< 36) $BMDL_{01}$: 0.3 to 8 µg.kg bw^{-1}.d^{-1}	Reduce exposure.	• Obtain speciation data in foods (as a priority, jars of vegetable- and fish-based baby food, as well as infant rice and cereals - mainly rice-based ones). • Update ANSES's work on the assessment of the health risks associated with the quality limit of arsenic in water intended for human consumption and natural mineral water, and examine whether it is appropriate to lower this quality limit. • Conduct developmental toxicity studies on arsenic.
Nickel	**Chronic risk:** TDI exceeded in 8 to 98% of children (2.8 µg.kg bw^{-1}.d^{-1}) **Risk of hypersensitivity:** Limits may be exceeded for sensitised children ($BMDL_{10}$ = 1.1 µg.kg bw^{-1}.d^{-1})	Reduce exposure via the main contributors (chocolate-based products in children aged 13-36 months).	• Lower the analytical limits. • Obtain acute exposure data.
PCDD/Fs	Cases where the limits were exceeded significantly from seven months of age, non-representative cases where the limits were exceeded in children under seven months (TDI: 0.7 pg.kg bw^{-1}.d^{-1})	Reduce exposure, mainly via normal food products making a major contribution to exposure of the most exposed children to PCDD/Fs (milk, ultra-fresh dairy produce and fish).	
PCBs	Cases where the limits were exceeded significantly from 13 months of age Non-representative cases where the limits were exceeded in children aged 7-12 months Limits not exceeded for children under 7 months of age (TDI: 10 ng.kg bw^{-1}.d^{-1}).	ANSES recommendations: "in order to allow optimal coverage of nutrient needs while limiting the risk of overexposure to chemical contaminants, consuming two portions of fish per week, including one with a high EPA-DHA content (salmon, sardines, mackerel, herring, smoked trout), and varying the species and sources of supply (wild, farmed, fishing sites, etc.) […], in the framework of a varied diet." (See methylmercury for additional recommendations).	

Substances	Conclusions	Recommendations for management measures	Research recommendations
Acrylamide	**Genotoxic carcinogenic effects:** MOE < 10,000 (BMDL$_{10}$ = 0.17 mg.kg bw^{-1}.d^{-1}). **Neurotoxic effects:** Benchmark value of 0.2 µg.kg bw^{-1}.d^{-1}: limits exceeded significantly in children under three years of age. RfD of 2 µg.kg bw^{-1}.d^{-1}: Exceeded in 7% of children over 13 months of age Non-representative cases where the limits were exceeded in children aged 7-12 months.	Continue efforts to reduce contamination from the main contributors (biscuits, potatoes, jars of vegetable-based baby food with or without meat) and exposure by reducing the formation of acrylamide during food production or preparation processes, for example.	• Study the impact of a reduction in contamination/consumption of the major contributors. • Conduct additional toxicological studies to confirm the TRV to be adopted for neurotoxic effects in young children.
Furan	**Genotoxic carcinogenic effects:** MOE < 10,000 (BMDL$_{10}$= 0.96 mg.kg bw^{-1}.d^{-1}).	Reduce exposure, mainly by reducing furan levels in industrial products, in particular jars of vegetable-based baby food (alone or with meat or fish), through the optimisation of manufacturing processes.	Study the impact of reheating practices in the home for infant foods prepared industrially.
T-2 and HT-2 toxins	Exceeded in 5 to 10% of children aged 5-12 months under the LB Non-representative cases where the limits were exceeded under the LB in children under four months (PMTDI = 0.06 µg.kg bw^{-1}.d^{-1}).	Continue efforts to reduce exposure, especially by strengthening monitoring of infant formulas and the associated control measures	Pursue efforts to lower the analytical limits.
DON and acetyl derivatives	TDI of 300 ng.kg bw^{-1}.d^{-1}: Exceeded in between 7.5 and 27% of children from five months of age under the LB. TDI of 1,000 ng.kg bw^{-1}.d^{-1}: Non-representative cases where the limits were exceeded under the LB for all age groups	Continue efforts to reduce exposure, especially via the major contributors (infant milk drinks, especially those containing cereals, jars of fruit, jars of vegetables with or without meat, normal biscuits and bread).	• Conduct additional toxicological studies to be able to confirm the TRV to be adopted for young children. • Pursue efforts to lower the analytical limits.
Reduction in exposure to be considered as a precaution			
Aluminium	Limits not exceeded for children under five months of age. Non-representative cases where the limits were exceeded from five months of age (PTWI = 1 mg.kg bw^{-1}.week^{-1})	Reduce exposure by varying the vegetables consumed.	

Substances	Conclusions	Recommendations for management measures	Research recommendations
Methylmercury	Limits not exceeded for children under 12 months of age. Non-representative cases where the limits were exceeded in children aged 13-36 months (PTWI = 1.3 µg.kg bw⁻¹.week⁻¹)	ANSES recommendations: "in order to allow optimal coverage of nutrient needs while limiting the risk of overexposure to chemical contaminants, consuming two portions of fish per week, including one with a high EPA-DHA content (salmon, sardines, mackerel, herring, smoked trout), and varying the species and sources of supply (wild, farmed, fishing sites, etc.) […], in the framework of a varied diet. […] It is also recommended […] for children under three years of age, limiting the consumption of wild predator fish (monkfish or angler fish, bass, bonito, eel, orange roughy, grenadier, halibut, pike, sea bream, skate, cutlassfish, tuna, etc.), and avoiding, as a precaution, consumption of swordfish, marlin, deepwater spiny dogfish, shark and sea lamprey, due to the risk associated with methylmercury".	
Cadmium	Put the cases where the TWI was exceeded (36%) into perspective: long-term nephrotoxicity and exposure in the first three years of life only accounts for 3% of cumulative exposure over 50 years. (TWI = 2.5 µg.kg bw⁻¹.week⁻¹)	Reduce exposure from a very young age Reduce contamination in the main contributors (mainly vegetables and potatoes).	Confirm the existence of cognitive effects associated with low levels of exposure to cadmium.
Selenium (in children over one year of age)	Non-representative cases where the limits were exceeded in children aged 13-36 months. (UL = 60 µg.d⁻¹) *(no TRV for children under one year of age)*	Reiterate the general recommendations on fish consumption issued by ANSES for children under three years of age	
Strontium	Non-representative cases where the limits were exceeded in children under one year of age Limits not exceeded for children over 13 months of age (TDI = 0.6 mg.kg bw⁻¹.d⁻¹)	Remind parents that highly mineralised natural mineral water must only be used in infants under medical advice and for a limited time.	
Cobalt	Exposure levels close to the TRV deemed to be not very robust in children under three years of age (TDI = 1.6 µg.kg bw⁻¹.d⁻¹).	Efforts to reduce dietary exposure to cobalt should be continued.	Conduct the missing toxicological studies (perinatal period).
Genistein (in consumers of soy-based products)	MOS = 40 (below the provisional critical MOS of 300) LOAEL of 35 mg.kg bw⁻¹ d⁻¹	Limit the consumption of soy-based products by children under three years of age.	Re-assess the TRV in light of more precise data when these are available and have been validated.

3.5.2. Need for acquisition of knowledge

For certain substances, additional data need to be acquired in order to rule definitively on whether or not there is a risk for certain consumers. This relates to the substances listed in Table 10.

Table 10: Substances for which data need to be acquired in order to conduct a final HRA

Type of recommendations	Substances for which the risk cannot be ruled out	Substances for which no conclusions can be reached on the risk
Recommendations for overcoming the analytical uncertainties		
Acquire speciation data	**Trace elements:** chromium	**Trace elements:** tin, vanadium
Acquire data with lower analytical limits	**Pesticide residues:** dieldrin, lindane, propylene thiourea **Mycotoxins:** ochratoxin A, aflatoxins **Additives:** ascorbyl palmitate	
Screen for the missing metabolites		**Pesticide residues:** chlorothalonil, chlorpropham, fenpropimorph, flusilazole, tepraloxidim
Recommendations for reducing the uncertainties relating to characterisation of the concentrations		
Take other foods into account	**Additives:** phosphoric acid	**Additives:** tartaric acid **Pesticide residues:** chlorantraniliprole, dodine, oxyfluorfen, pyridaben, triflumizole, biphenyl, flucythrinate, tolfenpyrad
Update the occurrence data	**Substances migrating from FCMs:** BPA	
Recommendations for overcoming the toxicological uncertainties		

Conduct studies for establishing a TRV applicable to the general population while taking infant specificities into account		**Trace elements:** germanium, silver, inorganic tin, gallium, tellurium, vanadium **POPs:** PFAS, mixture of "dioxin-like" substances **Mycotoxins:** *Alternaria* toxins, other trichothecenes (DAS, FusX, Ver, MAS, NEO, T2-triol) **Ink photoinitiators:** *4-tert*-octylphenol, 4-hydroxybenzophenone **Phthalates:** DIBP, DEP, DCHP, DnP **Priority sex steroids of animal origin** (17β-testosterone & 5α-dihydrotestosterone, progesterone, 17α & 17β-oestradiol and oestrone) and other sex steroids of animal origin **Phyto-oestrogens:** isoflavones (other than genistein), coumestans and lignans **Pesticide residues:** fenuron, metolcarbe, propargite, tricyclazole **Substances migrating from FCMs:** chlorohydrin derivatives of BADGE
Conduct reproductive and developmental toxicity studies in order to determine a TRV while taking infant specificities into account	**Trace elements:** barium, cobalt **Mycotoxins:** ochratoxin A	**Trace elements:** copper and selenium (for children under one year)
Reassess the reference values in the near future	**Phyto-oestrogens:** genistein **Substances migrating from FCMs:** BPA	

The uncertainties relate to the assessment of exposure levels or the toxicity of substances. For certain substances, the exposure levels may need to be further specified by:

- additional speciation data in foods that are high contributors: chromium, tin, vanadium.
- analytical limits that are suitable for the TRVs used: aflatoxins, ascorbyl palmitate, propylene thiourea, lindane, dieldrin.
- taking into account the concentrations in other foods not analysed in the study of compounds such as certain pesticides (chlorantraniliprole, dodine, oxyfluorfen, pyridaben, triflumizole, biphenyl, flucythrinate, tolfenpyrad) and, for food additives, phosphoric acid, tartaric acid, ascorbyl palmitate. In addition, with regard to additives, their natural presence in food should be taken into account. For example, in the case of ascorbyl palmitate, EFSA has shown that its ingestion as a food additive accounted for only 3% of a normal diet (EFSA 2015).
- the updating of the occurrence data due to a significant regulatory change occurring after the study's sampling period: BPA.

For other substances, the uncertainties relating to the assessment of their toxicity in light of the estimated exposure levels meant that it was not possible to conduct a final HRA. These uncertainties related primarily to:

- the lack of a robust TRV: germanium, silver, inorganic tin, gallium, tellurium, vanadium, mixture of "dioxin-like" substances, certain phthalates, perfluoroalkyl compounds (other than PFOA and PFOS), *Alternaria* toxins, *4-tert*-octylphenol, 4-hydroxybenzophenone, 2-isopropylthioxanthone, 17β-testosterone & 5α-dihydrotestosterone, progesterone, 17α & 17β-oestradiol, oestrone and other sex steroids of animal origin, isoflavones (other than genistein), coumestans and lignans, certain pesticide residues. For these substances, toxicity studies should therefore be conducted for establishing a TRV applicable to the general population while taking infant specificities into account.
- the inability to confirm that the selected TRV takes infant specificities into account (by the existence of developmental toxicity studies, reprotoxicity studies or multi-generational studies for example): copper and selenium (for children under one year), ochratoxin A, barium, cobalt. For these substances, toxicity studies should therefore be conducted for determining a TRV taking infant specificities into account.
- the possibility of the selected TRV being called into question following the work in progress: BPA, genistein. A reassessment of the reference value may be conducted to rule on the risk.

Regarding minerals, physiological data need to be acquired for determining the nutritional references for children aged 0 to 3 years. In particular, tolerable upper intake levels should be established for iron, potassium, sodium, lithium and magnesium and, for children under one year of age, for manganese, molybdenum, selenium and copper. Similarly, in order to assess the risk of insufficient intake, nutritional references should be established for chromium, lithium and sodium, and the average requirement (AR) should be defined for nutrients for which only a satisfactory intake value has been proposed, i.e. for magnesium, manganese, molybdenum, potassium, copper and selenium for children under three years of age, for calcium for children under one year, and for iron and zinc for children under six months. Lastly, the validity of the value of the AR chosen for iron should be confirmed by direct studies of the iron status of children.

3.5.3. Need to maintain suitable surveillance

Approximately 90% of the substances or classes of substances for which the risk assessment was carried out, do not present a health concern.

Table 11: Substances for which the health situation was deemed tolerable or acceptable

Classes of substance	Substances for which the health situation was deemed tolerable or acceptable
Trace elementsand minerals	Cr III, Hg, Sb
Persistent organic pollutants	PBBs, PBDEs (7+209), HBCDDs, TBBPA, PFOA, PFOS
Mycotoxins	nivalenol, patulin, fumonisins, zearalenone
Heat-induced substances	PAHs
Substances derived from migration from FCMs	benzophenone, 4-MBP, nonylphenols, BADGE, DEHP, DnBP, DIDP & DiNP, BBP
Phyto-oestrogens	genistein (non-consumers of soy-based products)
Pesticide residues	278 pesticide residues

For some substances, maximum regulatory limits have been established in normal foods and/or infant foods. This is the case with mycotoxins (patulin, zearalenone and fumonisins), mercury and PAHs in European Regulation (EC) No 1881/2006. Similarly, Maximum Residue Limits (MRLs) have been defined for all the pesticide residues analysed (Regulation (EC) No 396/2005[16], Directive 2006/125/EC[17]) and quality limits (QL) for water intended for human consumption (tap water and spring water – Ministerial Order of 11 January 2007[18]) and for natural mineral water (Ministerial Order of 14 March 2007[19] as amended).

---

[16] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC.
[17] Commission Directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children.
[18] Ministerial Order of 11 January 2007 on the quality references and limits for raw water and water intended for human consumption listed in Articles R. 1321-2, R. 1321-3, R. 1321-7 and R. 1321-38 of the French Public Health Code.
[19] Ministerial Order of 14 March 2007 as amended on the quality criteria for bottled water, on specific treatments and labelling statements for bottled natural mineral water and spring water as well as natural mineral water distributed in public refreshment bars.

For non-regulated substances, monitoring to check any changes in the levels of contaminants/nutrients or in exposure where appropriate, must be maintained or implemented.

For BADGE, the occurrence data should be updated due to a significant regulatory change (in the framework of Bisphenol A) occurring after the study's sampling period.

For PFOS and PFOA, work in progress by the US EPA may call the selected TRV into question. Similarly, future work at ANSES on the effects associated with the endocrine-disrupting mechanism of certain phthalates may lead to the definition of a new reference value. The reference value could be re-assessed in order to rule on the risk.

For some contaminants (HBCDDs, TBBPA and nivalenol), abnormally high concentrations were observed in a few samples of infant foods (infant formulas or rice-based cream desserts). These levels did not lead to the toxicity reference values being significantly exceeded. Nevertheless, further investigations are needed to confirm these high levels and determine the origin.

In each case, efforts need to be encouraged to reduce the levels of contaminants in foods.

3.6. Prospects for the study

The results obtained in this study will help target the substances on which particular attention should be focused. However, other work themes should also be considered, in order to address the limitations and uncertainties associated with this study.

3.6.1. Breastfeeding

The present study focused exclusively on the diet of non-breastfed children. It therefore seems necessary to characterise the exposure of breastfed children to contaminants, since many substances present in the mother can be transmitted to the infant through breastfeeding (Fenton et al. 2005). In France, the prevalence of breastfeeding is 69.7% at birth (Wagner et al. 2015). Taking breastfed children into account seems essential to obtain an overall view of the exposure of children under three years of age to different contaminants present in the environment.

Data in the literature have shown that the presence of certain contaminants in breast milk could lead to a risk for children (Cerna et al. 2010, Chovancova et al. 2011, Cok et al. 2009, Johnson-Restrepo et al. 2007, Park et al. 2011, Ulaszewska, Zuccato, and Davoli 2011). At the present time, French data on the levels of these contaminants in breast milk are still rare and only relate to a limited number of substances: mainly PCBs, dioxins and furans, and brominated flame retardants (Antignac et al. 2009, Brucker-Davis et al. 2010, Cariou et al. 2008, INVS/CAREPS 2000, Kadar et al. 2011).

In order to gain a better understanding of the French situation, a specific study was set up to analyse the contamination of breast milk collected in various milk banks throughout France. This study, entitled CONTA-LAIT, will thus help obtain data on the contamination of breast milk in France. It will then be possible to conduct an assessment of the benefits and risks associated with breastfeeding.

3.6.2. Mixtures of substances

For most of the substances, the risk assessments were constructed according to the usual approach, which deals with each substance independently of any others. For some contaminants from the same chemical class, the choice was made to consider a mixture of congeners with a toxicity reference value (dioxins and furans, PCBs, PBDEs, HBCDDs, PBBs, PAHs, fumonisins) for assessing the risk. An identical source of contamination and mode of action shared by the different congeners were the essential elements justifying this type of approach.

However, the question of mixtures cannot be limited solely to a mixture of compounds belonging to the same chemical class. Through their diet, individuals are exposed to a multitude of contaminants from diverse chemical classes. Phenomena of competition, additivity or synergy can occur between several substances, which may lead to the organism responding in an unexpected way with regard to the known toxicological effects for each substance. Assessment methods are being developed to take these types of effects into account, for example the use of cumulative assessment groups (CAGs) for the cumulative risk assessment of pesticides (EFSA 2013c).

It is therefore necessary to identify mixtures (or "cocktails") of substances that are relevant in health terms and realistic from the point of view of population exposure. In this respect, the iTDS is an important source of

data for identifying the cocktails to which children are actually exposed, and could therefore provide input for studies of the potential associations between these cocktails of substances and the health effects.

Studying the effects of mixtures that are representative of food intakes would help better estimate the actual risk by incorporating the cumulative effects.

The iTDS data will in particular be used in the framework of the COCTELL project, funded by the French National Research Agency (ANR) and conducted jointly by Inserm and ANSES, whose aim is to estimate the level of exposure to mixtures of food contaminants in pregnant women and their children, and to study the association between exposure to these contaminants individually or in mixtures and development parameters such as growth and cognition.

Example of the mixture of "dioxin-like" compounds

The CES ERCA considered that the existing toxicological data made it impossible to consider dioxins/furans and DL-PCBs together, in the form of a mixture of "dioxin-like" compounds. It is relevant in health terms to take into account all substances acting like dioxins, but this cannot be limited solely to dioxins/furans and DL-PCBs and the binding to the Ah receptor (AhR). Other substances identified in food interact significantly with the AhR as agonists (hexachlorobenzene, biphenyls, polybrominated compounds, p-dioxins and polybrominated dibenzofurans, polychlorinated naphthalenes) or antagonists (NDL-PCBs). In addition, the principle legitimising the concept of toxic equivalency (TEQ), i.e. that most of the toxic effects of a substance or class of substances only depend on the binding to a receptor (in the present case, AhR), is relevant for dioxins but more reductive for other substances such as DL-PCBs, for example (for which many other receptors are involved in the toxic processes). Therefore, the current approach using calculation of a theoretical TEQ can potentially lead to an estimate that differs significantly from the actual toxic potential of a mixture of "dioxin-like" substances.

Knowledge of the occurrence of mixtures of food contaminants has evolved since the establishment of toxic equivalency factors; other toxic compounds can now be integrated in the list of "dioxin-like" compounds, in addition to the classes of PCDD/Fs and DL-PCBs[20]. To better assess the risk associated with exposure to "dioxin-like" compounds, it is recommended that toxicity studies be conducted with mixtures that reflect dietary exposure to "dioxin-like" substances. Pending these new data, the CES ERCA believes it is more relevant to assess the risk separately for dioxins/furans and PCBs with a view to establishing management measures tailored to these two classes of substances from different sources of pollution.

Example of the mixture of substances with "endocrine disrupting" effects

Some of the substances studied have "endocrine disrupting" toxicological mechanisms of action (sex steroids of animal origin, phyto-oestrogens, certain phthalates, certain plant protection products, etc.).

The diverse mixture of substances with hormone-mimicking activity provided by the diet implies that their chemical nature, interactions and mechanisms of action should be taken into account from an overall perspective. The CES ERCA therefore recommends that additional studies be conducted with mixtures that reflect dietary exposure to the substances in order to assess, through bioassays, the intensity of their hormonal activity (oestrogenic, anti-androgenic, etc.).

Work is needed to develop a method able to address the issue of mixtures and understand the risks associated with natural substances provided via food (phyto-oestrogens, sex steroids of animal origin, etc.) and xenobiotics with hormonal effects (plant protection products, dioxins, brominated flame retardants, bisphenols, PCBs, alkylphenols, etc.).

3.6.3. Aggregate exposure

The iTDS dealt exclusively with exposure via food and did not incorporate exposure via other routes (respiratory, dermal, etc.) in the risk assessment approach.

However, for certain substances, these other routes of exposure do exist. This is particularly the case with lead (ANSES 2014), certain phthalates (Beko et al. 2013, INSERM 2011, Schettler 2006), cadmium (EFSA 2009), certain perfluorinated compounds (Fromme et al. 2009) and brominated flame retardants (EFSA 2011), for which intakes *via* these non-dietary routes of exposure can be non-negligible in children. For these substances, it is therefore necessary to reiterate that the conclusions established in this study only correspond to the health risk associated with dietary exposure, and do not prejudge the overall risk. To

---

[20] Work is currently being finalised at ANSES to identify the main mixtures of substances to which consumers are exposed via food, using co-exposure data.

characterise this, the main routes of exposure would need to be considered by calculating exposure regarded as "aggregate". This would require quantified data on the other routes of exposure.

This work has already been conducted or is under way at ANSES for the following substances: bisphenol A, lead, perfluorinated compounds, brominated flame retardants and phthalates. The data from the iTDS will provide further input for these studies (ANSES 2013a, 2014).

3.6.4. Lifelong exposure

For a given substance, the exposure observed in children under three years of age can differ significantly from that of adults (see the TDS2). This is due to a diet and a "quantity of food consumed to body weight" ratio that differs between children and adults (see above). The TRVs used in this study were established in order to be applied on the basis of a scenario taking into account exposure throughout an individual's entire life. However, the exposures calculated in this study and compared with the TRVs cover a period of life that is limited to three years. Depending on the substance's mechanism of action (in particular for contaminants that accumulate in the body), the interpretation of cases where the limits were observed to have been exceeded in the iTDS should therefore be placed in the context of longer term exposure, mainly in adulthood, in order to confirm whether or not there is a risk for the general population. Work will be initiated to attempt to estimate "lifelong" exposure from data derived from the iTDS and the TDS2, in order to characterise the risk for substances identified as a concern in these two studies.

Example of cadmium and the associated nephrotoxic risks:

For substances whose effects appear after accumulation over a long period of exposure, the cases where limits were observed to have been exceeded over a limited time do not necessarily lead to a risk to the population. This is especially the case with cadmium, for which the nephrotoxic effects are associated with an exposure period of 40 to 50 years. The calculated risk may in this case be overestimated. Due to the "consumption/body weight" ratio, the estimate of exposure is generally higher in the infant population. Therefore, cases where the TRV was exceeded make it possible to identify substances potentially posing a risk and which should be studied more closely. The estimates of exposure obtained in this population should thus be considered in light of those for children over three years of age, in order to consider lifelong exposure while taking the potential windows of susceptibility into account.

3.6.5. Other substances

The iTDS made it possible to assess the exposure of children under three years of age to 522 substances. These substances were selected according to criteria of known or suspected health concern in light of the scientific literature studied at the time of implementation of the study.

The CES ERCA reiterates that there are many substances in food for which the toxicological effects and/or the optimisation (or development) of analytical techniques to identify them are currently being investigated, as well as substances whose presence in food remains to be demonstrated. These include, for example, substances added unintentionally, which migrate from food contact materials, or emerging heat-induced substances, which appear during food processing or preparation processes (for example chloropropanols such as 3-MCPD, 2-MCPD or glycidol) and chloropropanol esters derived from a process of acid hydrolysis of vegetable proteins, which can be found in infant food formulas (EFSA 2013a). Similarly, among the classes of known compounds such as brominated flame retardants, EFSA draws attention to new congeners to be studied (EFSA 2012), or poly- and perfluoroalkyl compounds (Munoz 2015).

3.6.6. Need for toxicology data

The infant population may present particular susceptibility to certain substances in the event of chronic exposure to low doses of contaminants. A specific approach was implemented to decide on the relevance of the reference values selected from a toxicological point of view for the infant population. The robustness and applicability of each of the selected values to the studied population were considered.

For some substances (e.g. cobalt, barium, cadmium, aflatoxins and furan), the toxicity reference value was found to be robust for the adult population, although its applicability to the infant population remains to be demonstrated. For these substances, the risk may therefore be underestimated and an additional literature review should be performed to determine the extent to which a new reference value should be defined for the infant population. In the course of the study, this work was conducted for two substances (deoxynivalenol and its derivatives, and acrylamide) and led to an additional safety factor being proposed to take the specificities of the infant population into account.

Lastly, some of the substances (phthalates, brominated flame retardants, perfluorinated compounds and alkylphenols in particular) will be undergoing expert appraisal at ANSES in the framework of the Working Group on "Endocrine Disruptors" (WG ED) for example. The ultimate objective of this work is to establish TRVs that take into account the endocrine-disrupting nature of the substances. It cannot therefore be ruled out that some values selected in the present study differ from those that may be proposed in the future.

4. AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety adopts the conclusions and recommendations of the Expert Committee on "Assessment of the physical and chemical risks in foods" (CES ERCA) and issues the following additional remarks.

4.1. Exposure to substances is generally well managed

The Agency conducted a specific study on the applicability of the toxicity reference values to the infant population, and in this regard proposed reference values for certain substances (acrylamide, and deoxynivalenol and its derivatives), which enabled a full risk assessment to be carried out for all these substances. The health risk assessments carried out on the basis of these results showed that, for more than 90% of the substances for which the risk assessment was carried out, exposure was deemed tolerable or acceptable. For the remainder, several situations were observed depending on the substances.

In order to take into account the exposure situations highlighted by the iTDS, the Agency formulated either management recommendations or research recommendations, in order to refine the conclusions relating to the risk associated with exposure to certain compounds. The measures adapted to each of these substances proposed by the CES ERCA have been endorsed by the Agency and are detailed above. All the actions recommended by the CES ERCA should be considered with the same degree of priority.

4.2. The substances identified as a concern

Nine substances or classes of substances were identified as a concern: inorganic arsenic, nickel, lead, dioxins and furans, polychlorinated biphenyls, acrylamide, furan, and the mycotoxins deoxynivalenol and its derivatives, and T-2 and HT-2. For these substances, it seems essential to establish or strengthen measures to reduce the exposure of the infant population.

For seven of these substances, exposure had already been identified as a concern in the framework of the second total diet study (TDS2). Consequently, these situations are not likely to disappear after the age of three and in particular once adulthood is reached, which reinforces the imperative to act to reduce exposure to these substances for the entire population.

Regarding inorganic arsenic, the Agency recommends obtaining speciation data in foods (as a priority, jars of vegetable- and fish-based baby food, as well as infant rice and cereals - mainly rice-based ones) in order to define the main contributors to exposure. At the same time, the Agency will update its work on the assessment of the health risks associated with the quality limit of arsenic in water intended for human consumption and natural mineral water, and examine whether it is appropriate to lower this quality limit.

With regard to nickel, the toxicity reference value adopted in the present study is lower than the one adopted in the framework of the second total diet study (TDS2) in 2011 (2.8 *versus* 22 µg.kg bw^{-1}.d^{-1}). Accordingly, and in light of the exposure calculated in the TDS2, exposure is also identified as a concern for the population studied in the framework of the TDS2, namely individuals over three years of age. The Agency will be conducting an expert appraisal in order to determine possible measures for reducing the exposure of the general population to nickel.

4.3. Minerals

The results of the iTDS show that intakes meet nutritional needs to a satisfactory level overall for children under three years of age. This is the case for iron and zinc in children under six months, for magnesium, calcium and copper in those under one year, and lastly for manganese, selenium, molybdenum and

potassium in children under three years of age. However, there were insufficient intakes of calcium in children aged 13-36 months, and of iron and zinc in children aged 7-36 months. Similarly, when reference is made to adequate intakes (i.e. the observed mean intake for a group of individuals in apparent good health), magnesium and copper intakes in children aged 13-36 months are below the benchmark considered. Thus, given the nature of this nutritional reference, the risk associated with an insufficient intake of magnesium and copper cannot be totally ruled out in children aged 13-36 months.

Concerning excessive intakes, cases where the tolerable upper intake levels were exceeded were observed for calcium in children under six months of age, and for manganese, selenium and copper in children aged one to three years, albeit without certainty due to the limitations associated with the sampling. Concerning calcium, all the children under six months of age in whom the tolerable upper intake level was exceeded had consumed normal milk (richer in calcium than infant formulas) during the three days of the survey, and in greater quantities than the average consumption. Lastly, for zinc, excessive intakes were observed for all age groups (up to 75% of children under the age of six months). A risk associated with the excessive intake of these minerals cannot be ruled out for certain groups of consumers.

The reference values relating to minerals cannot by themselves be used to propose dietary recommendations and require the reference values for all nutrients to be taken into account, some of which still need to be consolidated. The definition of these values for the infant population is included in ongoing work on the revision of food consumption benchmarks for the National Health and Nutrition Programme (PNNS).

4.4. General recommendations

The Agency recommends putting in place an integrated strategy to reduce exposure, which could combine different approaches depending on the substances considered.

4.4.1. Better understand the origin of the contamination

ANSES recommends:

- Clearly identifying the sources of contamination throughout the entire production chain, including the primary production environment, in order to reduce this contamination, for example by modifying agricultural practices. In particular, for environmental pollutants (persistent organic pollutants or trace elements, for example), this should entail the identification of the countries or large geographical areas where the foods originate, industrial or polluting sites, polluted sites and soils, and taking into account the previous uses and the condition of the soil (in conjunction with the persistence of prohibited compounds);

- Improving knowledge of the agronomic determinants contributing to the presence of certain contaminants in plants, in order to identify the risk factors and establish a control strategy: for example, conditions favouring the soil-plant transfer of pesticides that are now prohibited but still persist in the environment; conditions of growth of mycotoxin-producing moulds (in particular, deoxynivalenol and its derivatives);

- Analysing the processing methods promoting the emergence of heat-induced products and ensuring compliance with recognised good practices for controlling these contaminants, some of which are already identified (acrylamide, furan).

4.4.2. Reduce exposure

ANSES recommends:

- Continuing the efforts by all the stakeholders to determine best agricultural practices in order to limit the presence of contaminants in foodstuffs;

- Conducting a debate on the maximum values laid down by the regulations and the choice of matrices to be regulated (in particular, the major contributors to exposure). Indeed, for PCBs and PCDD/Fs, inorganic arsenic, lead, and deoxynivalenol and its derivatives, although the concentrations measured in the composite samples were below the maximum levels laid down by the regulations, exposure was identified as a concern for certain groups of consumers;

- Conducting a debate on the benefits of implementing regulations for contaminants that are not regulated at the present time, particularly those for which exposure was identified as a concern: acrylamide, furan, nickel, T-2 and HT-2 mycotoxins[21];

- Following the general recommendation to vary the diet and the sources of supply, based in particular on the recommendations of the PNNS, and continuing efforts on nutrition education.

4.4.3. Acquire the knowledge to refine the risk assessments

With regard to certain substances for which the risk could not be ruled out, since the situation is less clear due to the lack of data (see Table 10), ANSES recommends acquiring the missing data in order to refine the health risk assessment (in relation with analytical performance and speciation, or in relation with toxicological knowledge).

As regards pesticide residues, efforts should continue to improve risk assessments for the metabolites of the active substances authorised under the European regulations, in particular in terms of description (in raw and processed foods). As such, a guidance document from EFSA, to which ANSES is contributing, is currently being finalised. Furthermore, taking into account the effects of exposure to mixtures of substances that result from agronomic practices, the metabolism of pesticides and food consumption are also being addressed by a European research project in which ANSES is an active participant, and by work being coordinated by EFSA, to which the Agency is also contributing.

4.4.4. Methodological recommendations

Total diet studies make it possible to estimate dietary exposure to a large number of substances taking into account differences in dietary habits in the general population, which acquires its food by conventional channels in a diverse number of ways. In such a comprehensive study, it is not possible to take account of specific exposure situations: regular consumers of produce from organic agriculture, vegetarians, regular consumers of home-grown produce, etc. Moreover, the present infant total diet study does not cover the French overseas territories, where the situation may differ significantly from that presented here. The question therefore arises of the collection of contamination and consumption data specific to these particular exposure situations. After identifying priority sub-populations, other exposure studies should be set up, considering what exists already at international level.

The individual food consumption data used to estimate exposure come from declarative surveys that may suffer from bias or not be representative of normal consumption due to the brevity of the collection period (three consecutive days in the case of the present study). The individual food consumption surveys are currently undergoing validation and methodological improvements in order to improve the estimation of exposure and intakes over long periods of time, in particular for children under three years of age.

The question arises of the rate at which the TDSs should be updated and which substances to include: ANSES recommends perpetuating tools such as the TDSs for monitoring the estimation of population exposure. In particular, continuing the TDSs should at the very least make it possible to monitor the changes in concentrations of the substances of greatest concern (and new substances of emerging concern). Recent contamination data should be exploited, in particular for substances that may clearly be declining in foods: this was the case, for example, with PCDD/Fs, for which exposure has decreased in a drastic and well documented manner, mainly due to the filtration of smoke from household-waste incinerators; it is also likely to be the case with bisphenol A, which has been prohibited in all food containers since 2012 (the iTDS samples were collected prior to this ban). This, however, requires verification and confirmation.

---

[21] T-2 and HT-2 mycotoxins appear in Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs, without any maximum level being specified.

Lastly, alongside the TDSs, ANSES indicates that for the issues related to chemical contaminants, it is essential to conduct monitoring and vigilance at the national, European and international levels. This makes it possible to rapidly identify early warning signs, even weak ones, concerning new hazards or risks.

4.5. Specific recommendations

4.5.1. Food diversification[22]

The examination of food consumption of children used in the present study highlighted the consumption of normal milk by several children under one year of age. This practice, besides the nutritional considerations mentioned earlier, led to significantly higher exposure levels being observed, in particular for contaminants vectored by dairy products: primarily persistent organic pollutants (in particular PCBs and PCDD/Fs). In this context, the Agency reiterates the conclusions of its opinion of 5 February 2013, which indicated that only breast milk or infant formulas can cover an infant's needs (ANSES 2013c). In addition the PNNS stresses that cow's milk is regarded as unsuited to the nutritional needs of children under one year of age.

More broadly, the present study did not set out to make recommendations on food diversification. Nevertheless, the results showed that food diversification leads to higher exposure to certain contaminants than that generated by the consumption of infant formulas. At the present time, therefore, the Agency advocates following the recommendations issued in the framework of the 2005 National Health and Nutrition Programme, namely beginning food diversification from the age of six months for optimal benefit and in any event, never before four months of age. Furthermore, an update to these recommendations is planned; this work will take into account both the nutritional needs and the risks associated with the presence of contaminants in food.

4.5.2. Water used for reconstitution

Water used to reconstitute infant formulas accounted for a significant share of the food consumed by non-breastfed infants. The iTDS showed that water is a major contributor to exposure only for a few substances (antimony, silver, arsenic, barium, lead and strontium). Given the small number of infants consuming bottles prepared with tap water, the study is unable to recommend a type of water to use preferentially (from the tap or bottled). Nevertheless, the Agency reiterates that unsoftened and unfiltered tap water is only suitable for reconstituting infant formula under certain conditions: it is important to ensure, in particular in older dwellings (where the pipes can be made of lead), that the water does not contain more than 10 µg L^{-1} of lead.

4.5.3. Food contact materials

In order to take into account differences in contamination in the estimation of exposure according to the food containers, specific sampling was carried out.

The results show that for the phthalates measured in the framework of the study, the impact of plastic containers on exposure was not significant. In the case of bisphenol A, it was shown that the exposure of children not consuming canned products was lower than that of children consuming some of these products. This can be explained by significantly higher concentrations of bisphenol A in the canned products. Nevertheless, some exposure may be higher than the toxicological benchmark established by ANSES, including in children not consuming canned products liable to release bisphenol A. These exposure levels indicate a situation that may be a concern.

Note that the samples for the present study were collected before the law prohibiting bisphenol A in food containers came into force. Contamination levels now may therefore be lower than those measured in the framework of the iTDS. Analyses of the foods contributing most to exposure are therefore needed to define the current levels of bisphenol A contamination. The Agency reiterates the need to limit exposure to bisphenol A, particularly in the more vulnerable child population. It is therefore necessary to determine current contamination levels, i.e. after the implementation of these regulations, in order to establish whether new recommendations to reduce exposure are necessary.

---

[22] Food diversification is the gradual introduction of foods other than milk (maternal or infant formulas, excluding cow's milk, as this is included in the diversification).

4.6. Outlook for further study

Concerning future studies, in addition to those identified by the CES ERCA (associated with: the effects of exposure to mixtures, aggregate exposure, lifelong exposure, emerging substances, breastfed children and needs in toxicology), the Agency draws attention to:

- The fact that the present study was unable to determine the exposure of breastfed children to different substances. In this framework, the CONTA-LAIT study under way will help obtain data on the contamination of breast milk in France, and therefore enable the benefits and risks associated with breastfeeding to be assessed.

- The need to examine the risk associated with nanoparticle preparations. On this issue, the Agency recommends a dedicated approach to these substances, in both children and adults, which is already on the Agency's agenda. In addition, the present study has helped with the establishment of a sample bank, which may be useful for the identification of emerging substances of concern.

- The need to acquire data on the endocrine-disrupting nature of certain substances, through suitable research projects and an adequate expert appraisal on these bases, like the work conducted in the framework of the Third National Environmental Health Action Plan and the National Endocrine Disruptor Strategy, in which the Agency is a stakeholder.

Roger GENET

REFERENCES

ANSES. 2011. Avis de l'ANSES relatif à la révision des teneurs maximales en cadmium des denrées alimentaires destinées à l'homme [ANSES Opinion on the revision of maximum levels of cadmium in foodstuffs intended for humans]. (Request No 2011-SA-0194). Maisons-Alfort: ANSES.

ANSES. 2013a. Avis de l'ANSES et rapport d'expertise collective relatifs à l'évaluation des risques du bisphénol A (BPA) pour la santé humaine [ANSES Opinion and Collective Expert Appraisal Report on the assessment of the risks associated with bisphenol A (BPA) for human health]. (Request Nos 2009-SA-0331 and 2010-SA-0197). Maisons-Alfort: ANSES.

ANSES. 2013b. Avis de l'ANSES relatif aux recommandations sur les bénéfices et les risques liés à la consommation de produits de la pêche dans le cadre de l'actualisation des repères nutritionnels du PNNS [ANSES Opinion on the recommendations on the benefits and risks of consumption of fishery products in the context of updating the PNNS nutritional guidelines]. (Request No 2012-SA-0202). Maisons-Alfort: ANSES.

ANSES. 2013c. Avis de l'ANSES relatif aux risques liés à l'utilisation de boissons autres que le lait maternel et les substituts du lait maternel dans l'alimentation des nourrissons de la naissance à 1 an [ANSES Opinion on the risks of feeding beverages other than breast milk or breast milk substitutes to infants from birth to one year of age]. (Request No 2011-SA-0261). Maisons-Alfort: ANSES.

ANSES. 2014. Rapport d'appui scientifique et technique relatif à l'exposition agrégée au plomb : prise en compte des différentes voies d'exposition [Scientific and technical support report on aggregate exposure to lead: inclusion of the different routes of exposure]. (Support for Request No 2013-SA-0092). Maisons-Alfort: ANSES.

Antignac, J. P., R. Cariou, D. Zalko, A. Berrebi, J. P. Cravedi, D. Maume, P. Marchand, F. Monteau, A. Riu, F. Andre, and B. Le Bizec. 2009. "Exposure assessment of French women and their newborn to brominated flame retardants: determination of tri- to deca- polybromodiphenylethers (PBDE) in maternal adipose tissue, serum, breast milk and cord serum." *Environ Pollut* 157 (1):164-73. doi: 10.1016/j.envpol.2008.07.008.

Beko, G., C. J. Weschler, S. Langer, M. Callesen, J. Toftum, and G. Clausen. 2013. "Children's phthalate intakes and resultant cumulative exposures estimated from urine compared with estimates from dust ingestion, inhalation and dermal absorption in their homes and daycare centers." *PLoS One* 8 (4):e62442. doi: 10.1371/journal.pone.0062442.

Bemrah, N., J. Jean, G. Riviere, M. Sanaa, S. Leconte, M. Bachelot, Y. Deceuninck, B. L. Bizec, X. Dauchy, A. C. Roudot, V. Camel, K. Grob, C. Feidt, N. Picard-Hagen, P. M. Badot, F. Foures, and J. C. Leblanc. 2014. "Assessment of dietary exposure to bisphenol A in the French population with a special focus on risk characterisation for pregnant French women." *Food Chem Toxicol* 72:90-7. doi: 10.1016/j.fct.2014.07.005.

Brucker-Davis, F., K. Wagner-Mahler, L. Bornebusch, I. Delattre, P. Ferrari, J. Gal, M. Boda-Buccino, P. Pacini, C. Tommasi, P. Azuar, A. Bongain, and P. Fenichel. 2010. "Exposure to selected endocrine disruptors and neonatal outcome of 86 healthy boys from Nice area (France)." *Chemosphere* 81 (2):169-76. doi: 10.1016/j.chemosphere.2010.06.068.

Cariou, R., J. P. Antignac, D. Zalko, A. Berrebi, J. P. Cravedi, D. Maume, P. Marchand, F. Monteau, A. Riu, F. Andre, and B. Le Bizec. 2008. "Exposure assessment of French women and their newborns to

tetrabromobisphenol-A: occurrence measurements in maternal adipose tissue, serum, breast milk and cord serum." *Chemosphere* 73 (7):1036-41. doi: 10.1016/j.chemosphere.2008.07.084.

Cerna, M., V. Bencko, M. Brabec, J. Smid, A. Krskova, and L. Jech. 2010. "Exposure assessment of breast-fed infants in the Czech Republic to indicator PCBs and selected chlorinated pesticides: area-related differences." *Chemosphere* 78 (2):160-8. doi: 10.1016/j.chemosphere.2009.09.062.

Chovancova, J., K. Conka, A. Kocan, and Z. S. Sejakova. 2011. "PCDD, PCDF, PCB and PBDE concentrations in breast milk of mothers residing in selected areas of Slovakia." *Chemosphere* 83 (10):1383-90. doi: 10.1016/j.chemosphere.2011.02.070.

Cok, I., M. K. Donmez, M. Uner, E. Demirkaya, B. Henkelmann, H. Shen, J. Kotalik, and K. W. Schramm. 2009. "Polychlorinated dibenzo-p-dioxins, dibenzofurans and polychlorinated biphenyls levels in human breast milk from different regions of Turkey." *Chemosphere* 76 (11):1563-71. doi: 10.1016/j.chemosphere.2009.05.032.

de Lauzon, B., J. L. Volatier, and A. Martin. 2004. "A Monte Carlo simulation to validate the EAR cut-point method for assessing the prevalence of nutrient inadequacy at the population level." *Public Health Nutr* 7 (7):893-900.

EFSA. 2009. Scientific opinion of the EFSA Panel on Contaminants in the Food Chain on Cadmium in food. In *The EFSA journal*. Parma: EFSA.

EFSA. 2010. Scientific Opinion of the EFSA panel on Dietetic Products, Nutrition, and Allergies on principles for deriving and applying Dietary Reference Values. In *The EFSA journal*. Parma: EFSA.

EFSA. 2011. Scientific Opinion of the EFSA Panel on Contaminants in the Food Chain on Polybrominated Diphenyl Ethers (PBDEs) in Food. In *The EFSA journal*. Parma: EFSA.

EFSA. 2012. Scientific Opinion of the EFSA Panel on Contaminants in the Food Chain on Emerging and Novel Brominated Flame Retardants (BFRs) in Food. In *The EFSA journal*. Parma: EFSA.

EFSA. 2013a. Analysis of occurrence of 3-monochloropropane-1,2-diol (3-MCPD) in food in Europe in the years 2009-2011 and preliminary exposure assessment. In *The EFSA journal*. Parma: EFSA.

EFSA. 2013b. Scientific Opinion of the EFSA Panel on Dietetic Products, Nutrition and Allergies on nutrient requirements and dietary intakes of infants and young children in the European Union. In *The EFSA journal*. Parma: EFSA.

EFSA. 2013c. Scientific Opinion of the EFSA Panel on Plant Protection Products and their Residues on the identification of pesticides to be included in cumulative assessment groups on the basis of their toxicological profile. In *The EFSA journal*. Parma: EFSA.

EFSA. 2015. Scientific Opinion of the EFSA Panel on Food Additives and Nutrient Sources Added to Food on the re-evaluation of ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives. In *The EFSA journal*. Parma: EFSA.

Fantino, M., and E. Gourmet. 2008. "Apports nutritionnels en France en 2005 chez les enfants non allaités âgés de moins de 36 mois." *Arch Pediatr* 15 (4):446-55. doi: 10.1016/j.arcped.2008.03.002.

Fenton, S. E., M. Condon, A. S. Ettinger, J. S. LaKind, A. Mason, M. McDiarmid, Z. Qian, and S. G. Selevan. 2005. "Collection and use of exposure data from human milk biomonitoring in the United States." *J Toxicol Environ Health A* 68 (20):1691-712. doi: 10.1080/15287390500225708.

Fromme, H., S. A. Tittlemier, W. Volkel, M. Wilhelm, and D. Twardella. 2009. "Perfluorinated compounds--exposure assessment for the general population in Western countries." *Int J Hyg Environ Health* 212 (3):239-70. doi: 10.1016/j.ijheh.2008.04.007.

Hulin, M., N. Bemrah, A. Nougadère, J. L. Volatier, V. Sirot, and J. C. Leblanc. 2014. "Assessment of infant exposure to food chemicals: the French Total Diet Study design." *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* 31 (7):1226-39. doi: 10.1080/19440049.2014.921937.

INSERM. 2011. Reproduction et environnement. In *Expertise collective*. Paris: INSERM.

INVS/CAREPS. 2000. Etude sur les dioxines et les furanes dans le lait maternel en France.

IOM. 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. edited by National Academy Press. Washington, D.C.: IOM.

IOM. 2011. Dietary Reference Intakes for Calcium and Vitamin D. edited by The National Academies Press. Washington, DC IOM.

Johnson-Restrepo, B., R. Addink, C. Wong, K. Arcaro, and K. Kannan. 2007. "Polybrominated diphenyl ethers and organochlorine pesticides in human breast milk from Massachusetts, USA." *J Environ Monit* 9 (11):1205-12. doi: 10.1039/b711409p.

Kadar, H., B. Veyrand, A. Barbarossa, G. Pagliuca, A. Legrand, C. Bosher, C. Y. Boquien, S. Durand, F. Monteau, J. P. Antignac, and B. Le Bizec. 2011. "Development of an analytical strategy based on liquid chromatography-high resolution mass spectrometry for measuring perfluorinated compounds in human breast milk: application to the generation of preliminary data regarding perinatal exposure in France." *Chemosphere* 85 (3):473-80. doi: 10.1016/j.chemosphere.2011.07.077.

Munoz, G. 2015. "Ecodynamique des composés poly- et perfluoroalkylés dans les écosystèmes aquatiques." Thèse de doctorat en Chimie analytique et environnementale, École doctorale des Sciences chimiques (Bordeaux).

Park, J. S., J. She, A. Holden, M. Sharp, R. Gephart, G. Souders-Mason, V. Zhang, J. Chow, B. Leslie, and K. Hooper. 2011. "High postnatal exposures to polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) via breast milk in California: does BDE-209 transfer to breast milk?" *Environ Sci Technol* 45 (10):4579-85. doi: 10.1021/es103881n.

PNNS. 2004. Livret d'accompagnement du "Guide nutrition des enfants et ados pour tous les parents" destiné aux professionnels de santé. AFSSA, InVS, Ministère de la Santé et des Sports, L'assurance Maladie, INPES.

Schettler, T. 2006. "Human exposure to phthalates via consumer products." *Int J Androl* 29 (1):134-9; discussion 181-5. doi: 10.1111/j.1365-2605.2005.00567.x.

Touvier, M, S Lioret, I Vanrullen, J C Boclé, M C Boutron-Ruault, J L Berta, and J L Volatier. 2006. "Vitamin and mineral inadequacy in the French population: estimation and application for the optimization of food fortification." *Int J Vitam Nutr Res* 76 (6):343-51. doi: 10.1024/0300-9831.76.6.343.

Ulaszewska, M. M., E. Zuccato, and E. Davoli. 2011. "PCDD/Fs and dioxin-like PCBs in human milk and estimation of infants' daily intake: a review." *Chemosphere* 83 (6):774-82. doi: 10.1016/j.chemosphere.2011.02.066.

Wagner, S., C. Kersuzan, S. Gojard, C. Tichit, S. Nicklaus, B. Geay, X. Humeau, M.A. Charles, S. Lioret, and B. De Lauzon-Guillain. 2015. "Durée de l'allaitement en France selon les caractéristiques des parents et de la naissance. Résultats de l'étude longitudinale française Elfe, 2011." *Bull Epidémiol Hebd* 29:522-32.

ANNEX

Changes to the version dated 30 August 2016.

Page 3 and 15: The number of substances for which the exposure was assessed is 500 (instead of 490)
Page 15: The number of substances for which the risk was assessed is 400 (instead of 366) and clarification was added on the substances requiring a reduction in exposure
Page 18, and Table 9 page 21: Clarification relating to selenium was provided
Page 24: The number of substances for which the risk was assessed was removed

COLLECTIVE EXPERT APPRAISAL:
SUMMARY AND CONCLUSIONS

on "the infant total diet study (iTDS)"

This document, which has been validated by the Expert Committee on "Assessment of physico-chemical risks in food", summarises the report on the infant total diet study

---

Presentation of the issue

On 17 September 2010, the French Agency for Food, Environmental and Occupational Health & Safety issued an internal request for an opinion on the total diet study concerning dietary exposure of children under three years of age to certain substances in France.

All the data produced in the course of the infant total diet study (iTDS) have been examined in a scientific expert appraisal report. The present summary, drawn up by the Expert Committee on "Assessment of physico-chemical risks in food" (CES ERCA), focuses on the objectives, the method and the main results by class of substances. Lastly, a cross-sectional analysis of the data, carried out by the CES ERCA and supplemented by ANSES's main conclusions on this study, is available in the opinion.

Scientific background and purpose of the study

Knowledge of the possible contamination and nutrient composition of foods constitutes a major tool for protecting health, as it helps document dietary exposure to microbiological, chemical and physical agents, as well as nutrient intakes. This exposure is then used to assess the risks for the population and therefore to inform decision-making in risk management (control and regulation), at the national, European and international levels.

In France, monitoring of food contamination by substances regularly takes place in a regulatory framework through control and surveillance plans, led by the competent ministries. However, the resulting contamination data are insufficient (restricted sampling method, products not prepared, limited coverage of the total diet, no nutrients, etc.) for precisely estimating the exposure or intake levels of the French population.

"Total Diet Studies" (TDSs) are cross-cutting national surveys designed to analyse a large number of substances in food samples defined with the aim of reflecting the diet of the population under study. To achieve this, they rely on food surveys. TDSs make it possible to identify the substances for which there is a risk of inadequate intake (for minerals) and/or excessive exposure (for contaminants) in the population, and the food vectors contributing most to this intake or exposure. In France, two total diet studies have been conducted to date (TDS1 in 2005 and TDS2 in 2011), targeting adults and children over three years of age.

The infant total diet study (iTDS) is one of the first studies to estimate the dietary exposure of children under three years of age (non-breastfed infants) to 670 substances (mainly environmental contaminants, minerals and pesticide residues). The population of children under three years of age has two specific characteristics that justify this study: they are more vulnerable individuals (possible impact of certain substances on the stages of development), and they consume specific food products (foods intended for infants and young children) for which there are very few concentration data (on contamination or nutrients).

Given the methodology of the present study, issues related to breastfeeding have not been taken into account. Nevertheless, a specific study of this practice has been set up by ANSES to determine the exposure of breastfed children to certain environmental contaminants.

This study therefore makes it possible to describe the composition and contamination levels of foods consumed by children under three years of age as well as the chronic exposure levels of this population. On the basis of these data, a health risk assessment (HRA) was carried out to identify the substances for which a risk of insufficient and/or excessive intake or exposure cannot be ruled out. Apart from this first assessment, presented in this report, these data constitute a source of information for more complex questions requiring longer term analysis, such as that of mixtures of exposure or aggregate exposure.

Organisation of the expert appraisal

Overall, the study method, all the results, their interpretation and the conclusions and recommendations were discussed and validated by the iTDS Working Group (iTDS WG) and the Expert Committee (CES) on "Assessment of physico-chemical risks in food" (ERCA).

An additional working group was created in the framework of this study: the WG on "Analytical methods in food" (AMF WG), in order to appraise the methods and the analytical results. Moreover, the CES rapporteurs carried out an in-depth reflection on the applicability of the toxicity reference values to the child population.

Selection of the reference values and interpretation of the results were entrusted to the:

- CES ERCA for chemical contaminants;

- CES on "Human nutrition" for minerals;

- CES on "Plant protection products: chemical substances and preparations" for pesticide residues.

- WG on "Assessment of substances and processes subject to authorisation in human food" for food additives.

The CES on "Water" and the WG on "Assessment of the health risks associated with chemical parameters of water intended for human consumption" (WG HRA WIHC) were consulted on issues specific to the water matrix.

Lastly, this opinion was submitted to the CES ERCA for validation.

Description of the method

Choice of the substances

The iTDS was established to follow on from TDS2, and therefore all the groups of substances considered in the TDS2 were analysed here: metal and mineral trace elements, polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/Fs), polychlorinated biphenyls (PCBs), perfluoroalkyl acids (PFAAs, more commonly known as perfluorinated compounds), brominated flame retardants, mycotoxins, phyto-oestrogens, heat-induced compounds, plant protection product residues and food additives. For these last two groups, a selection process specific to the population of children under three years of age was conducted.

The additives were selected on the basis of the step-by-step approach recommended by the European Commission for assessing chronic exposure to food additives (European Commission 1998). Only baby foods and the additives authorised in these foodstuffs were considered.

Concerning pesticide residues, a priority list was drawn up. It includes active plant protection substances approved according to Regulation (EC) No 1107/2009 during the study's sampling period, substances that are not approved but that were detected within the framework of national surveillance plans, and older pesticide residues that are prohibited as persistent organic pollutants (POPs). A total of 84 priority pesticide residues and their metabolites were identified. As multi-residue analytical methods were often used, analytical results were ultimately obtained for 469 pesticide residues and their metabolites.

Other substances that were not screened for in the TDS2 were analysed specifically in the iTDS because of questions being raised about the health risk, of a general nature or specific to the population considered, and for which there are few French data on food contamination. This particularly concerns substances migrating from food contact materials (FCMs): certain bisphenols (BPA and bisphenol A diglycidyl ether or BADGE), phthalates, ink photoinitiators and alkylphenols.

Some substances such as tocopherols (E306-E309), as well as twelve priority pesticide residues, were not included in the study because of their chemical instability and the sampling method. Sodium acetate was also excluded from the study because the share of exposure attributable to its use as an additive is negligible in comparison to intake via natural sources in food (TemaNord 2002). Nitrosamines, which were initially targeted, were not ultimately screened for because exposure via food represents a minority compared to that from the endogenous transformation of nitrates/nitrites in the body (AFSCA 2010).

In total, 670 substances were screened for in the foods, and dietary exposure was assessed for 500 of them. The full list of substances is provided in an annex (Annex 1).

Consumption data

In order to determine the foods to be sampled in the infant TDS, the latest French food consumption data for children under three years of age available at the time of implementation

of the sampling plan[1] were used. These are data from the "BEBE-SFAE" 2005 study, carried out by TNS-Sofres-CHU Dijon for the French Association for Children's Food (SFAE) (Fantino and Gourmet 2008). This cross-sectional survey was conducted between January and March 2005, on a representative national sample of infants and young children in France, non-breastfed (even partially) at the time of the study.

For each child, the care-givers (most often the mother and/or the nanny, with the participation of the father) were asked to note all food consumption using a food diary over three consecutive days, including a weekend day. The portion sizes of each food consumed were noted as well as the body weight of each child.

A total of 705 children were considered. In order to take into account possible dietary differences between 1 and 36 months, the study population was divided into four age groups. These groups were defined on the basis of the stages of food diversification (

Table 1): an exclusively milk-based diet, the beginning of food diversification with the introduction of vegetables and/or fruit, introduction of meat/fish/eggs, etc.

TABLE 1: BREAKDOWN BY AGE GROUP CORRESPONDING TO THE DIFFERENT STAGES OF FOOD DIVERSIFICATION

Age groups	Introduction of foods*
1-4 months	First infant formulas[2]
5-6 months	Follow-on formulas
7-12 months	+ dairy products, fruits, vegetables, potatoes, meat, fish, hard-boiled eggs, added fat
13-36 months	+ growing-up milk, fruit and vegetables in pieces, pulses, salt

*Extract from the companion booklet to the Nutrition Guide for children and teens intended for health professionals (PNNS 2004).

Choice and collection of the foods studied

In order to better reflect reality, the selection of foods to be sampled was based on data on consumption but also on purchases and preparation practices. The foods selected were therefore:

- the most widely consumed in terms of quantity and/or percentage of consumers;

- identified as major known or assumed contributors for at least one of the targeted substances.

A study was set up in 2011 to determine the common preparation practices of parents of children under three years of age (Hulin et al. 2014). The information thus collected helped define how to prepare the different foods to be analysed.

---

[1] The sampling plan was drawn up between October 2010 and June 2011.
[2] This name commonly refers to industrial formulas intended specifically for young children. Their regulatory designation is "formula" and not "milk". Indeed, while the majority of these foods are manufactured from constituents of cow milk, certain formulas are made from other products (for example, soy). But regardless of their designation, they are all foods specifically designed for a healthy full-term child, from birth to the age of three years (Source: INPES, Nutrition Guide from birth to three years).

In order to reduce the number of samples for analysis, foods were organised into groups according to:
- their similarity in nutritional composition, and their level of contamination (for example biscuits that were filled or covered with chocolate, etc.),

- if possible, the associated brand, in order to take brand loyalty into account for certain products (especially for infant formulas and jars of baby food).

Lastly, because the type and brands of water used to dilute the infant formulas were not provided in the consumption study, a specific study was conducted to obtain this information and take it into account in the process for selecting the foods to be considered.

After organising the foods into groups, 314 food items were defined: 219 infant foods and 68 normal foods, accompanied by a further 27 common foods that are major potential contributors.

To take into account seasonal variability, possible different flavours, and different ways of consuming or preparing foods, all the analysed samples, referred to as "composites" or "pools", were formed of 12 sub-samples of the same food and of equal weight. This approach has the advantage of covering a wide variety of foods while limiting the number of samples to be analysed. It also makes it possible to obtain a close estimate of the mean content of a food item, although it limits the detection of high one-time contamination.

Lastly, for some items for which the packaging type can influence the content of certain substances derived from FCMs, several samples were taken.

In total, the sampling plan consisted of 457 composite food samples, corresponding to 5,484 food products (sub-samples) purchased and prepared. The sampling phase took place between July 2011 and July 2012 in a single region of France (the Centre region).

The products purchased were prepared in a way that reflected as closely as possible what is done in the home: preparation (removal of the non-edible part, washing of foods, etc.) and cooking (duration and power, addition or not of salt, fat, etc.). The infant formulas were diluted and heated most of the time, prepared baby dishes were reheated, vegetables (excluding raw vegetables), meat and fish were cooked according to the practices reported in the survey on practices.

The 12 sub-samples, stored at -18°C until the end of the sampling stage, were then pooled and placed in batches. Pooling consisted in first cryogrinding[3] an equivalent quantity of the 12 sub-samples and then homogenising the composite sample without thawing.

Defining the sampling plan in this way enabled it to cover more than 95% of the diet of children under 36 months of age: between 92 and 100% for normal food and between 95 and 98% for infant food, depending on the age group. For certain substances, the use of concentration data from the TDS2, and other sources of data for water ultimately made it possible to achieve a

---

[3] Cryogrinding involves crushing the entire sub-sample initially in a frozen state and then maintaining this state through the addition of liquid nitrogen, which avoids the warming of the sample and all the peroxidation processes that generate toxic by-products.

coverage rate for all of the sampling (iTDS + other sources) of between 97% and 98% depending on the age group.

The different steps, from the selection of foods through to the despatch of the batches to the laboratories, are shown in Figure 1.

FIGURE 1: THE FOOD SAMPLING STEPS FOR THE ITDS

Implementation of the sampling plan

Selection of foods to be sampled
-Updating of consumption data
-Identification of the foods consumed most often and the known or assumed contributors to exposure from a consumption study ("BEBE-SFAE" 2005)

Identification of the preparation practices
-Establishment of a national study on preparation practices
-Determination of the most common practices

Identification of composite samples and sub-samples
-Definition of the list of samples
-Determination of the 12 sub-samples making up each sample (the composite sample) on the basis of data on household consumption/purchasing and preparation practices

Collection and preparation of samples

Constitution of the sub-samples
-1 sub-sample per month for 12 months for each composite sample
-5,484 products purchased and prepared "as consumed"

Grouping of sub-samples into composite samples
-Storage of sub-samples at -18°C
-After 12 months, creation of 457 "pools" of composite samples from the different sub-samples
-Homogenisation and batching of composite samples

Sending of batches to the different laboratories

Analysis of samples

Analysis of samples

The choice of the food-substance pairs analysed drew on the data available in the TDS2, the literature on concentration levels in the different foods and/or the regulations, the opinions of experts or expert appraisals by laboratories. In most cases, the substances targeted in this study were not screened for in all of the food matrices but only in those known or assumed to be contributors to exposure.

In order to obtain an estimate of exposure that was as accurate as possible and limit the uncertainties associated with the processing of results below the analytical limits (known as censored data), the analytical limits to be achieved (limits of detection and quantification) were calculated to obtain an estimate of exposure that would enable a conclusion to be reached as to the risk, even in the absence of quantification (Hulin et al. 2014). For each of the substances, the laboratories were asked to achieve analytical limits as close as possible to these target limits. Consequently, the analytical limits for several substances or groups of substances were lowered compared to the TDS2 or to other previous assessments.

The analyses were carried out by around ten analytical laboratories, depending on the substances and matrices targeted.

Processing of analytical results

Validation of the analytical results included the assessment of firstly the analytical methods and secondly the quality of the datasets, including the taking into account of analytical blanks.

Censored data (results below the limits of detection (LOD) and quantification (LOQ)) were processed according to a substitution method that involved framing the actual level using the lowest (low assumption or lower-bound (LB)) and highest (high assumption or upper-bound (UB)) values possible. The low assumption was calculated by assuming that all values below the LOD are equal to zero and those between the LOD and the LOQ are equal to the LOD. The high assumption was calculated by assuming that all values below the LOD are equal to the LOD and those between the LOD and the LOQ are equal to the LOQ.

Mercury, arsenic and chromium were analysed in foods in their total form. However, the toxicity of these elements is dependent on their chemical form. In order to estimate the risk associated with each of these forms, speciation assumptions, most often from the literature, were applied to the concentration data.

In some cases, it made more sense from a toxicology point of view to group several substances together for the HRA. For example, the levels of several congeners of dioxins and furans were added together for each sample, through the use of a toxic equivalency factor (TEF). This approach was also used for PBBs, HBCDDs, PBDEs, PCBs, and aflatoxins and pesticide residues falling within the same regulatory definition.

Assessment of intakes and exposure

Exposure to contaminants was calculated individually for all the children in the consumption study, according to the following formula:

$$E_{i,j} = \frac{\sum_{k=1}^{n} C_{i,k} \times L_{k,j}}{BW_i}$$

where $E_{i,j}$ is the mean daily exposure to contaminant j of individual i, n is the number of foods in the diet, $C_{i,k}$ is the daily consumption of food k by individual i, $L_{k,j}$ is the level of contaminant j in food k, and BW_i is the body weight of individual i.

Similarly, the nutrient intakes were calculated according to the formula:

$I_{i,j} = \sum_{k=1}^{n} C_{i,k} \times L_{k,j}$ where $I_{i,j}$ is the mean daily intake of nutrient j by individual i, n is the number of foods in the diet, $C_{i,k}$ is the daily consumption of food k by individual i, and $L_{k,j}$ is the level of nutrient j in food k.

Allocation of the concentration data to each food consumed by an individual took into account:

- their home region for the regional concentration data produced by studies other than the iTDS (TDS2, SISE-EAUX, Lead in the Home[4]),

- the type of packaging for the food consumed,

- the type and brand, where appropriate, of water used to reconstitute the products to be diluted (mainly the infant formulas).

On the basis of these data, different descriptive statistics were calculated: mean, median (p50), p90 (and p10 in the case of nutrient intakes). Mean exposure of the most exposed individuals, i.e. those whose exposure was above the p90 of exposure for their age group, was also calculated, as were the mean dietary intakes of children with the lowest intakes (<p10). The share (%) of intake or exposure attributable to each category of food was then calculated in order to identify the major contributors to this intake or exposure.

Health risk assessment process from a toxicological perspective

Choice of toxicity reference values (TRVs)

In order to characterise the risks to the infant population, the calculated exposures were compared with the reference values, referred to as "TRVs" in this study: acceptable or tolerable daily intake (ADI or TDI), provisional tolerable weekly intake (PTWI), provisional tolerable monthly intake (PTMI), no-effect level, benchmark dose limit (BMDL), tolerable upper intake levels (UL).

For each substance, selection of the TRV drew on an analysis of the TRVs established by the main French, European or international scientific bodies (ANSES, EFSA, WHO, US-EPA, ATSDR, JECFA, etc.) and on criteria of robustness.

As the infant population was specifically targeted in this study, at the very least the experts determined whether the selected TRVs could be applied to this population, mainly by confirming that toxicological data specific to the infant population (perinatal and postnatal toxicity studies, developmental toxicity studies, reproduction studies over several generations, etc.) had been taken into account when establishing each of these TRVs.

---

[4] (Lucas et al. 2012)

Thus, depending on the contaminant considered, four groups of TRVs were defined:

- Group 0: Total absence of a TRV or absence of a robust TRV for the adult population.
- Group 1: Robust TRV for the adult population but no data for deciding on its applicability to the infant population.
- Group 2: TRV applied to the infant population because reprotoxicity/developmental or multigenerational studies had been taken into account, but in the absence of a comprehensive expert appraisal of the toxicological data.
- Group 3: Protective TRV for the infant population (this is the case with deoxynivalenol (DON) and acrylamide) following a comprehensive expert appraisal of the toxicological data.

For each substance, any possible limitations relating to the applicability of the selected TRVs to the infant population have been taken into account in the interpretation of the HRA results.

Lastly, some of the substances (phthalates, brominated flame retardants, perfluorinated compounds and alkylphenols in particular) will be undergoing expert appraisal at ANSES in the framework of the Working Group on "Endocrine Disruptors" (WG ED) for example. The ultimate objective of this work will be to establish TRVs that take into account the endocrine-disrupting nature of the substances. It cannot therefore be ruled out that some values proposed in the present study differ from those that may be proposed in the future.

The different HRA approaches from a toxicological perspective

The health risk assessment (HRA) was conducted bearing in mind the limitations to the applicability of the selected TRVs to the infant population (

Table 2).

TABLE 2: HEALTH RISK ASSESSMENT (HRA) FROM A TOXICOLOGICAL PERSPECTIVE ACCORDING TO THE RELEVANCE OF THE SELECTED REFERENCE VALUES

Categories of TRV according to their robustness (group defined above)	HRA process
Absence of a TRV or TRV not deemed to be robust for the adult population (Group 0)	No HRA
Robust TRV for the adult population but no evidence relating to its applicability to the infant population (Group 1)	HRA, but uncertainty taken into account in the interpretation of the results*
TRV applied to the infant population because reprotoxicity/developmental or multigenerational studies had been taken into account, but in the absence of a comprehensive expert appraisal of the toxicological data (Group 2)	HRA
Protective TRV for the infant population (Group 3)	

* If no excessive exposure was observed for the population under three years of age but the estimated exposure was close to the selected TRV, it was considered that the health risk could not be ruled out with certainty. Exposure is

considered to be close to a reference value when the ratio between the two is less than a factor of 10. This factor of 10 corresponds to the default factors generally used to establish TRVs.

For substances with a "threshold" TRV (ADI/TDI, (P)TWI, (P)TMI, etc.) individual exposures were compared directly to the TRVs. For each age group, the percentage of individuals in the study whose exposure was above the TRV was calculated, accompanied by its confidence interval at 95%. When this excessive exposure concerned fewer than five children, it was indicated that the limits had been exceeded, but that it was difficult to estimate the proportion in light of limitations related to the sampling or to the measurement of exposure (excessive exposure not robust).

In the case of substances with a BMDL ("threshold" or "non-threshold" substance), the risk was characterised by calculating a margin of exposure (MOE) or margin of safety (MOS), corresponding to the ratio between a critical exposure (BMDL, for example) and the mean exposure of the population or exposure at a high percentile. This margin was then compared to a critical margin defined when the BMDL was established by national and international bodies, in order to conclude as to the risk to the population.

On the basis of these results, and depending on the robustness of the TRV and its applicability to the infant population, characterisation of the risk for all the substances studied was summarised into four categories (Table 3).

TABLE 3: CONCLUSIONS REACHED ACCORDING TO CHARACTERISATION OF THE TOXICOLOGICAL RISK

Results	Risk phrase
TRV exceeded significantly or low margin of exposure	**Situation identified as a concern**
Limits not exceeded significantly or robustly or Limits exceeded significantly and robustly under the high assumption (UB) only, i.e. the scenario that overestimates levels and therefore exposure or Limits not exceeded with a robust TRV only for the adult population but exposure close	**Risk cannot be ruled out**
TRV not exceeded or margin of exposure sufficiently high (proposed for each substance)	**Risk considered tolerable* or acceptable***
Conditions are not conducive to conducting a relevant HRA. Example: toxicological point of departure not established due to a lack of data or not considered sufficiently robust	**Impossible to reach a conclusion as to the risk**

* The term "tolerable" is used for substances found unintentionally in foods (for example, persistent organic pollutants or mycotoxins). A TRV such as a tolerable daily/weekly/monthly intake (TDI, TWI, TMI, etc.) is then used. The term "acceptable" is used to characterise the risk in the case of substances whose use is subject to a

prior assessment (for example, additives or residues of plant protection products). A TRV such as an acceptable daily intake (ADI) is then used.

Health risk assessment process from a nutritional perspective

Choice of nutritional references

Work to update the nutritional references for minerals for children under three years of age was carried out for this study on the basis of data and nutritional references from different European (EFSA[5]), North American (IOM[6]) and international (WHO[7]) organisations.

Concerning the population of infants under six months of age, the adequate intakes (AIs) presented by EFSA in 2013 (EFSA 2013) and regarded by ANSES as adequate intakes (AS - *apports satisfaisants*) or, where they were lacking, other intakes regarded by EFSA as adequate, were used. The AS corresponds to the mean intake level observed or estimated for a group of individuals in apparent good health and regarded as satisfactory.

Concerning children over six months of age, the nutritional reference selected was the AS or the average requirement (AR) updated by EFSA from 2013. The AR corresponds to the average daily nutritional intake able to cover the needs of half of the healthy individuals in a population group of a given age and sex (Touvier et al. 2006).

Regarding the tolerable upper intake levels (ULs) for minerals, the values proposed by EFSA in 2006 were used. When EFSA was unable to establish ULs, due to a lack of data, the values proposed by the IOM (IOM 2001, 2011) were taken into consideration. All these ULs were established either from studies on the infant population, or when relevant, by extrapolation of the ULs established for the adult population, on the basis of body weight.

The different HRA approaches from the nutritional perspective

Concerning the health risk assessment (HRA) of excessive mineral intake, the percentage of children whose intakes were higher than the selected UL was calculated, as well as its confidence interval at 95%. The same assumptions of robustness were used to calculate this percentage, and the method of interpretation was the same as for the toxicological risk.

Concerning the HRA of insufficient intake, the approach described by EFSA in 2010 was followed for minerals for which only an AS (adequate intake or, where it was lacking, another intake regarded as adequate) had been established (EFSA 2010). In these cases, the mean intakes were compared directly to the AS in order to appraise the situation (Table 4). For minerals for which the average requirement (AR) had been determined, inadequate intake was calculated on the basis of the AR cut-off point method (de Lauzon, Volatier, and Martin 2004) by

---

[5] European Food Safety Authority
[6] Institute of Medicine
[7] World Health Organisation

calculating the proportion of children whose intakes were lower than the AR[8] with its confidence interval at 95%.

On the basis of the results, and according to the nutritional references adopted, the degree to which intakes meet needs was summarised into four categories (
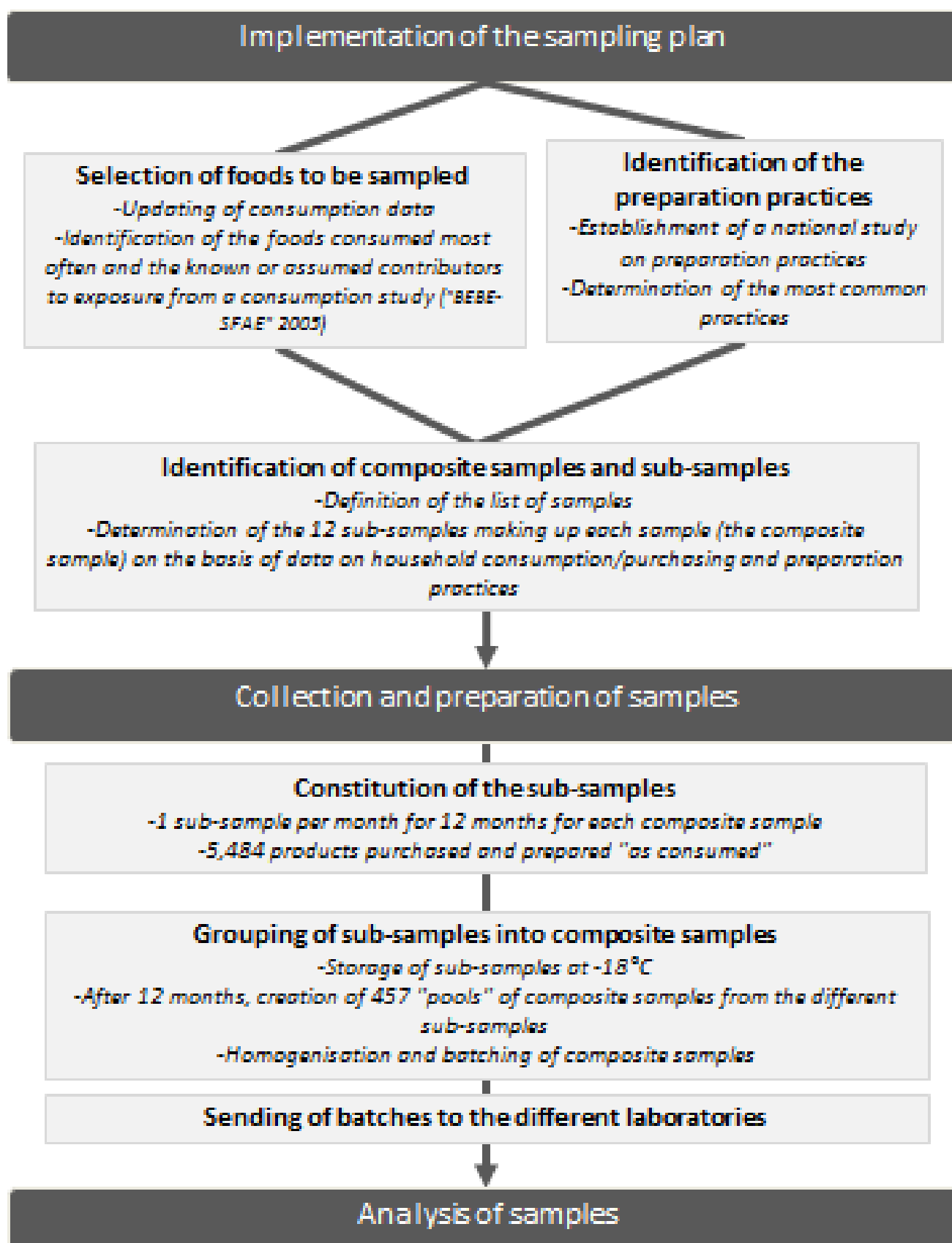
Table 4).

TABLE 4: CONCLUSIONS REACHED ACCORDING TO CHARACTERISATION OF THE RISK OF INSUFFICIENT NUTRIENT INTAKE IN MINERALS

Results	Risk phrase
Mean intake of the population above the AS or intake above the AR for the whole of the population considered	**Intakes meet needs at a generally satisfactory level**
Intake below the AR for a significant number of individuals	**Risk of insufficient intake for some groups of consumers**
Mean intake of the population below the AS	**Impossible to know whether needs are met and to what extent**
No nutritional reference selected for the age group considered, or nutritional reference deemed not to be robust	**No conclusion possible regarding inadequate intake**

Figure 2 summarises the steps leading to the exploitation of the results, from the analysis of samples through to the conclusion in terms of risk.

FIGURE 2: THE MAIN STEPS OF THE iTDS, FROM THE ANALYSIS OF SAMPLES THROUGH TO THE CONCLUSION IN TERMS OF RISK

---

[8] This proportion, usually called "prevalence of inadequate intake", will be referred to in this document as "prevalence of insufficient intake", in order to clearly distinguish cases of excessive and insufficient intake.

Implementation of the sampling plan

Selection of foods to be sampled
-Updating of consumption data
-Identification of the foods consumed most often and the known or assumed contributors to exposure from a consumption study ("BEBE-SFAE" 2005)

Identification of the preparation practices
-Establishment of a national study on preparation practices
-Determination of the most common practices

Identification of composite samples and sub-samples
-Definition of the list of samples
-Determination of the 12 sub-samples making up each sample (the composite sample) on the basis of data on household consumption/purchasing and preparation practices

Collection and preparation of samples

Constitution of the sub-samples
-1 sub-sample per month for 12 months for each composite sample
-5,484 products purchased and prepared "as consumed"

Grouping of sub-samples into composite samples
-Storage of sub-samples at -18°C
-After 12 months, creation of 457 "pools" of composite samples from the different sub-samples
-Homogenisation and batching of composite samples

Sending of batches to the different laboratories

Analysis of samples

Limitations

The limitations of the study are defined as being any situation that is not covered by the present study. Some of them will be addressed in the framework of future work to be conducted by ANSES.

As the population of breastfed children was excluded from the consumption study, it was not taken into account for the exposure calculations. However, international data have shown that the presence of certain contaminants in breast milk may lead to a risk for children (Cerna et al. 2010, Chovancova et al. 2011, Cok et al. 2009, EFSA 2011a, Johnson et al. 1986, Johnson-Restrepo et al. 2007, Park et al. 2011, Ulaszewska, Zuccato, and Davoli 2011). In order to gain a better understanding of the French situation, a specific study (CONTA-LAIT) was set up to analyse the contamination of breast milk collected in various milk banks spread throughout France.

Similarly, preterm children and children living outside mainland France (Corsica, the overseas territories) were not included in the consumption study. It was not therefore possible to assess the risk associated with their diet in the iTDS.

The iTDS did not set out to assess acute exposure to a substance at a given time, nor exposure resulting from specific situations such as contamination of food by the local environment (polluted sites, for example), the occasional consumption of food supplements, or specific diets (exclusively "organic" food, for example).

This study mainly targeted substances for which earlier work (toxicological and/or health risk assessments) had suggested a potential risk. However, there are other food contaminants that remain unidentified at the present time, or for which the hazard has only been poorly characterised, or not at all.

This study does not take into account routes of exposure other than food. For certain substances (lead, perfluorinated compounds, cadmium, flame retardants, etc.), these other routes of exposure may be non-negligible in children.

For certain substances that can accumulate in the body (POPs, etc.), exposure of the foetus via maternal exposure can lead to a non-negligible body burden for the child at birth. This prenatal exposure was not taken into account in the present study.

Lastly, "mixture" effects or the potential cumulative effects of different substances were only taken into account when TRVs on the mixtures were selected by the expert committees (this is the case with dioxins and furans, for example). These effects have so far been poorly documented and are still only rarely taken into account when establishing toxicological values. The iTDS will be an important source of data for identifying the cocktails to which children are actually exposed and will make it possible to better study the potential associations between these cocktails of exposures and the health effects.

Uncertainties

The uncertainties listed in Table 5 below may be present at the different steps of the risk assessment and have an impact on the results of the risk assessments conducted in this study. They may lead to the risks being overestimated or underestimated, without it always being possible to correct their impact on the estimates. Where applicable, methodological tools have been used to limit the impact of these uncertainties, always with a view to improving protection.

TABLE 5: SOURCES OF UNCERTAINTY NOTED IN THE iTDS

Sources of uncertainty
Reference values and risk assessment
Validity of the reference value and the available data
Applicability over the period 0-3 years: - From the point of view of the hazard - From the point of view of the comparison with the exposure data (versus lifelong)
Assessment of the hazard associated with several substances ("cocktail" effect), congeners or metabolites
Consumption data and sampling plan
Information not collected in the consumption study
Representativeness of the consumption data
Only taking into account major practices or consumer profiles
Collection of samples and composition and contamination data
Representativeness of the contamination and composition data
Robustness of the data
Use of contamination data for exposure calculations

The sources of uncertainty in the different steps of the health risk assessment, described in the iTDS report, were identified and analysed using a qualitative approach, with the aim of questioning the direction of the impact of each source of uncertainty on the risk estimate. However, it was not possible to reach a conclusion as to the overall impact of these uncertainties on the risk estimate. In most cases, it may underestimate or overestimate the risk. In light of this analysis, the uncertainties that may have a major impact in terms of underestimating the risk are probably those related to the nutritional and toxicological reference values and specifically in connection with the period examined in this study (applicability of values to children aged 0-3 years in terms of susceptibility and exposure) and the failure to take into account the potential cumulative effects of different substances in the health risk assessment. To obtain a more precise estimate of the impact of these uncertainties, their amplitude should be analysed and characterised for each of the substances considered.

Concerning the question of the applicability of the reference values to the population under three years of age, two uncertainties remain:

1. The infant population may have particular susceptibility to certain substances. A specific process was therefore set up to decide on the relevance of the reference values, usually defined for the general population, in light of the specificities of the infant population (see the toxicological HRA process).
   For some substances, it was not possible to demonstrate the applicability of the selected TRV to the infant population. In this case and where the TRV was not exceeded, the risk may be underestimated. To compensate for this uncertainty:

- the health risk was not ruled out when exposure was considered to be too close to this value[9];
- an additional literature review is needed to determine the extent to which a new reference value should be defined for the infant population and a new risk assessment conducted.

2. There may also be uncertainties according to the mechanism of action (particularly for substances that accumulate in the body) due to the comparison of TRVs, which are normally established for "lifelong" exposure, with a duration of exposure that is limited in time (here, less than three years). Despite this uncertainty, it was considered that cases where the TRV was exceeded nonetheless made it possible to identify substances that could present a potential risk and that should therefore be studied more specifically.

Regarding the cumulative effects, for certain classes of substances, the hazard is characterised not for one given substance but for several congeners (in the case of PCBs for example) or for a parent substance and its metabolites (in the case of certain pesticides, for example). Thus, within the same class of substances, toxic equivalency factors were taken into account to express the toxic potential of the congeners or metabolites compared to the reference substance, according to the principle of additivity of effects. The risk calculated substance by substance may therefore underestimate the actual risk considering the cumulative effects.

Results of the collective expert appraisal

Summary of results by class of substances

The daily dietary exposure of an individual to a substance is the daily intake of this substance via food relative to the body weight. This intake corresponds to the sum, for all foods consumed, of the quantity of each food consumed multiplied by the concentration of the substance in this food.

The consumption study on children under three years of age identified different stages in their diet (Table 1): an exclusively milk-based diet, and then the beginning of food diversification with the introduction of vegetables and/or fruit, introduction of meat/fish/eggs, etc.

In order to take into account the development of the diet as the individuals grow, exposure was estimated at the different stages of the diet corresponding to the following age groups: 1-4 months, 5-6 months, 7-12 months and 13-36 months.

1.1   Metal and mineral trace elements (MTEs): arsenic, lead, nickel, aluminium, mercury, strontium, chromium, selenium, cobalt, barium, cadmium, copper, antimony, germanium, silver, tin, gallium, tellurium, vanadium

As mentioned in the methodological section, for certain MTEs (inorganic mercury and methylmercury, inorganic and organic arsenic, chromium VI and chromium III) whose total form

---

[9] Exposure is considered to be close to a reference value when the ratio between the two is less than a factor of 10. This factor of 10 corresponds to the default factors generally used to establish TRVs.

was analysed, speciation assumptions were made given the knowledge acquired on the toxicity of some of their chemical forms.

For the vast majority of these MTEs and minerals, exposure of children under one year of age was lower than that of older children. This is generally explained by the increasing consumption by older children of normal foods, which are more contaminated.

1.1.1   A situation of concern for inorganic arsenic, lead and nickel

For these contaminants, the exposure level of a significant number of individuals exceeded the toxicological benchmarks selected.

With regard to lead and inorganic arsenic, an equivalent situation had already been described in children over three years of age in the TDS2. For these MTEs, efforts to reduce infant dietary exposure should be continued.

- For lead, food contamination is ubiquitous and some foods contain high levels. As a result, it is difficult to reduce lead contamination levels in foods. ANSES therefore recommends providing all children with a varied diet to ensure that they are not systematically consuming the most contaminated foods.

- For arsenic, it is above all necessary to obtain analytical speciation data in foods in order to determine the categories of foods on which efforts should be focused. It would be useful to have this information for jars of vegetable- and fish-based baby food, as well as infant rice and cereals (mainly rice-based ones). Furthermore, the Agency will update its work on the assessment of the health risks associated with the quality limit of arsenic in water intended for human consumption and natural mineral water, and examine whether it is appropriate to lower this quality limit. Lastly, the developmental toxicity of inorganic arsenic should be better documented.

For adults and children over three years of age (ANSES 2011), the situation had not been identified as a concern for nickel. In the iTDS, a more recent and lower TDI was adopted (2.8 µg.kg bw^{-1}.d^{-1}) (EFSA 2015b) and the situation was identified as a concern in children under three years of age. Regardless of the calculation assumptions, the TDI was confirmed to have been exceeded in at least 10% of children. It is therefore recommended that exposure levels be reduced, especially via the main contributors identified (such as chocolate-based products in children aged 13-36 months). Moreover, a further lowering of the analytical limits may be necessary to refine this exposure with regard to the TDI selected.

The situation may also be a concern for nickel-sensitised populations, and specific exposure data should be acquired to assess the acute risk for these populations.

1.1.2   A risk cannot be ruled out for aluminium, methylmercury, strontium, chromium VI, cobalt, barium, cadmium, copper and selenium

The risk could not be ruled out for these substances because of a major uncertainty.

Due to the limitations inherent in the study (related to the sampling or the measurement of exposure) and the very small number of children concerned (less than five individuals), the percentage of children in whom the TRVs were exceeded could not be quantified with certainty for:

- o **aluminium.** Non-representative cases where the limits were exceeded were observed in children aged 5-36 months, a priori in high consumers of spinach (excluding jars of baby food) which has higher contamination levels than the mean for vegetables. Efforts to reduce exposure should therefore be continued, by varying the vegetables consumed.

   As a reminder, cases where the TRVs were exceeded slightly in adults and children over three years of age have already been observed (ANSES 2011).

- o **methylmercury.** Only one child had an exposure level higher than the TWI selected, due to high consumption of sole. The contamination data in the iTDS only focused on a limited number of fish species, but the literature shows that other fish species can contain methylmercury levels equal to or higher than sole (Sirot et al. 2008). The recommendations on fish consumption formulated by ANSES should therefore be taken into account in order to allow optimal coverage of nutrient needs while limiting the risk of overexposure to chemical contaminants, i.e. "consuming two portions of fish per week, including one with a high EPA-DHA content (salmon, sardines, mackerel, herring, smoked trout), and varying the species and sources of supply (wild, farmed, fishing sites, etc.) […], in the framework of a varied diet. […]". Moreover, with regard to the risk associated with methylmercury for children under three years of age, ANSES specifically recommends limiting the consumption of wild predator fish (monkfish or angler fish, bass, bonito, eel, orange roughy, grenadier, halibut, pike, sea bream, skate, cutlassfish, tuna, etc.) (ANSES 2013). It also recommends avoiding, as a precaution, consumption of swordfish, marlin, deepwater spiny dogfish, shark and sea lamprey. As a reminder, cases where the TRVs were exceeded slightly, mainly related to high consumption of fresh tuna, were described in the TDS2.

- o **strontium**. Non-representative cases where the TRV was exceeded were observed in children under one year of age. These exceeded limits were associated with high daily consumption of infant formula reconstituted with a natural mineral water with a high strontium concentration generally used in infants for cases of constipation. It should be noted that highly mineralised natural mineral water must only be used in infants under medical advice and for a limited time.

- o **chromium VI (Cr VI).** Comparing exposure levels with the toxicological benchmarks indicated a situation for which the risk cannot be ruled out, whether for neoplastic effects (MOE < 10,000 for all age groups) or non-neoplastic effects (guidance value of 1 $\mu g.kg\ bw^{-1}.d^{-1}$ exceeded in infants aged 1-4 months and 7-12 months). However, in the absence of reliable speciation data, a conservative assumption was adopted for Cr VI (using a maximalist approach to consider that Cr VI accounts for 10% of chromium in food). Analytical speciation data on

chromium in foods therefore need to be obtained in order to refine this speciation assumption, or even to discard it.

- o **selenium.** Non-representative cases where the tolerable upper intake level was exceeded in children aged 13-36 months were mainly linked to high fish consumption. It is worth recalling the recommendations formulated by ANSES for children under three years of age (ANSES 2013), i.e. two portions of fish per week, including one with a high EPA-DHA[10] content (salmon, sardines, mackerel, herring, smoked trout), and varying the species and sources of supply (wild, farmed, fishing sites, etc.), in the framework of a varied diet.

- o **copper.** Non-representative cases where the tolerable upper intake level was exceeded in children aged 13-36 months were also observed.

For **cobalt** and **barium**, the TRVs selected by default do not take into consideration toxicological studies covering the perinatal period. The exposure levels observed in children under three years of age seem high, however, in light of these TRVs. The risk cannot be ruled out for these substances and additional toxicological studies are needed. For cobalt, non-representative cases where the limits were exceeded were observed in children over one year of age. Therefore, despite uncertainties about the TRV, efforts to reduce dietary exposure should also be continued.

For **cadmium**, the PTWI was exceeded in children aged 5 to 36 months (15 to 36% depending on the age group). This PTWI was established on the basis of cadmium's nephrotoxicity due to its accumulation over time in the renal cortex, with its effects becoming apparent at around 50 years of age. Protection from the critical effect therefore involves limiting the accumulation of cadmium. As was demonstrated for children aged 3 to 17 years (TDS2), these exceeded limits must be put into perspective, mainly because:

- they may be partly linked to the standardisation of exposure by the children's body weight and should no longer be observed in these proportions once adulthood is reached;
- they do not reflect the exceeding of the critical renal burden. On the basis of the results of this study and those from the TDS2, it can be seen that exposure between the ages of 1 and 36 months only makes a very small contribution (<3%) to cumulative exposure over 50 years.

Nevertheless, because the PTWI was observed to have been exceeded in the adult population (0.6%) (ANSES 2011) and because of the existence of cognitive effects associated with low exposure levels, the exposure to cadmium is not regarded as tolerable and it is recommended that efforts be continued to reduce exposure from a very young age, by acting on the same contributors as those identified for the adult population (mainly potatoes and vegetables).

1.1.3   A risk deemed tolerable for copper, inorganic mercury, chromium III and antimony

---

[10] Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) belong to the family of omega-3 fatty acids.

For **inorganic mercury** and **chromium III**, the exposure levels observed were lower than the TDIs regarded as applicable to the infant population. The risk for children under three years of age is deemed tolerable.

For **antimony**, the lack of relevant reprotoxicity and developmental toxicity studies means that no conclusions can be reached as to the applicability of the TRV to children under three years of age. Nevertheless, because the exposure levels were far lower than the TRV selected (around a factor of 10 to 100), the risk for children under three years of age is deemed to be tolerable.

For **copper**, a tolerable upper intake levels (UL) of 1 mg d^{-1} was selected for children aged 1 to 3 years. No TRV was selected for children under one year of age. Thus, in light of the estimated exposure for children aged 13 to 36 months, the risk is deemed tolerable, but could not be assessed for children under one year of age.

1.1.4 Impossible to reach any conclusions for germanium, silver, tin, organic arsenic, gallium, tellurium, vanadium

For certain contaminants, because of the lack of robust toxicological data (for germanium, silver, organic arsenic, gallium, tellurium, vanadium) or speciation data (for tin and vanadium), it was not possible to reach any conclusions as to the risk associated with dietary exposure.

For these substances and in particular for copper (in children under one year of age), tin and vanadium, *ad hoc* toxicological studies should be conducted and/or the necessary analytical developments should be initiated (see table below).

TABLE 6: SUMMARY TABLE OF RESULTS RELATING TO MTEs AND CERTAIN MINERALS

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which the situation was identified as a concern			
Lead	Very low MOEs (< 10) BMDL$_{10}$: 0.63 µg.kg bw^{-1} d^{-1}	Reduce exposure by providing all children with a varied diet	
Inorganic arsenic	Very low MOEs (< 36) BMDL$_{01}$: 0.3 to 8 µg.kg bw^{-1}.d^{-1}	• Reduce exposure	• Obtain speciation data in foods (as a priority, jars of vegetable- and fish-based baby food, as well as infant rice and cereals - mainly rice-based ones) • Update ANSES's work on the assessment of the health risks associated with the quality limit of arsenic in water intended for human consumption and natural mineral water, and examine whether it is appropriate to lower this quality limit. • Conduct developmental toxicity studies on arsenic
Nickel	**Chronic risk:** TDI exceeded in 8 to 98% of children (2.8	Reduce exposure via the main contributors (chocolate-based products in children aged 13-36	• Lower the analytical limits • Obtain acute exposure data

Substances	Conclusions	Recommendations for management measures	Research recommendations
	$\mu g.kg\ bw^{-1}.d^{-1}$) **Risk of hypersensitivity**: Limits may be exceeded for sensitised children ($BMDL_{10}$ = 1.1 $\mu g.kg\ bw^{-1}.d^{-1}$)	months).	
Substances for which the risk cannot be ruled out			
Aluminium	Limits not exceeded for children under five months of age Non-representative cases where the limits were exceeded from five months of age ($PTWI$ = 1 mg.kg $bw^{-1}.week^{-1}$)	Reduce exposure by varying the vegetables consumed.	
Methylmercury	Limits not exceeded for children under one year of age Non-representative cases where the limits were exceeded in children aged 13-36 months ($PTWI$ = 1.3 $\mu g.kg\ bw^{-1}.week^{-1}$)	ANSES recommendations: "in order to allow optimal coverage of nutrient needs while limiting the risk of overexposure to chemical contaminants, consuming two portions of fish per week, including one with a high EPA-DHA content (salmon, sardines, mackerel, herring, smoked trout), and varying the species and sources of supply (wild, farmed, fishing sites, etc.) […], in the framework of a varied diet. […] It is also recommended […] for children under three years of age, limiting the consumption of wild predator fish (monkfish or angler fish, bass, bonito, eel, orange roughy, grenadier, halibut, pike, sea bream, skate, cutlassfish, tuna, etc.), and avoiding, as a precaution, consumption of swordfish, marlin, deepwater spiny dogfish, shark and sea lamprey, due to the risk associated with methylmercury".	
Strontium	Non-representative cases where the limits were exceeded in children under one year of age Limits not exceeded for children over 13 months of age (TDI = 0.6 mg.kg $bw^{-1}.d^{-1}$)	Remind parents that highly mineralised natural mineral water must only be used in infants under medical advice and for a limited time	
Chromium VI	Neoplastic effects: MOE < 10,000 (for all age groups) ($BMDL_{10}$ = 1 mg.kg $bw^{-1}.d^{-1}$) Non-neoplastic effects: guidance value of 1		Obtain analytical speciation data on chromium in foods in order to refine the speciation assumptions, or even to discard them.

Substances	Conclusions	Recommendations for management measures	Research recommendations
	$\mu g.kg$ $bw^{-1}.d^{-1}$ exceeded in children aged 1-4 months and 7-12 months		
Selenium (in children over one year of age)	Non-representative cases where the limits were exceeded in children aged 13-36 months. (UL = 60 $\mu g.d^{-1}$) *(no TRV for children under one year of age)*	Reiterate the general recommendations on fish consumption issued by ANSES for children under three years of age	
Copper (in children over one year of age)	Non-representative cases where the limits were exceeded in children aged 13-36 months. (UL =1 $mg.d^{-1}$) *(no TRV for children under one year of age)*		
Cobalt	Exposure levels close to the TRV deemed to be not very robust in children under three years of age (TDI = 1.6 $\mu g.kg$ $bw^{-1}.d^{-1}$)	Efforts to reduce dietary exposure to cobalt should be continued	Conduct the missing toxicological studies (perinatal period)
Barium	Exposure levels close to the TRV deemed to be not very robust in children under three years of age (RfD = 0.2 $mg.kg$ $bw^{-1}.d^{-1}$)		Conduct the missing toxicological studies (perinatal period)
Cadmium	Put the cases where the TWI was exceeded (36%) into perspective. Long-term nephrotoxicity, and exposure in the first three years of life only accounts for 3% of cumulative exposure over 50 years. (TWI = 2.5 $\mu g.kg$ $bw^{-1}.week^{-1}$)	Reduce exposure from a very young age Reduce contamination from the main contributors (mainly vegetables and potatoes).	Confirm the existence of cognitive effects associated with low levels of exposure to cadmium.
Substances for which the risk is considered tolerable			
Chromium III	Limits not exceeded P_{90} <2% of the TDI (300 $\mu g.kg$ $bw^{-1}.d^{-1}$)		
Inorganic mercury	Limits not exceeded P_{90} < 18% of the TDI (4 $\mu g.kg$ $bw^{-1}.week^{-1}$)		
Antimony	Limits not exceeded P_{90} < 3% of the TDI (6 $\mu g.kg$ $bw^{-1}.d^{-1}$)		

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which no conclusions can be reached			
Germanium	No robust TRV		Conduct toxicity studies for establishing a TRV applicable to the general population while taking infant specificities into account.
Copper (in children under one year of age)	No robust TRV for children under one year of age		Conduct studies to determine an UL for this age group
Selenium (in children under one year of age)	No robust TRV for children under one year of age		Conduct studies to determine an UL for this age group
Silver	No robust TRV		Conduct toxicity studies for establishing a TRV applicable to the general population while taking infant specificities into account.
Organic arsenic	No robust TRV		
Tin	No speciation studies or data for establishing speciation assumptions	• Apply analytical methods for the speciation of tin in foods • Determine the origin of the high levels observed in certain jars of fruit	Conduct toxicity studies for establishing a TRV applicable to the general population while taking infant specificities into account.
Gallium	No robust TRV		Conduct toxicity studies for establishing a TRV applicable to the general population while taking infant specificities into account.
Tellurium	No robust TRV		Conduct toxicity studies for establishing a TRV applicable to the general population while taking infant specificities into account.
Vanadium	Lack of a robust TRV and no speciation studies or data for establishing speciation assumptions		Conduct studies making it possible to differentiate the concentrations of the different forms of vanadium in food matrices. Conduct toxicity studies for establishing a TRV applicable to the general population while taking infant specificities into account.

1.2   Persistent organic pollutants

1.2.1   Dioxins and furans

In total, 17 polychlorinated dibenzo-p-dioxin (PCDD) and polychlorinated dibenzofuran (PCDF) congeners were analysed and detected in 49 to 100% of the samples tested, depending on the congener in question.

In children over seven months of age, the TDI proposed by the US EPA in 2012 for dioxins and furans (i.e. 0.7 pg.kg bw^{-1}.d^{-1}) was observed to be significantly exceeded. In children under six

months of age, it was not possible to estimate precisely the extent to which the limits were exceeded, given the limited number of children concerned.

The cases in which the TRV was exceeded can mainly be explained by higher consumption of normal milk (the single main contributor in children under six months), fish and ultra-fresh dairy produce than in consumers as a whole.

Dietary exposure to dioxins and furans is identified as a concern. Exposure, mainly via normal food products making a major contribution to exposure of the most exposed children to these compounds (milk, ultra-fresh dairy produce and fish), should therefore be reduced.

1.2.2   PCBs

In total, 18 congeners of polychlorinated biphenyls (PCBs) were analysed and detected on average in 88% of samples tested.

The cases in which the TDI selected for PCBs (i.e. 10 ng.kg bw^{-1}.d^{-1}) was exceeded seem significant from the age of one year. The limits were not observed to have been exceeded for children under six months of age.

The cases in which the TRV was exceeded were mainly observed in children who are high fish consumers (especially of salmon).

Dietary exposure to PCBs is identified as a concern. Efforts to reduce exposure, especially via fish, should therefore be continued. The contamination data in this study only focused on a limited number of fish species, but the literature shows that other fish species can contain PCB levels equal to or higher than salmon (Marchand et al. 2006). Even though PCB levels in fish have been falling over the past few years (ANSES 2015), ANSES's recommendations for children under three years of age, with regard to the risk associated with PCBs, should be reiterated (ANSES 2013): "The Agency recommends, in order to allow optimal coverage of nutrient needs while limiting the risk of overexposure to chemical contaminants, consuming two portions of fish per week, including one with a high EPA-DHA content (salmon, sardines, mackerel, herring, smoked trout), and varying the species and sources of supply (wild, farmed, fishing sites, etc.) […], in the framework of a varied diet." ANSES reiterates that these recommendations may be supplemented, with regard to the risk associated with methylmercury.

1.2.3   Brominated flame retardants: PBDE, HBCDD, PBB, TBBPA

Hexabromocyclododecane (HBCDD): Three isomers of HBCDD were analysed and detected in 32 to 77% of samples tested.

Regardless of the age group, the margins of safety calculated with regard to the BMDL$_{10}$ established by EFSA for the sum of the three HBCDDs (3000 ng.kg bw^{-1}.d^{-1}) were higher than the critical value of 25 selected for the iTDS. **The situation is therefore deemed to be tolerable**.

However, the sampling revealed an unexpectedly high level for a composite sample of first infant formula (more than ten times higher than the levels measured in the other milk samples). Such a high contamination situation had already been found in foods of animal origin (eggs,

poultry meat) as part of the surveillance plans of the General Directory for Food (DGAL). Consequently, the potential sources of contamination remain to be identified given the low margin of safety observed in the most exposed children.

Polybrominated diphenyl ethers (PBDEs): Eight isomers of PBDE were analysed and detected in 20 to 93% of samples tested.

Due to its specific characteristics in terms of pharmacokinetics and toxicity, BDE-209 was considered separately from the other seven congeners, whose chemical structure and mechanism of action are similar to those of NDL-PCBs. The threshold of 10 ng.kg bw^{-1}.d^{-1} defined for the six NDL-PCBs most frequently encountered in food (neurodevelopmental effects) was therefore adopted. This threshold value was not observed to have been exceeded. Similarly, the margin of safety calculated for BDE-209 (with regard to the BMDL$_{10}$ of 1700 µg.kg bw^{-1}.d^{-1}) is far higher than the margin deemed tolerable by EFSA. **For PBDEs, the situation is therefore deemed to be tolerable.**

Polybrominated biphenyls (PBB): Three congeners of PBB were analysed and detected in 4 to 12% of samples tested.

The margins of safety calculated using the no-effect level observed by EFSA for the sum of the three PBBs (0.15 mg.kg bw^{-1}.d^{-1}) are sufficiently high to conclude that the **situation is tolerable.**

Tetrabromobisphenol-A (TBBPA): The overall detection rate for TBBPA was 30%.

The margins of safety calculated using the BMDL$_{10}$ established by EFSA (16 mg.kg bw^{-1}.d^{-1}) are sufficiently high to conclude that the **situation is tolerable.**

1.2.4 Perfluoroalkyl compounds (PFAs)

In total, 16 compounds were analysed and detected in 0 to 6% of samples tested.

Given the toxicological data available, only the risks associated with exposure to PFOS and PFOA could be assessed. Based on the RfD calculated by the US EPA in 2009 for PFOA (0.2 µg.kg bw^{-1}.d^{-1}) and PFOS (0.08 µg.kg bw^{-1}.d^{-1}) **the situation is deemed to be tolerable**.

However, in 2014, the US EPA calculated new lower RfD values, based on the result of pharmacokinetic modelling of serum values in animals in conjunction with the criteria of selected effects and their extrapolation to humans. As this document is currently out for public consultation before finalisation, these values cannot be put forward in the context of the current study, but the conclusions related to dietary exposure to PFOS and PFOA may be reviewed after this new work has been finalised and assessed by experts.

For the other PFAs, given the absence of data that would enable a toxicological point of departure to be established, **it is not currently possible to reach any conclusions as to the health risk** associated with dietary exposure to these substances.

TABLE 7: SUMMARY TABLE OF RESULTS RELATING TO PERSISTENT ORGANIC POLLUTANTS

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which the situation was identified as a concern			
PCDD/Fs	Cases where the limits were exceeded significantly from seven months of age. Non-representative cases where the limits were exceeded in children under seven months. (TDI: 0.7 pg.kg bw^{-1}.d^{-1})	Reduce exposure, mainly via normal food products making a major contribution to exposure of the children most exposed to PCDD/Fs (milk, ultra-fresh dairy produce and fish).	
PCBs	Cases where the limits were exceeded significantly from 13 months of age. Non-representative cases where the limits were exceeded in children aged 7-12 months. Limits not exceeded for children under 7 months of age (TDI: 10 ng.kg bw^{-1}.d^{-1})	ANSES recommendations: "in order to allow optimal coverage of nutrient needs while limiting the risk of overexposure to chemical contaminants, consuming two portions of fish per week, including one with a high EPA-DHA content (salmon, sardines, mackerel, herring, smoked trout), and varying the species and sources of supply (wild, farmed, fishing sites, etc.) […], in the framework of a varied diet." (See methylmercury for additional recommendations).	
Substances for which the risk is considered tolerable			
7 PBDEs	Limits not exceeded. P$_{90}$ < 15% of the TDI (10 ng.kg bw^{-1}.d^{-1})		
BDE-209	Very high MOS (> 450,000) (BMDL$_{10}$ of 1700 µg.kg bw^{-1}.d^{-1})		
PBB	Very high MOS (> 740,000) (NOAEL: 0.15 mg.kg bw^{-1}.d^{-1})		
HBCDD	MOS (>70) above 25 (but take care with certain foodstuffs) (BMDL$_{10}$: 3000 ng.kg bw^{-1}.d^{-1})	Identify potential sources of contamination	
TBBPA	Very high MOS (> 500,000) (BMDL$_{10}$: 16 mg.kg bw^{-1}.d^{-1})		
PFOS	Limits not exceeded but possible reassessment following publication of the work by the US EPA. P$_{90}$ < 6% of the RfD (0.08 µg.kg bw^{-1}.d^{-1})		
PFOA	Limits not exceeded but possible reassessment following publication of the work by the US EPA		

	P_{90} < 3% of the RfD (0.2 µg.kg bw^{-1}.d^{-1})		
Substances for which no conclusions can be reached			
PFAs (except PFOS and PFOA)	No robust TRV		Conduct toxicity studies for establishing a TRV applicable to the general population while taking infant specificities into account.

1.3 Heat-induced compounds

Three heat-induced compounds were analysed: acrylamide, furan and polycyclic aromatic hydrocarbons (PAHs)[11].

1.3.1 Acrylamide

Acrylamide was analysed and detected in 87% of samples tested.

The risk associated with dietary exposure to acrylamide was assessed with regard to its neurotoxic and genotoxic carcinogenic effects.

Firstly, for neurological effects, the RfD of 2 µg.kg bw^{-1}.d^{-1} established by the US EPA in 2010 was exceeded by 7% of children aged 13-36 months. In children aged 7-12 months, the limits were exceeded but it is difficult to estimate the proportion in light of limitations related to the sampling or the measurement of exposure. The failure to take into account infant sensitivity to the neurotoxicity of acrylamide and the uncertainties related to metabolism (elimination of acrylamide and glycidamide) led the experts to propose a benchmark value of 0.2 µg.kg bw^{-1}.d^{-1} for children under three years of age (by applying a default factor of 10 to the RfD of 2 µg.kg bw^{-1}.d^{-1}). In this case, this benchmark value was observed to have been exceeded significantly for all the age groups considered.

The BMDL$_{10}$ of 0.17 mg.kg bw^{-1}.d^{-1} set by EFSA (EFSA 2015a) was used as a reference to assess the risks relating to the neoplastic effects of acrylamide. The margins of exposure (MOE) calculated using EFSA's BMDL$_{10}$ were far lower than the value of 10,000 that EFSA deems appropriate for ruling out a risk associated with a genotoxic compound (EFSA 2012). An identical conclusion had been reached for adults and children over three years of age (see TDS2).

Dietary exposure to acrylamide is identified as a concern both regarding the neurological and neoplastic effects. The consumption of biscuits and potatoes largely explains the high levels of exposure in children over one year of age. In children under one year of age, the main contributors to the risk are jars of vegetable-based baby food, with or without meat.

Efforts should therefore be continued to decrease contamination from the main exposure contributors (by reducing the formation of acrylamide during food production or preparation

---

[11] Apart from being generated by thermal processes, PAHs can also be environmental contaminants.

processes, for example) and, consequently, exposure. Simulating the impact on exposure levels of a reduction in contamination and/or a change in the consumption of these major contributors would enable efforts to be targeted more effectively.

Lastly, additional toxicological studies may be necessary to confirm the TRV to be adopted for neurotoxic effects in young children.

1.3.2 Furan

Furan was analysed and detected in 83% of samples tested.

In 2011, the JECFA established a $BMDL_{10}$ of 0.96 mg.kg bw^{-1}.d^{-1} based on the increase in adenomas and hepatocellular carcinomas. Given its carcinogenic nature and uncertainties about a genotoxic mode of action, a critical MOE of 10,000 was considered to assess the health risk (EFSA 2012).

The margins of exposure calculated for children, regardless of the age group, were always below 10,000. **Dietary exposure to furan is therefore identified as a concern.**

The differences observed between the exposure levels of different age groups were rather unusual compared with those observed for the other substances. Exposure in children aged 5-6 and 7-12 months was higher than that of the rest of the infant population. This difference may be explained by the high consumption of jars of vegetables, vegetables with meat or vegetables with fish, as these food groups have higher concentrations of furan. Differences in exposure (of a factor of 3 to 6) were observed between children consuming jars of vegetables accompanied by meat or fish, and non-consumers. Moreover, it was shown that infant foods prepared at home contained less furan than those prepared industrially (EFSA 2011b).

Similar to what has been done to limit the population's exposure to acrylamide (in particular, creation of a "toolbox"), ways should be sought to reduce furan contamination of industrial products through the optimisation of manufacturing processes, in particular for jars of vegetable-based baby food (alone or with meat or fish). Moreover, given furan's volatility, it would be interesting to study reheating practices in the home for infant foods prepared industrially in order to limit the exposure.

1.3.3 Polycyclic aromatic hydrocarbons (PAHs)

A total of 20 PAHs were screened for in the iTDS. Their detection rates varied greatly (between 0.5 and 81% of samples tested) depending on the congeners.

Regardless of the approach used (PAH4[12] or PAH11[13]), dietary exposure of the infant population to PAHs was deemed to be tolerable with regard to the carcinogenic risk.

Recent studies indicate the onset of neurodevelopmental effects after exposure to low levels of light PAHs (≤4 cycles) during the perinatal period; however, these studies should be supplemented before they can potentially be taken into account for establishing a TRV

---

[12] Approach for assessing the risks associated with PAHs proposed by EFSA (EFSA 2008)
[13] Approach for assessing the risks associated with PAHs proposed by AFSSA (AFSSA 2003)

applicable to the infant population, with a view to confirming the absence of a health risk associated with dietary exposure to PAHs.

TABLE 8: SUMMARY TABLE OF RESULTS RELATING TO HEAT-INDUCED COMPOUNDS

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which the situation was identified as a concern			
Acrylamide	**Genotoxic carcinogenic effects:** MOE < 10,000 (BMDL$_{10}$ = 0.17 mg.kg bw^{-1}.d^{-1}) **Neurotoxic effects:** Benchmark value of 0.2 µg.kg bw^{-1}.d^{-1}: limits exceeded significantly in children under three years of age RfD of 2 µg.kg bw^{-1}.d^{-1}: Exceeded in 7% of children over 13 months of age Non-representative cases where the limits were exceeded in children aged 7-12 months.	Continue efforts to reduce contamination from the main contributors (biscuits, potatoes, jars of vegetable-based baby food with or without meat) and exposure, by reducing the formation of acrylamide during food production or preparation processes, for example.	• Study the impact of a reduction in contamination/consumption of the major contributors • Conduct additional toxicological studies to confirm the TRV to be adopted for neurotoxic effects in young children
Furan	**Genotoxic carcinogenic effects:** MOE < 10,000 (BMDL$_{10}$= 0.96 mg.kg bw^{-1}.d^{-1})	Reduce exposure, mainly by reducing furan levels in industrial products, in particular jars of vegetable-based baby food (alone or with meat or fish), through the optimisation of manufacturing processes.	Study the impact of reheating practices in the home for infant foods prepared industrially
Substances for which the situation was identified as of low health concern			
PAHs	**Carcinogenic effects:** PAH$_4$ approach: MOE > 10,000 (BMDL$_{10}$ = 0.34 mg.kg bw^{-1}.d^{-1}) PAH$_{11}$ approach: Excess risk < 10^{-6} (VSD = 5 ngTEQ.kg bw^{-1}.d^{-1})		Acquire toxicological data specific to light PAHs and neurodevelopmental effects following perinatal exposure

1.4 Mycotoxins

Seven classes of mycotoxins were assessed in the iTDS (aflatoxins, ochratoxin A, patulin, trichothecenes, zearalenone, fumonisins, *Alternaria* toxins). The mycotoxin detection rate varied in the foods sampled (infant and normal foods). For aflatoxins and zearalenone, the detection rate in infant foods was zero. It was very low for fumonisins, ochratoxins and *Alternaria* toxins.

The improvement in analytical performance since the TDS2 meant that conclusions could be reached for most mycotoxins, including under the UB assumption. **Thus, for patulin, nivalenol, zearalenone and fumonisins, the exposure levels calculated under the UB assumption were deemed tolerable as they were well below the selected TRVs regarded as applicable to the infant population for these mycotoxins**.

However, exposure levels for ochratoxin A were deemed to be too close (despite being lower) to the PTWI selected by default, given the uncertainties about its applicability to the infant population. **For ochratoxin A, the risk cannot be ruled out.** Reproductive and developmental toxicity studies should be conducted to determine a TRV taking infant specificities into account, and efforts should then be continued to lower the analytical limits in order to refine the estimation of exposure.

Aflatoxins were not detected in infant products and were only detected at very low levels in normal foods. However, under the high assumption, the margins of exposure with regard to the experimental $BMDL_{10}$ of 170 ng.kg $bw^{-1}.d^{-1}$ were below the critical value of 10,000 defined for carcinogenic and genotoxic compounds that EFSA deems necessary to rule out the risk. Accordingly, **the risk associated with dietary exposure to aflatoxins cannot be ruled out for children under three years of age**. Efforts should be pursued to lower the analytical limits in order to obtain more precise concentration data with which to refine the estimation of exposure.

The degree to which the limits were exceeded were quantified, including under the LB assumption, for T-2 and HT-2 toxins, and DON and its derivatives. **The situation is therefore identified as a concern for T-2 and HT-2 toxins, and DON and its derivatives.**

- For T-2 and HT-2 toxins, the cases where the provisional maximum tolerable daily intake (PMTDI) of 0.06 µg.kg $bw^{-1}.d^{-1}$ was exceeded under the LB concerned over 10% of children aged 5 to 6 months and 5% aged 7-12 months. In children under 4 months of age, the PMTDI was also exceeded, but it is difficult to estimate the proportion in light of limitations related to the sampling or the measurement of exposure. The limits were observed to have been exceeded in children consuming either jars of fruit containing rice with especially high levels, or higher than average quantities of follow-on formula in which T-2 and HT-2 toxins were detected or quantified. Efforts to reduce exposure should therefore be continued, especially by strengthening monitoring of infant formulas and the associated control measures. Concerning the other food products, efforts should be continued to lower the analytical limits in order to refine the estimation of exposure.

- For DON and its acetyl derivatives, the cases in which the JECFA's TDI of 1000 ng.kg $bw^{-1}.d^{-1}$ were exceeded under the LB concern every age group, but it is difficult to estimate the proportion in light of limitations related to the sampling or the measurement of exposure. The failure to take into account infant sensitivity in the establishment of this TDI nevertheless led the experts to propose a benchmark value of 300 ng.kg $bw^{-1}.d^{-1}$ for children under three years of age (by applying a default factor of 3). With regard to this value, the proportion of children concerned by the exceeded limits (under the LB) varied between 7.5 and 27%, from the age of seven months. **Dietary exposure to DON and its acetyl derivatives is identified as a concern.** Efforts to reduce exposure, especially via the major contributors (infant milk drinks, especially those containing cereals, jars of fruit, jars of vegetables with or without meat, normal

biscuits and bread), should therefore be continued. Additional toxicological studies are necessary to confirm the TRV to be adopted for young children. Efforts should subsequently be pursued to lower the analytical limits in order to obtain more precise concentration data with which to refine the estimation of exposure.

Given the absence of sufficient data that would enable a toxicological point of departure to be established, it is not currently possible to reach any conclusions as to the health risk associated with *Alternaria* toxins and other trichothecenes (DAS, FusX, Ver, MAS, NEO, T2-triol). Toxicity studies for establishing TRVs applicable to the general and infant populations should therefore be conducted. These studies should in particular focus on alternariol and alternariol monomethyl ether, given their genotoxic nature demonstrated *in vitro*.

TABLE 9: SUMMARY TABLE OF RESULTS RELATING TO MYCOTOXINS

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which the situation was identified as a concern			
T-2 and HT-2 toxins	Exceeded in 5 to 10% of children aged 5-12 months under the LB Non-representative cases where the limits were exceeded under the LB in children under four months (PMTDI = 0.06 µg.kg bw^{-1}.d^{-1})	Continue efforts to reduce exposure, especially by strengthening monitoring of infant formulas and the associated control measures	Pursue efforts to lower the analytical limits
DON and acetyl derivatives	TDI of 300 ng.kg bw^{-1}.d^{-1} Exceeded in between 7.5 and 27% of children from five months of age under the LB TDI of 1000 ng.kg bw^{-1}.d^{-1} Non-representative cases where the limits were exceeded under the LB for all age groups	Continue efforts to reduce exposure, especially via the major contributors (infant milk drinks, especially those containing cereals, jars of fruit, jars of vegetables with or without meat, normal biscuits and bread).	• Conduct additional toxicological studies to confirm the TRV to be adopted for young children • Pursue efforts to lower the analytical limits
Substances for which the risk cannot be ruled out			
Ochratoxin A	Exposure levels close to the TRV deemed to be not very robust in children under three years of age. (PTWI = 0.12 µg.kg bw^{-1}.week^{-1})		• Conduct reproductive and developmental toxicity studies in order to determine a TRV while taking infant specificities into account. • Pursue efforts to lower the analytical limits
Aflatoxins	MOE < 10,000 under the UB (BMDL$_{10}$ = 170 ng.kg bw^{-1}.d^{-1})		Pursue efforts to lower the analytical limits
Substances for which the risk is considered tolerable			
Nivalenol	The selected TRV was		

Substances	Conclusions	Recommendations for management measures	Research recommendations
	not exceeded under the UB $P_{90} < 7\%$ of the TDI ($1.2 \ \mu g.kg \ bw^{-1}.d^{-1}$)		
Patulin	The selected TRV was not exceeded under the UB $P_{90} < 30\%$ of the PMTDI ($0.4 \ \mu g.kg \ bw^{-1}.d^{-1}$)		
Fumonisins	The selected TRV was not exceeded under the UB $P_{90 \ (FB1 + FB2)} = 7\%$ of the PMTDI ($2 \ \mu g.kg \ bw^{-1}.d^{-1}$)		
Zearalenone	The selected TRV was not exceeded under the UB $P_{90} < 40\%$ of the TDI ($0.25 \ \mu g.kg \ bw^{-1}.d^{-1}$)		

Substances for which no conclusions can be reached			
Alternaria toxins	No robust TRV		Conduct toxicity studies for establishing TRVs applicable to the general and infant populations, in particular on alternariol and alternariol monomethyl ether given their genotoxic nature as demonstrated *in vitro*.
Other trichothecenes (DAS, FusX, Ver, MAS, NEO, T2-triol)	No robust TRV		Conduct toxicity studies for establishing TRVs applicable to the general and infant populations

1.5   Substances derived from migration from food contact materials

New substances were considered compared to the list defined in the TDS2, in particular those that have been the focus of growing interest in recent years, and with priority given to substances liable to be found in infant food (BPA and bisphenol A diglycidyl ether - BADGE, phthalates, ink photo initiators and alkylphenols).

1.5.1   Alkylphenols

Mixtures of 4-nonylphenol isomers and *4-tert*-octylphenol were analysed in the iTDS. The mixtures of 4-nonylphenol isomers were detected in 68% of the samples tested, unlike *4-tert*-octylphenol which was only detected in 1% of samples. No significant difference in contamination according to the packaging type was observed.

The exposure levels recorded for nonylphenols were far lower than the selected TRV considered applicable for children under three years of age (30 µg.kg bw^{-1}.d^{-1}). **The situation is therefore deemed to be tolerable.**

For *4-tert*-octylphenol, the lack of a robust TRV meant that it was not possible to reach a conclusion regarding the associated risk. Additional toxicity studies are needed to establish this TRV.

1.5.2   Ink photoinitiators

The ink photoinitiators screened for in the context of the iTDS were benzophenone, 4-methylbenzophenone (4-MBP), 4-hydroxybenzophenone (4-HBP), 4-benzoylbiphenyl (PBZ) and 2-isopropylthioxanthone (ITX).

The detection rate was low. Only benzophenone was detected in certain samples (1.9%). **The exposure levels (assessed under the UB) for benzophenone and 4-MBP were deemed tolerable** with regard to the selected TRVs considered applicable for children under three years of age. However, the absence of robust TRVs for PBZ, 4-HBP and ITX mean that it is not possible to reach a decision in terms of the risk, even though they were not detected.

1.5.3   Bisphenol A (BPA)

Because of its oestrogen-mimicking effects, BPA has been classed as a Category 1 endocrine disruptor (EC 2002). In terms of assessment of its effects, many publications have studied the toxicity and endocrine effects of BPA in animals. Many epidemiological studies have also sought to link BPA exposure to effects on human health.

The rate of detection of BPA in the samples tested in the iTDS was 26%. BPA levels in infant products were lower than the background level of 5 µg kg^{-1}, defined previously when analysing the TDS2 samples. The highest levels were found in normal foods, especially canned foods.

Mean daily exposure to BPA varied from 10.2 to 99.4 ng.kg bw^{-1}.d^{-1}, depending on the age group. Exposure had a tendency to increase with age and varied by a factor of 3 to 10, under the UB, depending on whether or not canned foods such as vegetables or filled pasta (ravioli) were consumed.

EFSA's temporary Tolerable Daily Intake, or tTDI (4 µg.kg bw^{-1}.d^{-1}) was not observed to have been exceeded (even under the UB). However, on the basis of the lowest toxicological value (TV) proposed by ANSES (0.08 µg.kg bw^{-1}.d^{-1}), the limits were exceeded significantly in children aged 5-36 months under the low assumption, and for all age groups under the high assumption. With regard to children who had not consumed canned products, the TV of 0.08 µg.kg bw^{-1}.d^{-1} was only observed to have been exceeded under the high assumption, affecting between 2 and 28% of children depending on the age group.

With regard to EFSA's temporary value, the health risk associated with dietary exposure to BPA can be ruled out, whereas it cannot be excluded for certain consumers on the basis of the TVs proposed by ANSES.

In conclusion, **the risk for the infant population associated with exposure to BPA cannot be ruled out**, even though both ANSES and EFSA consider that their toxicological values are liable to change following the conclusions of the long-term studies currently under way. Moreover, as the samples from the present study were collected in 2011-2012, i.e. before BPA was prohibited in food packaging, the contamination and therefore the exposure reported are most likely higher than those that would be measured today. It is therefore important to determine current exposure levels, i.e. after the introduction of these prohibition measures, in order to be able to rule on the need for new recommendations.

1.5.4   BADGE

The analyses focused on BADGE, and its hydrolysis products and chlorohydrin derivatives.

The detection rate of these compounds was zero, apart from in vegetables and mixed dishes in canned form.

Exposure levels were far below the selected TDI (0.15 mg.kg bw^{-1}.d^{-1}) considered to be applicable in children under three years of age. **The situation is therefore deemed tolerable for BADGE and its hydrolysis products**.

Given the absence of a toxicological point of departure, it is impossible to reach a conclusion as to the risk associated with dietary exposure to chlorohydrin-type derivatives.

1.5.5   Phthalates

The analyses concerned nine phthalates (DEHP, DnBP, DiDP & DiNP, BBP, DiBP, DEP, DCHP and DnOP). A robust toxicity reference value applicable to children under three years of age was selected only for the DEHP, DIDP, DINP, BBP and DnBP congeners.

The detection percentages varied widely depending on the phthalate considered, but were generally low. Only three phthalates were detected in more than 10% of samples (DiBP, DINP and DEHP). Due to the low detection rates for most of the phthalates, it is difficult to test the differences in contamination rates according to the packaging type. However, significantly higher DEHP concentrations were found in dishes of vegetables with meat or vegetables with fish packaged in plastic plates or bowls, compared to those packaged in glass jars.

Apart from DEHP, the estimates calculated suggest that the mean daily exposure decreased with age under the high assumption. For these substances, because of the low detection rate, exposure was dependent on the analytical limits and the ratio of quantity consumed to body weight. The decrease in the value of this ratio explains the change in exposure between the different age groups. However, for DEHP, exposure increased with age, probably due to an increase in the share attributable to normal foods (which are more contaminated) in the diet.

The limits were not observed to have been exceeded for the five phthalates (DEHP, DIDP, DINP, BBP, DnBP) for which a TDI was selected in this study (see table below). Moreover, for these substances, under the high assumption (UB), the 90th percentile of exposure for each compound accounted for less than 5% of the TDI. **Exposure to these phthalates is deemed tolerable.**

Some literature data describe endocrine-disrupting effects in phthalates at doses below those used to establish the toxicity reference values selected in the present study. However, these data are not currently sufficiently numerous or robust to be used to establish toxicological points of departure based on this mechanism of action. Future work at ANSES on the effects associated with an endocrine-disrupting mechanism of certain phthalates may ultimately make it possible to establish certain TRVs. The risk conclusions issued in this study should therefore be reviewed on the basis of these new values.

In the absence of robust TRVs for DIBP, DEP, DnOP and DCHP, it is not possible to reach a conclusion as to the health risk associated with exposure to these phthalates. Toxicity studies for establishing TRVs applicable to the general population and taking infant specificities into account should be conducted.

TABLE 10: SUMMARY TABLE OF RESULTS RELATING TO SUBSTANCES DERIVED FROM FCMs

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which the risk cannot be ruled out			
BPA	ANSES TV = 0.083 µg.kg bw^{-1}.d^{-1}: Cases where the limits were exceeded significantly from 5 months of age under the LB EFSA tTDI = 4 µg.kg bw^{-1}.d^{-1}: not exceeded under the UB	Determine current exposure levels, following the recent regulatory changes, in order to be able to rule on the need for new recommendations.	Reassess the TRVs following the long-term toxicity studies currently under way in the United States.
Substances for which the risk is considered tolerable/acceptable			
Benzophenone	TDI not exceeded P$_{90}$ < 2% of the TDI (0.03 mg.kg bw^{-1}.d^{-1})		Given the endocrine-disrupting effects of certain benzophenones, conduct more studies, especially *in vivo,* on reproduction and development
4-methyl-benzophenone (4-MBP)	MOS (> 5,000) much higher than the critical MOS of 200 (BMDL$_{10}$ = 3.1 mg.kg bw^{-1}.d^{-1})		Given the endocrine-disrupting effects of certain benzophenones, conduct more studies, especially *in vivo,* on reproduction and development
Nonylphenols	TRV not exceeded P$_{90}$ < 1.5% of the TRV (30 µg.kg bw^{-1}.d^{-1})		
BADGE and hydrolysis products	TDI not exceeded P$_{90}$ < 1.5% of the TDI (0.15 mg.kg bw^{-1}.d^{-1})		
DEHP	TDI not exceeded P$_{90}$ < 3% of the TDI (0.05 mg.kg bw^{-1}.d^{-1})		
DnBP	TDI not exceeded P$_{90}$ < 21% of the TDI (0.002 mg.kg bw^{-1}.d^{-1})		
DiDP & DiNP	TDI not exceeded P$_{90}$ < 6% of the TDI (0.15 mg.kg bw^{-1}.d^{-1})		
BBP	TDI not exceeded P$_{90}$ < 0.1% of the TDI (0.5 mg.kg bw^{-1}.d^{-1})		

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which no conclusions can be reached			
4-tert-octylphenol	No robust TRV		Conduct additional toxicity studies to establish a robust TRV
4-hydroxy-benzophenone (4-HBP)	No robust TRV		Given the endocrine-disrupting effects of certain benzophenones, conduct more studies, especially *in vivo,* on reproduction and development
4-benzoylbiphenyl (PBZ)	No robust TRV		
2-isopropyl-thioxanthone (ITX)	No robust TRV		
Chlorohydrin derivatives of BADGE	No robust TRV		
DiBP	No robust TRV		Conduct toxicity studies for establishing TRVs applicable to the general population and taking infant specificities into account.
DEP	No robust TRV		Conduct toxicity studies for establishing TRVs applicable to the general population and taking infant specificities into account.
DCHP	No robust TRV		Conduct toxicity studies for establishing TRVs applicable to the general population and taking infant specificities into account.
DnOP	No robust TRV		Conduct toxicity studies for establishing TRVs applicable to the general population and taking infant specificities into account.

1.6 Phyto-oestrogens and sex steroids of animal origin

1.6.1 Sex steroids of animal origin (17β-testosterone & 5α-dihydrotestosterone, 17α and 17β-oestradiol, oestrone and progesterone)

In this study, sex steroids of animal origin relate to hormones synthesised naturally by domestic mammals. This group of steroids includes oestrogens, androgens and progestogens. Although several compounds were assayed, only data on 17β-testosterone, 5α-dihydrotestosterone, progesterone, oestrone, and 17β- and 17$\alpha-$œstradiol were exploited in this study. The criteria used to rank these steroids included firstly their ability to bind with high affinity to the steroid receptors (ERα, ERβ, AR, PR), secondly the access to robust, reliable analytical data, and lastly their confirmed presence in foodstuffs.

Detection percentages were very low for 17β-testosterone, 5α-dihydrotestosterone, 17α-œstradiol and 17β-œstradiol, but were high for progesterone (80% on average). Detection rates for oestrone were intermediate. As expected, the steroid profiles differed greatly from one food to another.

In the absence of a robust TV (large differences were noted between the values proposed by the JECFA and those proposed by the FDA), it is not possible to reach a conclusion as to the health risk associated with dietary exposure to these substances.

Work is needed to obtain more data on these substances, especially toxicological data.

1.6.2   Phyto-oestrogens: isoflavones, lignans, coumestans

Three major classes of phyto-oestrogens were analysed: isoflavones (genistein, daidzein and glycitein), enterolignan precursors (secoisolariciresinol, matairesinol and enterodiol) and coumestrol belonging to the class of coumestans.

The detection percentages were rather low for certain substances (enterodiol, biochanin A, glycitein) but were on the other hand high for genistein, daidzein, secoisolariciresinol and equol. The highest concentrations were measured in products containing soy, for isoflavones and lignans, and it seems necessary to distinguish consumers of soy-based products who are subject to very high exposure to these substances, from children who do not consume them.

Given the absence of a toxicological benchmark, it is impossible to reach a conclusion as to the health risk associated with dietary exposure to these substances, with the exception of genistein, for which the risk cannot be ruled out for children consuming soy-based products. For this substance, the mean exposure levels for non-consumers of soy-based products were between 0.70 and 6.58 µg.kg bw^{-1}.d^{-1} depending on the age group. These levels reached 880 µg.kg bw^{-1}.d^{-1} in children consuming soy-based products, which led to a margin of safety of 40, deemed to be too low with regard to the LOAEL[14] of 35 mg.kg bw^{-1}.d^{-1} and the critical MOE of 300 adopted in this study.

The consumption of soy-based products by children under three years of age should therefore be limited.

1.6.3   General recommendation for sex steroids of animal origin and phyto-oestrogens

The diverse mixture of substances with hormone-mimicking activity provided by the diet implies that their chemical nature, interactions and mechanisms of action should be taken into account from an overall perspective. The CES ERCA therefore recommends that additional studies be conducted with mixtures that reflect dietary exposure to the substances in order to assess, through bioassays, their hormonal potential (oestrogenic, anti-androgenic, etc.).

Work is needed to develop a method able to address the issue of mixtures and understand the risks associated with natural substances provided via food (phyto-oestrogens, sex steroids of animal origin, etc.) and xenobiotics with hormonal effects (plant protection products, dioxins, brominated flame retardants, bisphenols, PCBs, alkylphenols, etc.).

TABLE 11: SUMMARY TABLE OF RESULTS RELATING TO SEX STEROIDS OF ANIMAL ORIGIN AND PHYTO-OESTROGENS

---

[14] LOAEL: Lowest Observed Adverse Effect Level

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which the risk cannot be ruled out			
Genistein in consumers of soy-based products	MOS = 40 (below the provisional critical MOS of 300) LOAEL of 35 mg.kg^{-1}.d^{-1}	Limit the consumption of soy-based products by children under three years of age.	Re-assess the TRV in light of more precise data when these are available and have been validated
Substances for which the risk is considered tolerable			
Genistein in non-consumers of soy-based products	MOS > 5,300 LOAEL of 35 mg.kg^{-1}.d^{-1}		

Substances	Conclusions		Research recommendations
Substances for which no conclusions can be reached			
Priority sex steroids of animal origin: 17β-testosterone & 5α-dihydrotestosterone, progesterone,17α & 17β-oestradiol, and oestrone	No robust TRV		Assess their overall hormonal potential, using bioassays on mixtures that reflect dietary exposure. Develop a method able to address the issue of mixtures and understand the risks associated with natural substances provided via food and xenobiotics with hormonal effects
Other sex steroids of animal origin	No robust TRV		
Other isoflavones (daidzein and related compounds, and glycitein)	No robust TRV		
Enterolignans (secoisolariciresinol, matairesinol and enterodiol)	No robust TRV		
Coumestrol	No robust TRV		

1.7 Additives

Phosphoric acid (E338), tartaric acid (E334) and ascorbyl palmitate (E304) were screened for in the foods in which they are authorised, even though some of them were also found in foods in the natural state. The exposure levels only take into account the intakes of these compounds via their use as additives.

Phosphoric acid was detected very widely in the foods analysed, unlike tartaric acid and ascorbyl palmitate which were only detected sporadically in certain samples.

Concerning phosphoric acid, which is mainly found in protein-rich foods, dairy products were the main contributors regardless of the age group. Mean exposure to phosphates deriving from the only foods that can contain phosphoric acid or orthophosphates provided by food additives accounted for between 38 and 42% of the maximum tolerable consumption level (MTCL) of 70 mg.kg bw^{-1}.d^{-1} and reached a maximum of 66% at the 90th percentile in children aged 7-12 months. Non-representative cases were noted where the MTCL was exceeded, for all age groups. Given the exposure levels observed for food additives, and the fact that these levels did not take into account other sources of phosphate exposure (in particular its natural presence in

certain foods that were not analysed here), the possibility that overall exposure to phosphates significantly exceeds the established MTCL cannot be ruled out. **A health risk associated with dietary exposure to phosphates as additives cannot be ruled out.** However, an overall analysis (including natural food sources) of all forms of phosphates is needed to confirm the total exposure level.

Levels of exposure to ascorbyl palmitate in children under six months of age exceeded the selected ADI only under the UB assumption. However the limits were not exceeded at all under the LB assumption. For this additive, the risk cannot be ruled out for children under three years of age. A lowering of the analytical limits seems necessary to refine the exposure calculations.

Exposure to tartaric acid was lower than the selected ADI (with a P90 less than 10% of the ADI) but this does not take into account the natural presence of tartaric acid at high levels in certain foods (in particular, bananas and grapes). This uncertainty means that it is not possible to reach a conclusion as to the risk associated with dietary exposure to tartaric acid.

TABLE 12: SUMMARY TABLE OF RESULTS RELATING TO THE ADDITIVES ANALYSED IN THE iTDS

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which the risk cannot be ruled out			
Phosphoric acid (E338) & orthophosphates	Non-representative cases where the ADI was exceeded, regardless of the age		Natural sources and other phosphate forms to be taken into account for calculating exposure
Ascorbyl palmitate (E304)	ADI exceeded under the UB in children under 6 months of age Not exceeded under the LB		Lower the analytical limits
Substances for which no conclusions can be reached			
Tartaric acid (E334) and its salts	Limits not exceeded P90 < 10% of the ADI		Natural sources to be taken into account for calculating exposure

1.8 Pesticide residues

The iTDS was characterised overall by better analytical performances than the TDS2, which helped reduce the uncertainty associated with the exposure assessment and obtain more realistic results in the high assumption (UB). Thus the limits of detection are two to 10 times lower than those used in the TDS2, or in the most recent surveillance and control programmes.

Pesticide residues were detected in 67% of the composite samples analysed, and quantified in 37% of them. Among the composite samples in which residues were detected, 17% contained a single active substance (AS), 61% contained 2 to 5 ASs and 22% contained more than 5 ASs. As a reminder, a composite sample consisted of 12 sub-samples of the same food and of equal weight (see methodology).

Among the 469 substances and metabolites screened for, 17% were detected and 8% quantified at least once. Concerning the 84 priority substances for surveillance when the study was launched, 42% were detected and 25% quantified.

Eleven substances were detected in over 10% of foods: the fungicides 2-phenylphenol (OPP), azoxystrobin, boscalid, captan (its metabolite THPI), carbendazim, cyprodinil, difenoconazole, dodine and tebuconazole, the herbicide metribuzin and the synergist piperonyl butoxide (PBO). Among these pesticides, metribuzin and OPP (18% of samples), carbendazim (14%), tebuconazole (12%) and captan (11%) had been defined as priorities for surveillance due to their unfavourable toxicological profiles. The toxicity reference values (TRVs) for these eleven substances were not exceeded. The maximum exposure was 2% of the TRV for carbendazim. With the exception of PBO, these were all active plant protection substances approved under Regulation (EC) No 1107/2009 at the time of the study's sampling phase. Carbendazim has not been authorised in France since 2008, but it is also the metabolite of an authorised substance, thiophanate-methyl.

Concerning infant foods, at least one residue was detected in 67% of the 219 composite samples analysed, and quantified in 27% of samples. Among the substances and metabolites screened for in the infant foods, 19% were detected and 5% quantified at least once. All the jars of fruit, vegetables and vegetables with fish or meat, as well as the infant fruit juices, contained the residues detected. However, in the growing-up milks and infant formulas, 2-phenylphenol (OPP) was detected (but not quantified) in one sample of follow-on formulas. No pesticide residues were detected in the first infant formulas.

Concerning normal foods, at least one residue was detected in 68% of the 90 composite samples analysed, and quantified in 60% of samples. Among the substances and metabolites screened for in the normal foods, 8% were detected and 7% quantified at least once.

These detection and quantification rates are indicative and cannot be compared between different categories of foods. Similarly, they cannot be compared with those of the TDS2, given the methodological differences between the two studies. The detection rate in normal foods, which was higher in the iTDS than in the TDS2, can mainly be explained by the improved analytical performances in the iTDS.

The dietary risk was characterised for 281 substances with a TRV (see summary table), of which 78 are priority substances. Under the low contamination assumption (LB), which tends to underestimate exposure, the TRV was not observed to have been exceeded in any case. Under the high contamination assumption (UB), which tends to overestimate exposure, the TRV was exceeded by three priority pesticides for one or more age groups: these were two persistent organic pollutants (POPs), dieldrin and lindane, which are older pesticides prohibited at the international level and environmental contaminants, and a relevant metabolite (propylene thiourea, PTU) of propineb, a fungicide that has approval at EU level. The risk cannot be entirely ruled out for these three substances, because the TRVs were exceeded only under the UB assumption overestimating exposure and the actual risk. This overestimated risk under the UB is related to the limits of detection not being low enough with regard to the TRV. For these three pesticides, it is therefore recommended that the exposure and risk be re-assessed based on new analyses with better analytical performances.

The risk is deemed to be tolerable/acceptable for 278 active substances, due to the fact that no TRVs were exceeded under either of the assumptions used. For these substances, a high level of coverage (70 to 100%) of the theoretically contributing diet was noted. The risk associated with chronic exposure to these substances does not constitute a health problem.

For 188 substances, in particular 17 regarded as relevant (priority and/or detected), the risk could not be characterised because of the lack of TRVs (n=4) and/or insufficient coverage of the theoretically contributing diet (n=8) and/or the lack of reference substances (standards) for certain metabolites included in the residue definitions (n=5) (see summary table). For the eight substances for which coverage was insufficient, it is recommended that surveillance be broadened to all the theoretically contributing foods. Concerning fenuron, a herbicide that has not been authorised in Europe since 2002, it is recommended that new analyses be performed on more recent samples of the three natural mineral waters concerned. Lastly, the reference substances for the metabolites included in the residue definitions need to be made commercially available, for the risk assessment of the five priority substances.

Despite a satisfactory level of coverage of the contributing diet for the majority of pesticides, one of the uncertainties affecting this study is the lack of sampling of certain fresh fruits and vegetables (strawberries, grapes, melon, cucumber), given the period of the consumption study. Note that consumption of these fruits was taken into account in the processed state (purees, jars of baby food, etc.). An additional assessment based on the theoretical contribution levels of these fruits shows that taking them into account in the exposure calculation does not significantly alter the initial conclusions. Nevertheless, it is recommended that these fresh fruits and vegetables be included in a future study.

A higher number of pesticide residues was screened for in the iTDS (n=469) compared to the TDS2 (n=283), given the greater number of mono- and multi-residue analytical methods, and samples screened per method.

TABLE 13: SUMMARY TABLE OF RESULTS RELATING TO PESTICIDE RESIDUES

Substances	Conclusions	Recommendations for management measures	Research recommendations
Substances for which the risk is considered tolerable/acceptable			
278 pesticide residues	TRV not exceeded. High level of coverage of the theoretically contributing diet (70 to 100%).	-	-
Substances for which a risk cannot be entirely ruled out, because the TRVs were exceeded only under the high assumption (UB) overestimating exposure and the actual risk (1)			
Dieldrin (incl. aldrin) *POP listed in the Stockholm Convention (environmental contaminant)*	TRV exceeded in 49% of children aged 1-4 months, limits not exceeded significantly in children aged 5-12 months.	Risk management should draw on the results of new analyses with lower limits of detection. In the context of the surveillance plans, it is recommended that screening for PTU be included in fruits where the use of propineb is authorised in Europe.	Improve analytical performance.
Lindane (HCH-gamma) *POP listed in the Stockholm Convention (environmental contaminant)*	JMPR's TRV not exceeded (2003). ATSDR's TRV exceeded significantly (2005).		
PTU (propylene thiourea) *A metabolite of propineb, a fungicide approved under Regulation (EC) No 1107/2009*	TRV exceeded in between 5 and 40% of children, depending on the age group.		
Relevant substances (priority and/or detected) for which no conclusions can be reached			
Fenuron (NA) (2) Metolcarb (NA) Propargite (NA) Tricyclazole (ongoing)	TRV not available or not finalised	Strengthen surveillance: increase the number of analyses in the context of the surveillance plans (theoretical contributors, in particular)	Conduct new more recent analyses in order to identify whether it is necessary to establish TRVs.
Chlorantraniliprole (A) Dodine (A) Oxyfluorfen (A) Pyridaben (A) Triflumizole (A) Biphenyl (NA) Flucythrinate (NA) Tolfenpyrad (NA)	Insufficient coverage of the theoretically contributing diet (< 70%).		Increase the number of foods to be analysed in order to improve the level of coverage of the theoretically contributing diet, and re-assess exposure in more detail.
Chlorothalonil (A) Chlorpropham (A) Fenpropimorph (A) Flusilazole (A) Tepraloxydim (A)	Reference substances (standards) not available for analysing metabolites included in the residue definitions, and conversion factors non-existent.	Make available the reference substances for the metabolites included in the residue definitions, for the risk assessment.	Supplement the analyses by screening for the missing metabolites.

(1) This overestimated risk under the UB is related to the limits of detection not being low enough with regard to the TRV. Lindane and PTU were not detected. Dieldrin was detected and quantified in a composite sample of cooked courgettes and in 0.01% of tap water samples.
(2) Status according to Regulation (EC) No 1107/2009: A (approved), NA (not approved) or ongoing

1.9   Minerals

Twelve minerals were analysed in the context of the iTDS. The results of this study show that intakes meet needs to a satisfactory level overall for children under three years of age. This is the case for iron and zinc in children under six months, for magnesium, calcium and copper in those under one year, and lastly for manganese, selenium, molybdenum and potassium in children under three years of age.

However, there were insufficient intakes of zinc (37% in children aged from 7 months to 3 years), calcium (14%) in children aged 13-36 months and iron in children aged 7-36 months (48% in those aged 7-12 months and 81% in those aged 13-36 months). For magnesium and copper in children aged 13-36 months, levels were below the adequate intake, i.e. the observed mean intake for a group of individuals in apparent good health. Given the nature of this nutritional reference, the health risk associated with an insufficient intake cannot be assessed.

As no nutritional reference has been adopted for chromium, lithium and sodium, the prevalence of inadequate intake could not be calculated. The health risk associated with an insufficient intake of these elements could not be assessed for children under three years of age. Studies should be conducted in order to determine nutritional references.

Concerning excessive intakes, the tolerable upper intake levels (UL) set for molybdenum in children aged 1-3 years, and for calcium in children aged 7-36 months, was not exceeded. The risk associated with excessive intake can therefore be ruled out for these age groups.

However, the ULs were observed to have been exceeded for calcium in children under six months of age, and for manganese, selenium and copper in children aged one to three years. It is, however, difficult to estimate the proportion of the population exposed given the limitations related to the sampling or the measurement of exposure. Concerning calcium, all the children in whom the UL was exceeded had consumed semi-skimmed milk during the three days of the survey, and in greater quantities than the mean consumption. Moreover, milk is higher in calcium than infant formulas. These exceeded ULs are therefore attributable to the consumption of normal milk. Lastly, for zinc, the limits were observed to have been exceeded in all age groups (up to 75% of children under the age of six months). A risk related to the excessive intake of these minerals cannot therefore be ruled out for certain groups of consumers.

For iron, potassium, sodium, lithium and magnesium, in the absence of any ULs, it is impossible to reach a conclusion as to a possible excessive intake for children under three years of age. Similarly, for manganese, molybdenum, selenium and copper, in the absence of any ULs for children under one year of age, it is impossible to reach a conclusion as to a possible excessive intake. Studies should be conducted in order to determine a UL for these age groups.

Conclusions of the collective expert appraisal

The Expert Committee on "Assessment of physico-chemical risks in food" adopted the collective expert appraisal work and its conclusions and recommendations, which are covered in this report, at its meeting of 23 February 2016 and informed ANSES's General Directorate accordingly.

Date of validation of the report by the Expert Committee: 23 February 2016

Annex

TABLE A1: LIST OF SUBSTANCES ANALYSED IN THE INFANT TDS

Group	Substances or congeners
Mycotoxins	**Aflatoxins:** AFB1, AFB2, AFG1, AFG2, AFM1
	Ochratoxins: OTA
	Patulin
	Trichothecenes: DON, DON3, DON15, Niv, T2, HT2, DAS, FusX, Ver, MAS, T2-triol
	Zearalenone: ZEA
	Fumonisins: FB1, FB2
	Alternaria **toxins:** AOH, AME, TA
Phyto-oestrogens:	**Isoflavones:** Genistein, daidzein, glycitein, biochanin A, formononetin and equol
	Coumestans: coumestrol
	Lignans and enterolignans: Matairesinol, secoisolariciresinol and enterodiol
Sex steroids of animal origin:	**Oestrogens:** a-oestradiol, b-oestradiol, oestrone
	Androgens: Dihydrotestosterone, epitestosterone, 4-androstenedione, testosterone, 5b-dihydrotestosterone, androsterone, 5a-dihydrotestosterone, 17b-testosterone, 17a-testosterone, epiandrosterone, 5b-androstane-3one-17b-ol, etiocholanolone, DHEA
	Progestogens: progesterone
Minerals	Calcium, Sodium, Magnesium, Potassium, Iron, Zinc
Trace metal elements	Aluminium, Antimony, Silver, Arsenic, Barium, Cadmium, Chromium, Cobalt, Copper, Tin, Gallium, Germanium, Lithium, Manganese, Mercury, Molybdenum, Nickel, Lead, Strontium, Selenium, Tellurium and Vanadium
Dioxins and furans	**PCDDs:** TCDD_2378, PCDD_12378, HCDD_123478, HCDD_123678, HCDD_123789, HCDD_1234678, OCDD
	PCDFs: TCDF_2378, PCDF_12378, PCDF_23478, HCDF_123478, HCDF_123678, HCDF_234678, HCDF_123789, HCDF_1234678, HCDF_1234789, OCDF
PCBs	**DL-PCBs:** PCB_77, PCB_81, PCB_126, PCB_169, PCB_105, PCB_114, PCB_118, PCB_123, PCB_156, PCB_157, PCB_167, PCB_189
	NDL-PCBs: PCB_28, PCB_52, PCB_101, PCB_138, PCB_153, PCB_180
Brominated flame retardants	**PBDEs:** BDE 28, BDE 47, BDE 99, BDE 100, BDE 153, BDE 154, BDE 183, BDE 209
	PBBs: BB52, BB101, BB153
	HBCDs: α, β, γ
	TBBPA
Perfluorinated compounds	PFOS, PFBS, PFHxS, PFHpS, PFDS
	PFOA, PFBA, PFPA, PFHxA, PFHpA, PFNA, PFDA, PFUnA, PFDoA, PFTrDA, PFTeDA
Phthalates	DnBP, DEHP, DINP, DIDP, DEP, DiBP, BBP, DCHP, DOP, di-butyl sebacate, di-(2-ethylhexyl)adipate
Alkylphenols	*4-tert*-octylphenol and mixtures of 4-nonylphenol isomers
Bisphenols	BPA and BADGE
Ink photoinitiators	Benzophenone, 4-MBP, 4-HBP, PBZ, ITX
Polycyclic aromatic hydrocarbons	PHE, AN, FA, PY, BaA, CPP, CHR, 5-MCH, BaP, IP, DBahA, BghiP, DbalP, DbaeP, DbaiP, DbahP, Benzo[c]fluorene
Acrylamide	
Furan	

Group	Substances or congeners
Pesticide residues (priority substances)	**Phosphinic acid:** glufosinate
	Tetronic acid (derivative): spirodiclofen
	Amide: propyzamide
	Quaternary ammonium: diquat
	Anilide: propanil
	Anilinopyrimidine: mepanipyrim
	Avermectins: abamectin, emamectin benzoate
	Benzimidazoles: carbendazim, thiabendazole
	Benzoylphenylurea: flufenoxuron
	Carbamates: carbaryl, carbofuran, chlorpropham, methomyl, oxamyl, thiophanate-methyl
	Chloroacetamide: alachlor
	Chloronitrile: chlorothalonil
	Cyclohexene oxime: profoxydim, tepraloxydim
	Dicarboximide: captan, cinidon, flumioxazin, iprodione, procymidone
	Dinitroaniline: trifluralin
	Dithiocarbamates and their metabolites: dithiocarbamates, ethylene-thiourea (ETU) and propylene thiourea (PTU)
	Glycine derivative: glyphosate
	Hydroxybenzonitriles: bromoxynil, ioxynil
	Imidazoles: imazalil, prochloraz
	Isoxazole: isoxaflutole
	Morpholine: fenpropimorph
	Organochlorides: chlordane, DDT, dieldrin, endosulfan, endrin, HCH, heptachlor, hexachlorobenzene, lindane (HCH-gamma)
	Organophosphates: chlorpyriphos-ethyl, chlorpyriphos-methyl, dimethoate, malathion, phosmet, pyrimiphos-methyl
	Phenol: 2-phenylphenol (OPP)
	Phenoxy herbicide: 2,4-D, 2,4-DB
	Phenylpyrazole: fipronil
	Phenylureas: chlorotoluron, diuron, isoproturon, linuron
	Pyrethroids: acrinathrin, bifenthrin, cyfluthrin, deltamethrin, esfenvalerate, tau-fluvalinate
	Pyridine (carboxylic acid): picloram
	Spinosyn: spinosad
	Strobilurins: dimoxystrobin, kresoxim-methyl
	Sulphite ester: propargite
	Thiocarbamate: molinate
	Triazines: atrazine, simazine
	Triazinone: metribuzin
	Triazoles: amitrole, cyproconazole, epoxiconazole, fluquinconazole, flusilazole, metconazole, myclobutanil, tebuconazole, triadimenol
Additives	**Ascorbyl palmitate (E304)**
	Tartrates: tartaric acid (E334), sodium (E335), potassium (E336) and calcium (E354) tartrates
	Phosphates: phosphoric acid (E338), sodium (E339) and calcium (E341) phosphates

References

AFSCA. 2010. Avis du comité scientifique de l'Agence fédérale belge pour la sécurité de la chaîne alimentaire sur les risques cancérogènes et/ou génotoxiques dans les denrées alimentaires: contaminants liés aux processus de transforation (dossier Sci Com 2007/09bis : auto-saisine). Bruxelles, Belgique: AFSCA.

AFSSA. 2003. Avis de l'AFSSA relatif à une demande d'avis sur l'évaluation des risques présentés par le Benzo(a)pyrène (B(a)P) et par d'autres hydrocarbures aromatiques polycycliques (HAP), présents dans diverses denrées ou dans certaines huiles végétales, ainsi que sur les niveaux de concentration en HAP dans les denrées au-delà desquels des problèmes de santé risquent de se poser [A*FSSA Opinion on a request for an opinion on the risk assessment presented by Benzo(a)pyrene (B(a)P) and other polycyclic aromatic hydrocarbons (PAHs), found in various foodstuffs or in certain vegetable oils, as well as on the PAH concentration levels in foodstuffs above which health problems may arise*]. (Request No 2000-SA-0005). Maisons Alfort: AFSSA.

ANSES. 2011. Avis de l'ANSES et rapport d'expertise relatifs à l'Etude de l'Alimentation Française 2 (EAT2) - Tome 1 : Contaminants inorganiques, minéraux, poluants organiques persistants, mycotoxines, phyto-estrogènes [*ANSES opinion and expert report on the Second Total Diet Study (TDS2) - Volume 1: Inorganic contaminants, minerals, persistent organic pollutants, mycotoxins and phytoestrogens*]. Maisons-Alfort: ANSES.

ANSES. 2013. Avis de l'ANSES relatif aux recommandations sur les bénéfices et les risques liés à la consommation de produits de la pêche dans le cadre de l'actualisation des repères nutritionnels du PNNS [*ANSES opinion on the recommendations on the benefits and risks of fish consumption in the context of the updating of the PNNS's nutritional guidelines*]. (Request No 2012-SA-0202). Maisons-Alfort: ANSES.

ANSES. 2015. Avis de l'ANSES et rapport d'expertise collective relatifs à la consommation de poissons d'eau douce et PCB : aspects réglementaires, méthodologiques et sanitaires [ANSES opinion and collective expert assessment report on the consumption of freshwater fish and PCBs: regulatory, methodological and health aspects]. (Request Nos 2014-SA-0122 and 2011-SA-0039). Maisons-Alfort: ANSES.

Cerna, M., V. Bencko, M. Brabec, J. Smid, A. Krskova, and L. Jech. 2010. "Exposure assessment of breast-fed infants in the Czech Republic to indicator PCBs and selected chlorinated pesticides: area-related differences." *Chemosphere* 78 (2):160-8. doi: 10.1016/j.chemosphere.2009.09.062.

Chovancova, J., K. Conka, A. Kocan, and Z. S. Sejakova. 2011. "PCDD, PCDF, PCB and PBDE concentrations in breast milk of mothers residing in selected areas of Slovakia." *Chemosphere* 83 (10):1383-90. doi: 10.1016/j.chemosphere.2011.02.070.

Cok, I., M. K. Donmez, M. Uner, E. Demirkaya, B. Henkelmann, H. Shen, J. Kotalik, and K. W. Schramm. 2009. "Polychlorinated dibenzo-p-dioxins, dibenzofurans and polychlorinated biphenyls levels in human breast milk from different regions of Turkey." *Chemosphere* 76 (11):1563-71. doi: 10.1016/j.chemosphere.2009.05.032.

de Lauzon, B., J. L. Volatier, and A. Martin. 2004. "A Monte Carlo simulation to validate the EAR cut-point method for assessing the prevalence of nutrient inadequacy at the population level." *Public Health Nutr* 7 (7):893-900.

EC. 2002. "Endocrine Disrupters: study on gathering information on 435 substances with insufficient data. European Commission, DG Environment RPS BKH Consulting Engineers, No. B4-3040/2001/325850/MAR/C2. Final Report.".

EFSA. 2008. Scientific Opinion of the Panel on Contaminants in the Food Chain on a request from the European Commission on Polycyclic Aromatic Hydrocarbons in Food. In *The EFSA journal*. Parma: EFSA.

EFSA. 2010. Scientific Opinion of the EFSA panel on Dietetic Products, Nutrition, and Allergies on principles for deriving and applying Dietary Reference Values. In *The EFSA journal*. Parma: EFSA.

EFSA. 2011a. Scientific Opinion of the EFSA Panel on Contaminants in the Food Chain on Polybrominated Diphenyl Ethers (PBDEs) in Food. In *The EFSA journal*. Parma: EFSA.

EFSA. 2011b. Update on furan levels in foods from monitoring years 2004-2010 and exposure assessment. In *EFSA Scientific Report*. Parma: EFSA.

EFSA. 2012. Reasoned Opinion on the modification of the existing MRL for glyphosate in lentils. In *The EFSA journal*. Parma: EFSA.

EFSA. 2013. Scientific Opinion of the EFSA Panel on Dietetic Products, Nutrition and Allergies on nutrient requirements and dietary intakes of infants and young children in the European Union. In *The EFSA journal*. Parma: EFSA.

EFSA. 2015a. Scientific Opinion of the EFSA Panel on Contaminants in the Food Chain on acrylamide in food. In *The EFSA journal*. Parma: EFSA.

EFSA. 2015b. Scientific Opinion of the EFSA Panel on Contaminants in the Food Chain on the risks to public health related to the presence of nickel in food and drinking water. In *The EFSA journal*. Parma: EFSA.

European Commission. 1998. Report on methodologies for the monitoring of food additive intake across the European Union. Final report submitted by the Task Coordinator, 16 January 1998. In *Reports of a Working Group on Scientific Cooperation on Questions Relating to Food, Task 4.2* Brussels: European Commission, Directorate General III Industry.

Fantino, M., and E. Gourmet. 2008. "Apports nutritionnels en France en 2005 chez les enfants non allaités âgés de moins de 36 mois." *Arch Pediatr* 15 (4):446-55. doi: 10.1016/j.arcped.2008.03.002.

Hulin, M., N. Bemrah, A. Nougadère, J. L. Volatier, V. Sirot, and J. C. Leblanc. 2014. "Assessment of infant exposure to food chemicals: the French Total Diet Study design." *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* 31 (7):1226-39. doi: 10.1080/19440049.2014.921937.

IOM. 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. edited by National Academy Press. Washington, D.C.: IOM.

IOM. 2011. Dietary Reference Intakes for Calcium and Vitamin D. edited by The National Academies Press. Washington, DC IOM.

Johnson-Restrepo, B., R. Addink, C. Wong, K. Arcaro, and K. Kannan. 2007. "Polybrominated diphenyl ethers and organochlorine pesticides in human breast milk from Massachusetts, USA." *J Environ Monit* 9 (11):1205-12. doi: 10.1039/b711409p.

Johnson, K. A., S. J. Gorzinski, K. M. Bodner, R. A. Campbell, C. H. Wolf, M. A. Friedman, and R. W. Mast. 1986. "Chronic toxicity and oncogenicity study on acrylamide incorporated in the drinking water of Fischer 344 rats." *Toxicol Appl Pharmacol* 85 (2):154-68.

Lucas, J. P., B. Le Bot, P. Glorennec, A. Etchevers, P. Bretin, F. Douay, V. Sebille, L. Bellanger, and C. Mandin. 2012. "Lead contamination in French children's homes and environment." *Environ Res* 116:58-65. doi: 10.1016/j.envres.2012.04.005.

Marchand, P., J. P. Antignac, A. Brosseau, C. Gade, A. Venisseau, M.-R. Sabatie, V. Sirot, A. Tard, J L Volatier, J. C. Leblanc, F. André, and B. Le Bizec. 2006. "Factors (trophic levels, fish species, habitat, fat content…) influencing PCDD/F, PCB and PBDE concentration in fish retailed in France." *Organohalogen Compounds* 68:608-11.

Park, J. S., J. She, A. Holden, M. Sharp, R. Gephart, G. Souders-Mason, V. Zhang, J. Chow, B. Leslie, and K. Hooper. 2011. "High postnatal exposures to polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) via breast milk in California: does BDE-209 transfer to breast milk?" *Environ Sci Technol* 45 (10):4579-85. doi: 10.1021/es103881n.

PNNS. 2004. Livret d'accompagnement du "Guide nutrition des enfants et ados pour tous les parents" destiné aux professionnels de santé. AFSSA, InVS, Ministère de la Santé et des Sports, L'assurance Maladie, INPES.

Sirot, V., T. Guerin, Y. Mauras, H. Garraud, J L Volatier, and J. C. Leblanc. 2008. "Methylmercury exposure assessment using dietary and biomarker data among frequent seafood consumers in France CALIPSO study." *Environ Res* 107:30-38.

TemaNord. 2002. *Food additives in Europe 2000 - Status of safety assessments of food additives presently permitted in the EU*. Copenhagen, Denmark: Nordic Council of Ministers.

Touvier, M, S Lioret, I Vanrullen, J C Boclé, M C Boutron-Ruault, J L Berta, and J L Volatier. 2006. "Vitamin and mineral inadequacy in the French population: estimation and application for the optimization of food fortification." *Int J Vitam Nutr Res* 76 (6):343-51. doi: 10.1024/0300-9831.76.6.343.

Ulaszewska, M. M., E. Zuccato, and E. Davoli. 2011. "PCDD/Fs and dioxin-like PCBs in human milk and estimation of infants' daily intake: a review." *Chemosphere* 83 (6):774-82. doi: 10.1016/j.chemosphere.2011.02.066.

anses