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French infant total diet study: Dietary exposure to heat-induced compounds (acrylamide, furan and polycyclic aromatic hydrocarbons) and associated health risks

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ABSTRACT

A total diet study (TDS) was conducted between 2010 and 2016 to assess the risk associated with chemicals in food of non-breast-fed children from 1 to 36 months living in France. Food samples were collected, prepared "as consumed", and analyzed for chemicals of public health interest. Acrylamide, furan and polycyclic aromatic hydrocarbons (PAHs) were analyzed as heat-induced compounds produced mainly during thermal processing of foods. Dietary exposure was assessed for 705 representative children using food consumptions recorded through a 3-consecutive-days record.

As all calculated margins of exposure (MOE) for PAHs exceeded 10 000, dietary exposure of the infant and toddler population was deemed tolerable with regard to the carcinogenic risk. Conversely, the exposure levels to acrylamide and furan were considered as of concern, requiring management measures to reduce the exposure essentially by reducing the formation of heat-induced compounds during food production or preparation processes. Efforts should mainly focus on major contributors to the exposure, i.e. sweet and savoury biscuits and bars, and potatoes and potato products for acrylamide, baby jars of vegetables, with or without meat or fish for acrylamide and furan.

1. Introduction

Humans are exposed through their diet to a large variety of chemicals that can induce adverse health effects. Some are already present in food, other compounds are generated during or after processing, particularly during heating and/or storage. Furan, acrylamide and polycyclic aromatic hydrocarbons (PAHs) are among chemicals that are mainly formed in food during thermal processing and can co-occur. Furan is an organic volatile compound produced from several precursors (EFSA, 2017). The main routes of furan formation are the Maillard reaction, thermal degradation of carbohydrates and some amino acids, thermal oxidation of polyunsaturated fatty acids, ascorbic acid and carotenoids, but also non-thermal treatments with the formation of free radicals during irradiation (Perez Locas and Yaylayan,

Abbreviations: ANSES, French agency for food, environmental and occupational health and safety; BfR, Bundesinstitut für Risikobewertung; BMDL, lower confidence limit of the benchmark dose; EFSA, European Food Safety Authority; FAO, Food and Agriculture Organization; FSA, Food Standard Agency; FSANZ, Food Standards Australia New Zealand; IARC, International Agency for Research on Cancer; JECFA, Joint FAO/WHO Expert Committee on Food Additives; LB, lowerbound approach; LOD, limit of detection; LOQ, limit of quantification; MOE, margin of exposure; MOS, margin of safety; RfD, reference dose; TDS, total diet study; UB, upperbound approach; WHO, World Health Organization

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2004; Limacher et al., 2007). Furan is found in a variety of food including coffee and canned and jarred food (EFSA, 2017). Furan is known to be hepatotoxic in rodents, leading to hepatocellular adenomas and carcinomas (EFSA, 2017), and was classified as possibly carcinogenic to humans (2B) by the International Agency for Research on Cancer (IARC) (IARC, 1995).

Acrylamide is a chemical formed during cooking at high temperatures (at least 120 °C) of foods rich in starch or sugars and in asparagine-type amino acid, by the Maillard reaction (Mottram et al., 2002). Potatoes (fries or crisps), biscuits and coffee are the foods most likely to be contaminated (EFSA, 2012a,b). Acrylamide is known to be mainly a neurotoxic and genotoxic carcinogenic compound (IARC, 1994; EFSA, 2015). Moreover, epidemiological studies on mother child cohorts showed that adduct levels of acrylamide and its metabolite glycidamide were significantly associated with a reduced birth weight and head circumference as well as increased risk of being small for gestational age (Pedersen et al., 2012; Duarte-Salles et al., 2013; Zhivagui et al., 2019).

With the exception of occupational or accidental exposures, smoking and food are the main route of exposure of humans to PAHs. Food contamination by PAHs is most often of environmental origin (fuel emissions, residential heating systems, combustion processes, marine pollution and degassing) or linked to food processing (drying, smoking, cooking, etc.) (EFSA, 2008). Low molecular weight PAHs cause systemic non-carcinogenic threshold effects: mainly kidney, liver and blood disorders, whereas other PAHs with a high molecular weight, are carcinogenic and genotoxic (EC (European Commission) 2002).

Complementary to monitoring programs, total diet studies (TDSs) are known as one of the most cost-effective ways to monitor dietary exposure of a population to chemical substances and to assess the corresponding health risk. TDSs rely on three major principles: coverage of at least 80% of the diet of the population, analysis of food composite samples and foods prepared “as consumed” by the population (EFSA, FAO et al., 2011), with the objective to gather a food sampling representative of the diet and as close as possible to the consumer's meal to be reflect the population exposure.

In France, two TDSs have been conducted on the adult population and on children over three years of age, the second one including acrylamide and PAHs as heat-generated compounds (Sirot et al., 2012; Veyrand et al., 2013). In addition, children under three years of age have to be considered as a specific and sensitive sub-population due to their metabolic specificities and their high food intake/body weight ratio. If several countries worldwide conducted TDSs including young children (Canada, United Kingdom, United States of America …), only the New Zealand, Australian, and the UK TDS included acrylamide or PAHs analyses (FSANZ, 2009; FSANZ, 2014; FSA, 2018a,b) and none included furan.

The first French “infant TDS” (https://www.anses.fr/fr/node/95844) was conducted between 2010 and 2016 in order to collect concentration data of chemical substances in foods consumed by children under three, to estimate their dietary exposure for health risks assessment. Concentration data have been collected for 670 substances including trace elements, persistent organic pollutants, pesticide residues, substances migrating from food packaging, etc. In line with the second French TDS, acrylamide and PAHs were analyzed in the infant TDS, and furan was analyzed following the 2010 recommendations of EFSA to collect new data on furan occurrence in food (EFSA, 2010). The present article focuses on dietary exposure to acrylamide, furan and PAHs, and associated health risk of non-breast-fed children under three years of age living in France.

2. Materials and methods

2.1. Population and consumption data

Consumption data were those from the cross-sectional survey on individual dietary consumption in children under 3 years, conducted by the Syndicat Français des Aliments de l’Enfance et de la Nutrition Clinique, © « Etude SOFRES 2005/Université de Bourgogne – Pr M. Fantino pour le Syndicat Français des Aliments de l’Enfance » already described (Fantino, 2005). Briefly, between January and March 2005, 705 children under 3 years of age have been recruited based on a proportionate quota sampling representative of the young children in France (according to the French 2002 census, taking into account the population structure in each region, the children age divided into 11 groups, a 60%-rate of working mothers, and taking into account the socio-professional category of the head of family). Breast-fed children, even partially, were not included in the survey. Food consumption including beverages had been recorded through a 3-consecutive-days record describing foods, quantities and portion sizes. Individual body weights were also measured.

2.2. Sampling plan and analysis

Food samples were collected to analyze acrylamide, furan and 20 PAHs: anthracene (AN), benzo[*a*]anthracene (BaA), benzo[*a*]pyrene (BaP), benzo[*b*]fluoranthene (BbF), benzo[*c*]fluorene (BcFL), benzo[*ghi*]perylene (BghiP), benzo[*j*]fluoranthène (BjF), benzo[*k*]fluoranthène (BkF), chrysene (CHR), cyclopenta[*cd*]pyrene (CPP), dibenzo[*a,e*]pyrene (DbaeP), dibenz[*a,h*]anthracene (DBahA), dibenzo[*a,h*]pyrene (DbahP), dibenzo[*a,i*]pyrene (DbaiP), dibenzo[*a,l*]pyrene (DbalP), fluoranthene (FA), indeno[1,2,3-*c,d*]pyrene (IP), 5-methylchrysene (MCH), phenanthrene (PHE) and pyrene (PY).

The sampling plan and occurrence data were previously described (Hulin et al., 2014; Lambert et al., 2018a,b). Briefly, the consumption survey allowed to select the most consumed foods in terms of quantity and/or consumer rates, or foods known to contribute significantly to the exposure to one of the studied chemicals. Because available infant foods on the market are constantly changing, the product list was updated before the sampling. The initial food list covered more than 97% of the children's diet, on a mean consumption basis (g/day). From this initial food list, 134 food items were selected for furan analysis, 141 food items were selected for acrylamide analysis, and 189 food items were selected for PAH analysis. On this basis, respectively 73, 87, and 97% of the diet theoretically contributing to the exposure (on a consumption basis) was covered by the analyses.

Between July 2011 and July 2012, foods were collected and prepared “as consumed” (i.e. peeled, cooked etc.) following habits recorded in a specific on-line survey (Hulin et al., 2014).

For each food item of the PAHs and acrylamide analysis lists, one subsample of equal weight of a same food was collected each month during one year in order to take into account possible seasonal variations. The 12 subsamples were chosen to be representative of the children consumption regarding brands, purchasing places, preparation modes etc. (Hulin et al., 2014). Each subsample was prepared “as consumed” then kept at −18 °C until all subsamples had been prepared. Then, they were pooled together by cryogrinding prior to analysis. Long-storage was not expected to significantly modify acrylamide level in foods, especially in cereal-based baby foods (Hoenicke and Gatermann, 2005; Michalak et al., 2016). PAH concentrations were also not excepted to be modified.

Due to volatility of furan, a specific sampling protocol was followed to limit losses of the substance during homogenization and storage steps (Lambert et al., 2018a,b). Then, for each food item, 6 subsamples representative of the consumption were collected, prepared, directly homogenized at room temperature to obtain the individual composite sample and analyzed in the 48 h. Once again, the preparation methods were allocated according to the results of the on-line survey described in Hulin et al., (2014), including time of heating (between 1 and 20 min depending on food item), utensils, heating power, etc. The homogenization step was carried out using a spoon (for liquid and semi-liquid items) and a blender (for solid items) to mimic the habits of the

Table 1
Dietary exposure to PAH4 in children less than 3 years old and associated health risk regarding the $BMDL_{10}$ of 0.34 mg kg $bw^{-1}.d^{-1}$.

		1–4 months	5–6 months	7–12 months	13–36 months
Mean exposure ± standard deviation (ng.kg $bw^{-1}.d^{-1}$)	LB	1.27 ± 1.26	1.07 ± 0.58	1.42 ± 0.77	2.25 ± 1.81
	UB	2.98 ± 1.39	3.15 ± 0.94	3.66 ± 1.31	3.78 ± 2.18
P90 (ng.kg $bw^{-1}.d^{-1}$)	LB	3.24	2.63	2.85	4.10
	UB	5.94	5.13	5.93	5.87
Margin of exposure for mean exposure	LB	268000	318000	239000	151000
	UB	114000	108000	93000	90000
Margin of exposure for P90	LB	105000	129000	119000	83000
	UB	57000	66000	57000	58000

BMDL, Benchmark dose limit; LB, Lowerbound; UB, Upperbound.

parents.

The analytical methods used for the determination of acrylamide and furan occurrences and the corresponding concentrations in the foodstuffs have already been published (Lambert et al., 2018a,b). The analytical method for the determination of PAHs in food is presented in supplemental method, and the concentrations are presented in supplemental results 1.

Left-censored data was managed by adapting the World Health Organization (WHO) recommendations (WHO, 2013), i.e. by using a lowerbound (LB) hypothesis and an upperbound (UB) hypothesis. Values lower than LOD have been replaced by 0 under LB and by LOD under UB, and values lower than LOQ but higher than LOD have been replaced by LOD under LB and LOQ under UB.

2.3. Exposure calculation

For each subject of the consumption survey, the dietary exposure was assessed 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 chemical j of individual i, n is the number of foods in the diet, $C_{i,k}$ is the mean daily consumption of food k by individual i (calculated as the mean of the 3 days of survey recording), $L_{k,j}$ is the concentration level of chemical j in food k, and BW_i is the body weight of individual i.

In order to cover a greater part of the whole diet, acrylamide and PAH concentration data from the second French TDS in common foods (Sirot et al., 2012; Veyrand et al., 2013) were compiled with the present one. Thus, 89 additional food items had an acrylamide level, as well as 223 food items for PAHs.

To take into account the dietary diversification periods, the population was divided into four age groups: 1–4 months, 5–6 months, 7–12 months and 13–36 months. For each age group and each substance, the mean exposure and 90th percentile (P90) were calculated. For PAHs, the exposure was calculated for the sum of 4 PAHs (PAH4): BaA, BaP, BbF and CHR, as recommended by EFSA (EFSA, 2008).

The food contribution to the mean exposure was calculated as the percentage of the total exposure due to the consumption of each food group analyzed, for each substance analyzed.

2.4. Risk assessment

For PAHs, the risk was assessed according to international recommendations (EFSA, 2012) by calculating a margin of exposure (MOE) based on the exposure of PAH4 and a benchmark dose lower limit ($BMDL_{10}$) of 0.34 mg.kg body weight $(bw)^{-1}$.day $(d)^{-1}$ (i.e. 340 µg.kg $bw^{-1}.d^{-1}$) derived from a 2-year study on oral carcinogenicity in mouse (EFSA, 2008).

For acrylamide, individual exposures were compared to the RfD of 2 µg.kg $bw^{-1}.d^{-1}$ established by the US EPA in 2010 (US-EPA, 2010). They were also compared to a guidance value of 0.2 µg.kg $bw^{-1}.d^{-1}$ proposed for children under three years of age by the French Expert Committee on "Assessment of the physical and chemical risks in foods" of the French agency for food, environmental and occupational health and safety (ANSES). This value was derived by applying a default factor of 10 to the RfD from US-EPA, to take into account infant sensitivity to the neurotoxicity of acrylamide and the uncertainties related to elimination of acrylamide and glycidamide (ANSES, 2016). The health risk associated with the dietary exposure was assessed by calculating the percentage of children exceeding the health-based guidance value and its 95% confidence interval ($CI_{95\%}$). When less than 5 children exceeded a health-based guidance value they were considered as non-representative cases and the percentage of exceedance was not calculated. The $BMDL_{10}$ of 0.17 mg. kg $bw^{-1}.d^{-1}$ set by EFSA (EFSA, 2015) was also used to assess the risks related to the neoplastic effects of acrylamide, by calculating the corresponding MOE.

In 2011, the JECFA established for furan a $BMDL_{10}$ at 0.96 mg.kg $bw^{-1}.d^{-1}$ (i.e. 960 µg.kg $bw^{-1}.d^{-1}$) based on the increase in adenomas and hepatocellular carcinomas (JECFA, 2011). 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, 2012a,b).

3. Results

3.1. PAHs

The mean and P90 of the daily exposure to the 20 PAHs analyzed in the study is presented in supplemental results. For the sum PAH4, the mean daily exposure ranged from 1.07 ng.kg $bw^{-1}.d^{-1}$ in the 5–6 months population to 2.25 ng.kg $bw^{-1}.d^{-1}$ in 13–36 months under the LB hypothesis and 2.98 ng.kg $bw^{-1}.d^{-1}$ in 1–4 months to 3.78 ng.kg $bw^{-1}.d^{-1}$ in 13–36 months under the UB hypothesis (Table 1). The P90 of exposure ranged 2.63 ng.kg $bw^{-1}.d^{-1}$ in 5–6 months to 4.10.ng kg $bw^{-1}.d^{-1}$ in 13–36 months under LB and 5.13 ng.kg $bw^{-1}.d^{-1}$ in 5–6 months to 5.94.ng kg $bw^{-1}.d^{-1}$ in 1–4 months under UB. Considering the $BMDL_{10}$ of 0.34 mg.kg $bw^{-1}.d^{-1}$, the MOE ranged from 57 000 to more than 300 000, depending on the age class, the hypothesis (LB-UB), and the exposure considered (mean or P90).The highest contributors to the mean exposure were infant formulae in 1–4 months, followed by follow-on formulae in 5–12 months, irrespective of the hypothesis considered (Table 2). After 12 months, ready-to-eat baby foods with meat or fish also appeared to contribute to more than 12% of the exposure, as well as some common food commodities such as: sweet and savoury biscuits and bars, and ultra-fresh dairy products.

3.2. Acrylamide

For acrylamide, the mean daily exposure ranged from 0.141 µg.kg $bw^{-1}.d^{-1}$ in 1–4 months to 0.708 µg.kg $bw^{-1}.d^{-1}$ in 13–36 months under the LB hypothesis, and ranged from 0.509 to 0.740 µg.kg $bw^{-1}.d^{-1}$ in the same age classes under the UB hypothesis (Table 3). The P90 of exposure reached 0.372–1.60 µg.kg $bw^{-1}.d^{-1}$ depending on

Table 2
Contributions of the different food groups to the mean lowerbound (LB) and upperbound (UB) exposure to PAH4, in children less than 3 years old.

Food groups	1–4 months		5–6 months		7–12 months		13–36 months	
	LB	UB	LB	UB	LB	UB	LB	UB
Cereals-based food	0.2	0.2	0.4	0.2	1.1	0.6	0.4	0.4
Follow-on formula	1	1.8	**39.7**	**36.3**	**12.4**	**13.4**	0	0.2
Fruit purée	0	0.1	0.3	1.5	0.3	1.1	0.1	0.6
Growing-up milk	.	.	.	.	0.1	0.8	0.1	1.1
Infant foods								
Infant formula	**95.1**	**89.6**	**13.1**	9.1	2.3	0.9	.	.
Meat/fish based ready-to-eat meal	.	.	5	5.2	**16.6**	**12.5**	2.8	3.2
Milk-based beverage	0.4	3.1	4.6	**11.3**	1.4	8.5	0	1.6
Milk-based dessert	0	0.7	0	8.8	0	**10.5**	0	1.3
Soup puree	1.1	0.9	5.7	3.3	**10.2**	5.7	2.4	2.4
Vegetable-based ready-to-eat meal	1.2	1	8.1	7.1	5.4	5	1	1.4
Total infant foods	99	97.5	76.9	82.8	49.7	59	6.8	12.2
Common foods								
Bread and dried bread products	.	.	0	0	1.3	0.5	4.5	3.1
Breakfast cereals	.	.	.	.	0	0	0.9	0.7
Butter	.	.	0.2	0.1	0.4	0.2	0.6	0.5
Cheese	.	.	0	0	0.6	0.7	1.1	2.3
Croissant-like pastries	.	.	.	.	0.4	0.2	5	3.6
Crustaceans and mollusks	.	.	.	.	0	0	1.2	0.8
Dairy-based desserts	.	.	0.3	0.4	0.9	1.4	3.4	6.1
Delicatessen meats	0	0	0.2	0.2	1.1	0.6	5.2	3.7
Eggs and egg products	.	.	.	.	0	0	0.9	0.8
Fish	.	.	.	.	1.5	0.6	5.6	3.7
Hot beverages	.	.	0	0	0.1	0	0.1	0.1
Margarine	.	.	0.2	0.1	0.2	0.1	1.7	1
Meat	.	.	0.2	0.2	1.8	2.4	3.2	6.6
Milk	0.2	1.8	1.8	2.3	1.4	2.4	2.1	5.2
Mixed dishes	.	.	.	.	0.3	0.1	4.6	3
Non-alcoholic beverages	.	.	.	.	.	.	0	0.2
Offal	.	.	.	.	.	.	0.2	0.2
Oil	.	.	4.6	1.6	1.1	0.4	4.2	2.5
Pastries and cakes	.	.	.	.	0.5	0.2	1.5	1.1
Pizzas, quiches and savoury pastries	.	.	.	.	0.1	0	3.5	2.2
Potatoes and potato products	0	0	1.6	1.2	3.4	2.4	6	5
Poultry and game	.	.	0.3	0.1	1.4	1.1	1.5	1.8
Seasonings and sauces	.	.	.	.	.	.	0.4	0.2
Soups and broths	.	.	4	1.5	2.5	1.1	3.2	2.1
Sweet and savoury biscuits and bars	.	.	.	.	5.5	2.1	**17.5**	**10.6**
Ultra-fresh dairy products	0.3	0.4	8	8.4	**15.9**	**19**	8.9	**16.2**
Vegetables (excluding potatoes)	0.3	0.2	1.7	1	**10**	5.3	6	4.6
Total common foods	1	2.5	23.1	17.2	50.3	41	93.2	87.8

In bold: main contributors (> 10% exposure) per age group.

the age class under the LB hypothesis, and ranged from 0.809 to 1.66 µg.kg $bw^{-1}.d^{-1}$ under the UB hypothesis. Considering the $BMDL_{10}$ of 170 µg.kg $bw^{-1}.d^{-1}$ for the neoplasic effects, the MOE ranged 100 to 1 200, depending on the age class, the hypothesis, and the exposure considered. Considering the neurological effects, the RfD of 2 µg.kg $bw^{-1}.d^{-1}$ established by the US EPA in 2010 (US-EPA, 2010) was exceeded by 7% of children aged 13–36 months. In children aged 7–12 months, the limit was exceeded but the proportion was difficult to estimate in light of limitations related to the sampling or the measurement of exposure. In addition, 26–98% of the children exceeded the

Table 3
Dietary exposure to acrylamide and associated health risk in children less than 3 years old.

		1–4 months	5–6 months	7–12 months	13–36 months
Mean exposure ± standard deviation (µg.kg $bw^{-1}.d^{-1}$)	LB	0.141 ± 0.186	0,296 ± 0.286	0.402 ± 0.332	0.708 ± 0.914
	UB	0.512 ± 0.261	0.509 ± 0.272	0.532 ± 0.342	0.740 ± 0.914
P90 (µg.kg $bw^{-1}.d^{-1}$)	LB	0.372	0.575	0.783	1.60
	UB	0.879	0.809	0.917	1.66
For neurotoxic effects					
% of exceeding the RfD of 2.0 µg kg $bw^{-1}.d^{-1}$ [$IC_{95\%}$]	LB	0	0	NC	7 [4.7; 9.3]
	UB	0	0	NC	7 [4.7; 9.3]
% of exceeding the benchmark value of 0.2 µg kg $bw^{-1}.d^{-1}$ [$IC_{95\%}$]	LB	26 [16; 94]	56 [40; 91]	71 [63; 88]	71 [67; 70]
	UB	98 [35; 100]	97 [72; 100]	93 [79; 97]	74 [75; 78]
For neoplasic effects ($BMDL_{10}$ 170 µg kg $bw^{-1}.d^{-1}$)					
Margin of exposure for mean exposure	LB	1200	600	400	200
	UB	300	300	300	200
Margin of exposure for P90	LB	500	300	200	100
	UB	200	200	200	100

RfD, reference dose; LB, Lowerbound; UB, Upperbound; NC, not calculated (less than 5 subjects were concerned).

Table 4
Contributions of the different food groups to the mean lowerbound (LB) and upperbound (UB) exposure to acrylamide, in children less than 3 years old.

Food groups	1–4 months		5–6 months		7–12 months		13–36 months	
	LB	UB	LB	UB	LB	UB	LB	UB
Infant foods								
Cereals-based food	6.3	2.5	3.8	3.7	3.9	4.1	0.8	1.1
Follow-on formula	0.1	1.1	4.1	**33**	1.6	**17**	0	0.3
Fruit purée	0	0	1.2	1.1	0.9	0.9	0.1	0.1
Infant formula	**73**	**90**	4	7.6	0.3	1	.	.
Meat/fish based ready-to-eat meal	.	.	**20**	**12**	**36**	**27**	4	3.9
Milk-based beverage	2.3	1.3	5.1	5	2.7	4.2	0.2	0.6
Milk-based dessert	0.4	0.3	2.4	3.5	2.5	4.7	0.2	0.4
Soup puree	5.2	1.4	**11**	6.1	9.2	7.3	2.4	2.3
Vegetable-based ready-to-eat meal	**12**	3.4	**47**	**28**	**24**	**18**	2.5	2.4
Total infant foods	100	100	99	99	81	84	10	11
Common foods								
Bread and dried bread products	.	.	0	0	0.6	0.5	2	2.1
Breakfast cereals	.	.	.	.	0	0	0.8	0.8
Chocolate	.	.	0	0	0.1	0.1	1.8	1.7
Compotes and cooked fruit	0	0.2	0	0.1	0	0.9	0	1.1
Croissant-like pastries	.	.	.	.	0.1	0.1	1.6	1.5
Dairy-based desserts	.	.	0	0.1	0	0.4	0.7	1.5
Fish	.	.	.	.	0.3	0.2	0.7	0.8
Hot beverages	.	.	0	0	0.6	0.5	0.8	0.8
Mixed dishes	.	.	.	.	0.1	0.1	0.9	1.1
Pastries and cakes	.	.	.	.	0.4	0.3	1.3	1.3
Pizzas, quiches and savoury pastries	.	.	.	.	0	0	1.6	1.5
Potatoes and potato products	.	.	.	.	6.6	5	**51**	**48**
Poultry and game	.	.	0.1	0.1	0.5	0.7	0.4	0.8
Sweet and savoury biscuits and bars	0.2	0	1.2	0.7	9.2	7	**27**	**25**
Total common foods	0.2	0.2	1.3	1	19	16	90	89

In bold: main contributors (> 10% exposure) per age group.

benchmark value of 0.2 µg.kg $bw^{-1}.d^{-1}$, depending on the age class and the hypothesis. The contribution to the mean exposure may vary according to the hypothesis considered (Table 4). The contributions remaining higher than 10%, whatever the hypothesis UB or LB, concerned infant formulae in 1–4 months old infants, vegetable-based and meat- or fish-based ready-to-eat meals in 5–12 months old children, potato-based products and biscuits after 1 year.

3.3. Furan

For furan, the mean daily exposure ranged from 0.09 µg.kg $bw^{-1}.d^{-1}$ in 1–4 months to 0.80 µg.kg $bw^{-1}.d^{-1}$ in 7–12 months under the LB hypothesis and from 0.14 µg.kg $bw^{-1}.d^{-1}$ to 0.84 µg.kg $bw^{-1}.d^{-1}$ under the UB hypothesis in the same age classes (Table 5). The P90 of exposure ranged from 0.26 to 0.28 (LB-UB) to 1.48–1.52 µg.kg $bw^{-1}.d^{-1}$ in the same age classes. It should be noted that children having consumed at least one product among baby jars of vegetables, with or without meat or fish, had a mean daily exposure ranging from 0.71 to 1.02 µg.kg $bw^{-1}.d^{-1}$, depending on the age class, whereas the children having consumed other foods presented a 3–6-fold lower exposure, ranging from 0.11 to 0.28 µg.kg $bw^{-1}.d^{-1}$. Indeed, ready-to-eat meals remained a major contributor to the mean furan exposure irrespective of the age class (Table 6). Considering the $BMDL_{10}$ of 960 µg.kg $bw^{-1}.d^{-1}$, the MOE calculated for the mean exposure ranged from 1100 to 10 700, depending on the age class and the hypothesis and the exposure considered (mean or P90), and the MOE calculated for the P90 of exposure ranged from 600 to 3700 (Table 5).

4. Discussion and conclusion

Only BaP and the sum PAH4 present regulatory levels in foods (Commission Regulation (EC) No 1881/2006 of 19 December 2006). All samples analyzed showed levels below those regulatory levels, especially for infant foods, which were 7–140 times below the limits (Supplemental results). Only 41 samples (22%) presented BaA and CHR levels higher than the LOQ. As concentrations were close to LOQs, data should be interpreted with care. Nevertheless, BaA/(BaA + CHR) ratios for those samples with quantification were in the range [0.24–0.53], tending to show a contamination of pyrolytic origin (Tobiszewski and Namiesnik, 2012). Indeed, all the foods sampled in the study were subject to heat treatment (pasteurization, sterilization, heating …). Four samples appeared however with a lower ratio (between 0.24 and 0.28), for which an environmental contamination could be suspected, three of them being spinach-based baby jars. Indeed, wide spinach leafs

Table 5
Dietary exposure to furan in children less than 3 years old and associated risk regarding the $BMDL_{10}$ of 960 µg kg $bw^{-1}.d^{-1}$.

		1–4 months	5–6 months	7–12 months	13–36 months
Mean exposure ± standard deviation (µg.kg $bw^{-1}.d^{-1}$)	LB	0.089 ± 0.180	0.562 ± 0.294	0.797 ± 0.398	0.326 ± 0.442
	UB	0.140 ± 0.180	0.604 ± 0.293	0.844 ± 0.397	0.370 ± 0.446
P90 (µg.kg $bw^{-1}.d^{-1}$)	LB	0.264	1.222	1.476	0.739
	UB	0.282	1.289	1.522	0.780
Margin of exposure for mean exposure	LB	10700	1700	1200	2900
	UB	6900	1600	1100	2600
Margin of exposure for P90	LB	3700	800	700	1300
	UB	3400	700	600	1200

BMDL, Benchmark dose limit; LB, Lowerbound; UB, Upperbound.

Table 6
Contributions of the different food groups to the mean lowerbound (LB) and upperbound (UB) exposure to furan, in children less than 3 years old.

Food groups	1–4 months		5–6 months		7–12 months		13–36 months	
	LB	UB	LB	UB	LB	UB	LB	UB
Infant foods								
Milk-based beverage	3.5	2.2	2.4	2.3	1.5	1.4	0.7	0.7
Cereals-based food	**22.6**	**14.4**	4.9	4.6	2.9	2.7	1.8	1.6
Milk-based dessert	0.2	0.4	0.4	1.2	0.4	1.3	0.1	0.4
Fruit juice	0.9	0.6	0.6	0.6	0.4	0.4	0.2	0.2
Growing-up milk	.	.	.	.	0.2	0.6	0.8	2.4
Soup puree	4.8	3.0	3.1	2.9	3.6	3.4	3.5	3.1
Fruit purée	3.1	2.0	4.8	4.4	3.5	3.3	1.7	1.5
Vegetable-based ready-to-eat meal	**33.2**	**21.1**	**38.5**	**35.8**	**23.0**	**21.7**	**15.4**	**13.6**
Meat/fish based ready-to-eat meal	.	.	**28.9**	**26.9**	**52.3**	**49.4**	**28.6**	**25.2**
Infant formula	**25.9**	**49.4**	0.3	0.8	0.0	0.1	.	.
Follow-on formula	3.0	2.5	**10.8**	**13.8**	3.7	5.1	0.2	0.3
Total infant foods	97.2	95.4	94.7	93.3	91.5	89.4	53.2	48.9
Common foods								
Hot beverages	.	.	0.0	0.0	0.1	0.1	0.7	0.6
Sweet and savoury biscuits and bars	.	.	.	.	0.2	0.2	2.6	2.3
Non-alcoholic beverages	.	.	.	.	0.1	0.1	1.5	1.6
Delicatessen meats	0.2	0.1	0.2	0.1	0.3	0.3	2.3	2.0
Chocolate	.	.	.	.	0.0	0.0	0.1	0.1
Breakfast cereals	.	.	.	.	0.0	0.0	3.5	3.1
Dairy-based desserts	.	.	0.0	0.0	0.0	0.1	0.4	0.9
Cheese	.	.	0.0	0.0	0.2	0.2	1.1	1.0
Milk	1.8	3.7	0.4	1.2	0.3	1.0	1.6	4.8
Vegetables (excluding potatoes)	0.4	0.4	0.8	1.1	1.2	1.7	4.1	4.6
Bread and dried bread products	.	.	.	.	0.1	0.1	0.9	0.8
Mixed dishes	.	.	.	.	0.1	0.1	2.5	2.2
Fish	.	.	.	.	0.1	0.0	0.7	0.6
Potatoes and potato products	0.4	0.2	2.2	2.1	3.1	3.0	8.4	7.6
Pasta	.	.	.	.	0.0	0.1	0.3	1.0
Rice and wheat products	.	.	.	.	0.2	0.1	0.4	0.6
Soups and broths	.	.	1.4	1.3	1.2	1.1	8.8	7.8
Sugars and confectionary	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ultra-fresh dairy products	0.1	0.1	0.3	0.8	0.6	1.8	1.7	4.9
Meat	.	.	0.1	0.1	0.7	0.7	4.8	4.2
Croissant-like pastries	.	.	.	.	0.0	0.0	0.0	0.1
Poultry and game	.	.	0.0	0.0	0.1	0.1	0.4	0.4
Total common foods	2.8	4.6	5.3	6.7	8.5	10.6	46.8	51.2

In bold: main contributors (> 10% exposure) per age group.

might be directly contaminated by soil contact, in that soils present high PAH levels.

Few data are available concerning baby food contamination by PAHs. The concentrations of the present study for PAH4 were in the same range as the 22nd Australian TDS, in which infant formulae and baby foods contents were lower than 0.010 and 0.044 $\mu g\,kg^{-1}$, respectively (FSANZ, 2009). Exposure levels were also in the same range. For example, BaP exposure was estimated to range from 0.2 (LB) to 4.3 (UB) ng.kg $bw^{-1}.d^{-1}$ for children from 9 months to 2 years old. In 2000, the UK TDS estimated the PAH4 exposure of 1.5–2.5 years old children at 12.7 ng.kg $bw^{-1}.d^{-1}$ and of 2.5–3.5 years old children at 11.8 ng.kg $bw^{-1}.d^{-1}$ (COT, 2002), which was higher than the exposures reported in the present survey. Nevertheless, 2002 UK data showed a decline in PAHs exposure compared to the 1979 TDS, and data from 2012 showed that the downward trend continued (FERA, 2012). In the present survey, the exposure slightly increased with age, especially in LB (Table 1), and the exposure of the children aged 13–36 months were in the same range as the exposure estimated for 3–6 years old children in the last French TDS (Veyrand et al., 2013). The highest contributors to the dietary exposure progressively changed from infant and follow-on formulae in 1–6 months old children (> 35%) to ready-to-meat meals in 7–12 months, then to current foods that represent more than 87% of the exposure after 1 year (Table 4). Regarding MOEs calculated for PAH4 all exceeding the critical MOE of 10 000, dietary exposure of the infant population was deemed tolerable with regard to the carcinogenic risk, which was already observed for the rest of the population (Veyrand et al., 2013).

One should note some uncertainties regarding the exposure calculation. The first one relied on the fact that only 3 days were recorded in the consumption survey, that may lead to an overestimation of the high percentiles of exposure. Variance reduction methods were not used in the present work as a conservative approach of risk assessment (Mancini et al., 2015), reinforcing the conclusion on the tolerable risk. Another uncertainty relied on the fact that occasional practices or consumptions were not represented in the sampling plan, such as charcoal grilled/barbecue foods or smoked fish or meat, which have been shown to present high levels of PAHs (EFSA, 2008). Nevertheless, the consumption survey used in the present work (unpublished data) and/or the last French consumption survey (ANSES, 2017) showed that young children consumption of smoked fish or meat is not a common practice in France and charcoal grilled/barbecue foods is limited to less than 0.5%.

Recent studies indicated the onset of developmental effects in animal models after treatment with low molecular weight PAHs (Incardona et al., 2004; Crepeaux, Bouillaud-Kremarik et al. 2012, 2013) and birth defects in human studies after PAHs exposure during the perinatal period (Naufal et al., 2010; Ren et al., 2011; Lupo et al., 2012). However, no health-based guidance value specific to the infant population has been established so far; this would allowed us to confirm the absence of a health risk associated with dietary exposure to PAHs in the present study.

Data on acrylamide exposure in infants and toddlers are sparse. Nevertheless, the exposure levels in the present study were generally lower than other estimations, with comparable analytical limits. In

2016, the UK COT published mean exposures based on TDS analyses from 2014 (FSA, 2018a,b) ranging from 0.061 (LB) to 0.53 (UB) μg.kg $bw^{-1}.d^{-1}$ for less than 4 months old infants exclusively fed with infant formulae (COT, 2016). The UB exposure was assessed at 0.30 μg.kg $bw^{-1}.d^{-1}$ for 4–6 months old infants, at 0.64–0.95 μg.kg $bw^{-1}.d^{-1}$ for 6–12 months old infants, and at 1.2–1.3 μg.kg $bw^{-1}.d^{-1}$ for 12–60 months old children. In New Zealand, mean acrylamide exposure was assessed at 1.77 μg.kg $bw^{-1}.d^{-1}$ for infants until 6 months and at 2.21 μg.kg $bw^{-1}.d^{-1}$ for 1–3 years old toddlers (MAF, 2012). Based on different European consumption surveys, the EFSA estimated mean exposure ranging from 0.78 (LB) to 1.0 (UB) μg.kg $bw^{-1}.d^{-1}$ for infants (P95 ranging from 1.8 to 2.1 μg.kg $bw^{-1}.d^{-1}$) and from 1.3 (LB) to 1.4 (UB) μg.kg $bw^{-1}.d^{-1}$ for toddlers (P95 ranging from 2.3 to 2.4 μg.kg $bw^{-1}.d^{-1}$) (EFSA, 2015). The median dietary intake of 1-year old Finnish toddlers was estimated around 0.4 μg.kg $bw^{-1}.d^{-1}$ (Hirvonen et al., 2011), which was close to the present results. The differences observed may be partly explained by a negligible consumption of fried or sautéed potatoes before the age of one in France (Hulin et al., 2014; ANSES, 2017), while potatoes-based products generally remained a main contributor in young children (EFSA, 2015). Potatoes and potato products in the present survey did not significantly contribute to the exposure before 6 months (Table 4), and then contributed only to 5–6% of the mean exposure in the 7–12 months old children, and 50% after. The consumption of biscuits also largely explained 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 were jars of vegetable-based baby foods, with or without meat or fish, and naturally infant formulae in 1–4 months old infants, as they almost exclusively consumed infant formulae. The risk associated with dietary exposure to acrylamide was assessed with regard to its neurotoxic and genotoxic carcinogenic effects (Table 3). The RfD of 2 μg.kg $bw^{-1}.d^{-1}$ established by the US EPA in 2010 for neurological effects (US-EPA, 2010) was exceeded in children aged 7–12 and 13–36 months. Moreover, the benchmark dose value of 0.2 μg.kg $bw^{-1}.d^{-1}$ proposed to take into account infant sensitivity and uncertainties related to metabolism (ANSES, 2016) was observed to have been exceeded significantly for all the age groups considered. In addition, the MOEs calculated using EFSA's $BMDL_{10}$ of 0.17 mg.kg $bw^{-1}.d^{-1}$ used to assess the risks related to the neoplasic effects of acrylamide (EFSA, 2015) were far lower than the value of 10 000 considered as appropriate for ruling out a risk associated with a genotoxic compound (EFSA, 2012a,b). An identical result was previously reached for adults and children over three years of age in France (Sirot et al., 2012). Dietary exposure to acrylamide was then identified as a concern both regarding the neurological and neoplasic effects, in compliance with previous studies (MAF, 2012; FSANZ, 2014; EFSA, 2015; COT, 2016). In the 2000s, industry has developed in collaboration with the national authorities and the European Commission a "toolbox", regularly updated, providing measures that can be applied by manufacturers to reduce acrylamide formation in their specific manufacturing processes and products (Food and Drink Europe 2014). Moreover, recommendations and regulations have been published in 2013 and 2017 to establish mitigation measures and indicative levels for the reduction of acrylamide concentration in food (Commission Recommendation, 2013/647/EU, 2013; Commission Regulation, 2017/2158/EU, 2017). Nevertheless, when compiling more than 13 000 data from annual monitoring programs of acrylamide levels in European foods from 2007 to 2010, EFSA failed to find any trend in decreasing concentrations (EFSA, 2012a,b). Efforts should therefore be continued to decrease contamination from the main exposure contributors and consequently exposure, by reducing the formation of acrylamide during food production or preparation processes for example. 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. Storage and preparation are known to have an impact on acrylamide concentration (Matthäus, 2002; Stadler and Scholz, 2004; Fiselier et al., 2006; Vinci et al., 2012; Bethke and Bussan, 2013). The Food Standards Australia New Zealand (FSANZ), the German Bundesinstitut für Risikobewertung (BfR), or the UK Food Standard Agency (FSA) propose on their website some recommendations to the consumer to reduce acrylamide exposure when preparing food at home (BfR, 2011; NZFSA, 2016; FSA, 2018a,b). As an example, it is advised to cook potato-based products around 180 °C maximum to limit acrylamide production, and to aim for "a light golden color only" when frying, baking, toasting or roasting starchy foods or bread. NZFSA also recommends not to store potatoes in the refrigerator or where exposed to light and to soak potatoes in water for 15–30 min, or blanch in boiling water before frying or roasting in order to reduce the components promoting acrylamide formation.

Due to its volatility, furan was not recommended to be analyzed in a TDS since pooling and homogenizing tend to decrease its concentration (Vin et al., 2014). That is why in the present study a specific sampling protocol was followed to limit furan losses during homogenization and storage steps (Lambert et al., 2018a,b). The exposure levels assessed were in the same range as the exposures calculated by EFSA based on different European consumption surveys including young children (EFSA, 2017). EFSA reported levels from 0.14 to 0.87 μg.kg $bw^{-1}.d^{-1}$ under LB to 0.21–0.99 μg.kg $bw^{-1}.d^{-1}$ under UB for infants (< 12 months), and from 0.22 to 0.52 μg. kg $bw^{-1}.d^{-1}$ under LB and 0.31–0.65 μg.kg $bw^{-1}.d^{-1}$ under UB for toddlers (13–36 months). Our exposure levels were slightly higher to those estimated in Norway, from 0.31 μg.kg $bw^{-1}.d^{-1}$ on average in non-breastfed 6 months old children to 0.10 μg.kg $bw^{-1}.d^{-1}$ in 24 months old children (P95 from 0.62 μg.kg $bw^{-1}.d^{-1}$ to 0.41 μg.kg $bw^{-1}.d^{-1}$ in the same age groups) (Husøy et al., 2012). That could be due to a higher number of food categories considered in our exposure calculations. The MOEs calculated for children, regardless of the age group, were below 10 000 (Table 5). Dietary exposure to furan was therefore identified as a concern. Exposure of children aged 5–6 and 7–12 months was higher than that of the rest of the infant population, due to their higher consumption of jars of vegetables, with or without meat or fish, these food groups having higher concentrations of furan (Lambert et al., 2018a,b). Differences in exposure (3–6-fold) were observed between children consuming jars of vegetables accompanied by meat or fish, and non-consumers. From a general point of view, it was shown that infant foods prepared at home contained less furan than those prepared industrially (EFSA, 2011). Evaporation of furan after heating highly depends on the food composition and interaction between furan and matrix components (Van Lancker et al., 2009). However, furan concentrations can remain stable in some food items after heating and decrease only after reheating (Fromberg, 2009). It was shown that in baby food samples, furan levels were reduced by up to 35% when heated with microwave and by up to 53% when heated in a hot-water bath (Altaki et al., 2017). Nevertheless, the EFSA concluded that the influence of reheating commercially processed foods on furan levels was limited and highly dependent on the consumer behavior (time, temperature, stirring, type of container, lid or not…), which is changeable and then not predictable (EFSA, 2017). Moreover, some people might consume these products without heating. According to the on-line survey specifically conducted for the present work (Hulin et al., 2014), in France, 40.6% of the parents used exclusively microwave to heat ready-to-eat baby foods, and 82.1% used it regularly (unpublished results). Only 3% used exclusively hot water bath, and around 6% never heated ready-to-eat baby foods. Similar to the "toolbox" proposed to limit the population's exposure to acrylamide, ways should be sought to reduce furan contamination of industrial products through the optimization of manufacturing processes, in particular for jars of vegetable-based baby food, alone or with meat or fish. Moreover, given the volatility of furan, it would be of interest to further study in-home reheating practices for infant foods prepared industrially in order to propose recommendations to the parents to limit exposure.

Moreover, if recent toxicological data are available for 3-methylfuran (Gill et al., 2018), data on other isomers are missing. It would also

be of interest to collect occurrence data in food of methylfurans, which are formed with furan during thermal processing and are likely to undergo a similar metabolic fate to furan (EFSA, 2017).

The present work focused on the dietary exposure to heat-induced compounds, but one should bear in mind that infants and toddlers are also exposed through passive smoking to furan and methylfurans (Hatzinikolaou et al., 2006), acrylamide (EFSA, 2015), and PAHs (EFSA, 2008). Some methodological works are ongoing to assess the combined exposure of populations to chemicals through different routes of exposure, in particular as concerns children (Vanacker, Tressou et al. Submitted). In addition to the different exposure sources, the potential cumulative effects of chemicals including heat-generated compounds that could have a same biological target should also be taken into account for risk assessment. Some works are also ongoing to identify mixtures of substances to which children are exposed through their diet, using a methodology already applied to the general French population including children over 3 and to cohorts of pregnant women (Traore et al., 2016; Traore et al., 2018). Nevertheless, toxicological studies are also needed to provide health-based guidance values for cumulative exposure.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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