Assessment of infant exposure to food chemicals: the French Total Diet Study design

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As part of the previous French Total Diet Studies (TDS) focusing on exposure to food chemicals in the population aged 3 years and older, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) launched a specific TDS on infants to complete its overall chemical food safety programme for the general population. More than 500 chemical substances were analysed in food products consumed by children under 3 years old, including nutrients, several endocrine disruptors resulting from human activities (polychlorinated biphenyls, dioxins and furans, brominated flame retardants, perfluorooalkyl acids, pesticide residues, etc.) or migrating from food contact materials such as bisphenol A or phthalates, but also natural substances such as mycotoxins, phytoestrogens and steroids. To obtain a representative and general view of infant food consumption, food items were selected based on results of a national consumption survey conducted specifically on this population. Moreover, a specific study on food was conducted on 429 households to determine which home-cooking practices are employed to prepare food consumed by infants. Overall, the targeted chemical substances were analysed in more than 450 food samples, representing the purchase and home-cooking practices of over 5500 food products. Foods included common foods such as vegetables, fruit or cakes as well as specific infant foods such as infant formula or jarred baby food. The sampling plan covered over 80% of the total diet. Specificities in infant food consumption and habits were therefore considered to define this first infant TDS. This study, conducted on a large scale and focusing on a particularly sensitive population, will provide accurate information on the dietary exposure of children under 3 years to food chemicals, especially endocrine disruptors, and will be particularly useful for risk assessment analysis under the remit of ANSES’ expert committees.

Keywords: infant; Total Diet Study; dietary exposure assessment; food chemicals; endocrine disruptors

Introduction

Evaluating individual exposure to potentially harmful substances is a key step in public health risk assessment. A better understanding of these exposures leads to informed decision-making for better managing risks at the national, European and international levels. When focusing on dietary exposure, the use of data from monitoring programmes of the food control system is often not suitable because it may not be representative of the whole diet and therefore of the “background level” of food contamination. Moreover, such a control programme is often carried out by several laboratories with analytical limits adapted to regulatory limits and not always appropriate for risk assessment.

Therefore, assessing the occurrence of chemicals of interest in foods as consumed to estimate accurately dietary exposure for different population groups requires an efficient, cost-effective and accurate approach such the Total Diet Study (TDS). The TDS approach has been promoted and endorsed by the WHO along with the FAO since the 1970s (WHO 1968a, 1968b) and more recently by EFSA in a joint guidance document in 2011 (EFSA et al. 2011a). In 2011, approximately 33 countries worldwide were in the process of carrying out a TDS or TDS-like studies (EFSA et al. 2011b; Moy & Vannoort 2013). Most focus on people over 3 years old. Only Australia, New Zealand, Canada and the United States have also collected data on infant products at time intervals ranging from 1 to 5 years (Moy & Vannoort 2013). In France, two TDSs based on individual food samples have been conducted, focusing on the general population aged over 3 years. The first TDS, established in the year 2000 by the French National Institute for Agricultural Research in collaboration with the French Food Safety Agency (AFSSA), focused on exposure to mycotoxins and trace elements and minerals (Leblanc, Guérin, et al. 2005; Leblanc, Tard, et al. 2005). In 2006, the second French TDS, called “TDS2”, was undertaken on a larger scale, including 445 chemical substances (pesticide residues, trace elements and minerals, environmental contaminants resulting from human activities, phytoestrogens, additives, etc.) in 20,000 samples of food belonging to 212 different core foods (Sirot et al. 2009). Nearly 250,000 analysis results were collected and used to provide a broad overview of exposure to food chemicals and in fine to provide a scientific basis for making decisions with regard to risk management to improve both food safety and consumer health.

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However, early stages of life, i.e. the foetal and early postnatal periods, correspond to periods of increased susceptibility (Makri et al. 2004; Sly & Flack 2008; Diamanti Kandarakis et al. 2009). Several pieces of evidence suggest that foetuses and infants may be more sensitive to pollutants (Landrigan et al. 2003). First, children’s metabolic pathways are immature, especially during the foetal period and the first months after birth, suggesting that metabolism and detoxification are not as efficient in infants as they are in adults (Spielberg 1992; NAS 1993). Development processes during these periods are also more easily disturbed. Lastly, infants are exposed to higher concentrations of pollutants through their diet because the ratio of the quantity consumed to body weight is higher in infants than in adults. Moreover, infant foods available on the market are very specific and ever-changing, differing from those of population groups considered in previous TDSs. The implementation of a TDS specific to infants is now necessary to obtain exposure data for a risk assessment of dietary and cooking practices and also to protect infants from adverse effects of food chemicals using the same TDS method to assess exposure as used for the general population. Therefore, in 2010, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) decided to launch the first French infant TDS focusing on children under 3 years old. This new study should be considered as an example of how to adapt the TDS sampling strategy to include not only in situ additives, persistent organic pollutants (POPs), pesticide residues, acrylamide, trace elements and minerals, but also other chemical substances known as endocrine disruptors (ED) that migrate from food contact and cookware, such as printing inks, bisphenol A (BPA), phthalates and phenols. To do so, the sampling plan integrates information that considers different home-cooking methods using various types of cookware known to be sources of contamination, and distinguished not only by different brands but also by packaging types (cans, plastic boxes, jars, etc.).

We present here the main methodological choices made in the French infant TDS in terms of substances screened and food sampling. The paper mainly focuses on the selection of core foods and the establishment of the sampling plan, which represents two of the main challenges for implementing and adapting the TDS approach.

Materials and methods

Components of the infant TDS

Given that the infant TDS expands on the TDS2, the same groups of substances were considered. This includes (1) substances naturally present in the environment or found due to contamination of environmental origin, either natural and/or arising from industrial, agricultural, domestic human activities; and (2) substances used for technological or agricultural reasons, or formed during the production, transformation or preservation of ingredients or the product. Therefore, the following groups of substances were targeted: inorganic contaminants and minerals, polychlorodibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/F), polychlorinated biphenyls (PCBs), perfluoralkyl acids, brominated flame retardants, myco-toxins, phytoestrogens, pesticide residues, food additives and heat-induced compounds. The TDS2 included those food additives and pesticides that may be found at levels that lead to an exceeding of the ADI in adults and children over 3 years old (Sirot et al. 2009). Therefore, these substances were specifically selected to focus on the risk for children under 3 years old. All methods used and the substances selected to be monitored in the infant TDS were reviewed and validated in the remit of the appropriate Expert Committees from ANSES’ Risk Assessment Department and ANSES’ Regulated Products Department.

Additives were first ranked by applying a tier-based approach as described in international guidelines for predicting chronic dietary intake of food additives (European Commission 1998). The method consists in calculating the theoretical maximum daily intake (TMDI) of the substance and defining a threshold of investigation according to a certain percentage of the ADI, which we set to around 50%. TMDI is based on maximum residues/permitted levels (MRL/MPL) combined with individual food consumption data, here those of newborns and infants (Fantino & Gourmet 2008). Only additives authorised in infant food products according to French regulations (Ministerial Order of 29 August 2011) were considered in this study. Additives for which no MPL has been set (e.g. quantum satis), but having a specified ADI, were included. In all, 14 additives were selected including sodium acetate (E262), ascorbyl palmitate (E304), tocopherols (E306–E309), tartaric acid (E334), sodium tartrate (E335), potassium tartrate (E336), calcium tartrate (E354), phosphoric acid (E338), sodium phosphates (E339), calcium phosphates (E341) and diphosphates (E450).

Priority pesticide residues screened were active phytopharmaceutical substances authorised during the sampling period and POPs that satisfied at least one of the five following criteria:

- Classified as carcinogenic, mutagenic, reprotoxic and/or with a specific target organ toxicity after repeated exposure (“STOT RE”) in category 1 or 2 according to Regulation (EC) No. 1272/2008.
- Potential endocrine disruptors from the European priority list (European Commission 2013).
- A mean estimated daily intake (EDI) higher than the ADI.
- Substances included in the national biomonitoring strategy (Fréry et al. 2013).
• Pesticides that exceeded the European Union MRLs in baby foods in the 2009 monitoring programs of European Union member states (EFSA 2011a).

The EDI was estimated under a “pessimistic” upper-bound scenario overestimating exposure levels by combining infant consumption data (Fantino 2005; Fantino & Gourmet 2008) and the results of the 2008 French monitoring programmes for common foods (vegetables, fruits, meat, etc.) and baby foods, when available, and/or the European Union MRLs (Regulation (EC) No. 396/2005). For baby foods, a general default MRL of 0.01 mg kg\(^{-1}\) was applied for all pesticides, except for 16 pesticides for which specific MRLs lower than 0.01 mg kg\(^{-1}\) have been established (Commission Directive 2006/125/EC; Commission Directive 2006/141/EC). In total, 82 priority pesticides, including their degradation products, were identified for this study. However, several mono- and multi-residue methods were developed and implemented, and the results for more than 300 other pesticides were also obtained, as in the TDS2 (Nougadère et al. 2012).

Other substances of health concern, in particular those coming from food contact materials (FCMs), some of which are known as EDs, were also added to the study: bisphenols (BPA and bisphenol A diglycidyl ether), phthalates, nitrosamines, ink photo-initiators and alkylphenols. In national and European publications and opinions BPA has been included to assess in more detail the level of contamination in food prepared as consumed, including heating baby bottles. Regarding phthalates, data indicate that dietary exposure for some phthalates is in the range of the TDI (EFSA 2005a, 2005b). In 2005, EFSA therefore recommended that an improved estimate of the exposure to these substances should be provided. Alkylphenols are products of biodegradation of non-ionic surfactants (alkylphenol ethoxylates) widely used in industrial applications including plastic food packaging or pesticides. Among them, 4-tert-octylphenol (4-t-OP) and 4-nonylphenol (4-NP) isomers have been classified as potential EDs (European Commission 2013; WHO & UNEP 2013). Moreover, they can be found in food, including baby foods (Guenther et al. 2002; Raecker et al. 2011), but data are needed to estimate dietary exposure better. Nitrosamines and ink photo-initiators have also been added given the lack of data on dietary exposure. Furan has also been added as a heat-induced compound based on the report of EFSA, which conclude that furan exposure estimates are highest in toddlers (EFSA 2011c). Trace elements and minerals, pesticides and alkylphenols were analysed in all samples. The other food chemicals were analysed in known contributors or in foods where these substances are thought to be detected (due to packaging, for example).

In this TDS, other data were collected on food contamination for EDs, allowing the assessment of exposure in infants, a particularly susceptible population (PCBs, PCDD/Fs, brominated flame retardants, perfluoroalkyl acids, BPA or phthalates, but also natural substances such as mycotoxins or phytoestrogens). In addition, natural steroids will also be analysed to obtain information on exposure to EDs from natural sources versus anthropogenic sources.

To obtain the most precise exposure estimation and to avoid insofar as possible sources of uncertainty due to processing censored data with high analytical limits, special care was made to reach analytical limits as low as technically possible in testing laboratories. Therefore, to help the laboratories reach this goal, theoretical calculations were made to evaluate the threshold limits necessary for a satisfactory evaluation. When a substance is not detected or cannot be quantified in a given sample (and its subsamples), two scenarios (upper and lower bound), based on the analytical limits, are used to estimate exposure (GEMS/Food-EURO 1995). In the upper-bound scenario (UB), all results under the analytical limit are considered to be equal to the analytical limit. In this TDS, to be able to conclude to a potential exposure risk for the population, we estimated the theoretical value of this analytical limit that would be required to obtain an UB exposure of between 10% and 50% of the ADI in the case of non-detection or quantification in all samples analysed. For the margin of exposure (MOE) calculation, we verified that the proposed analytical limits enable calculating MOE associated with low levels of concern. For each screened substance and priority pesticides, laboratories were required to have the lowest acceptable analytical limits and target LOQs. For one additive (E450), the target LOQ could not be reached; it was therefore excluded from the programme. All LODs targeted prior to analysis and actually reached by laboratories after analysis in this infant TDS will be described further in future articles dealing with analytical results. Moreover, with regard to the sampling method (see below), the stability of compounds in foods during the storage period of food samples (1 year at –18°C) was discussed with laboratories prior to analysis. If stability was not confirmed, the substance was excluded. For this reason, toco-pherols (E306–E309) and 12 pesticides were excluded from the study. The list of all substances analysed in the infant TDS is given in Table 1.

Establishment of the sampling plan

The infant TDS food list was established in three steps, as described in the guidance document on the TDS approach (EFSA et al. 2011a):

• Identification and selection of representative food items from food consumption data.
Table 1. Substances analysed in the infant Total Diet Study.

| Groups                  | Natural or environmental contamination of natural origin | Environmental contamination of anthropogenic origin | Used in food contact materials | Used for technological or agricultural reasons or formed during food process | Substances or congeners                                                                 |
|-------------------------|----------------------------------------------------------|-----------------------------------------------------|-------------------------------|-----------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Mycotoxins              | ×                                                        |                                                     |                               | Aflatoxins: AFB1, AFB2, AFG1, AFG2, AFM1 Ochratoxins: OTA Patulin Trichothecens: DON, DON3, DON15, Niv, T2, HT2, DAS, FusX, Ver, MAS, T2-triol Zearalenon: ZEA Fumonisins: FB1, FB2 Alternaria toxins: AOH, AME, TA Isoflavons: genistein, daidzein, glycitein, biochanin A, formononetin, equol Coumestans: coumestrol Lignans and enterolignans: matairesinol, secoisolariciresinol, enterodiol |                                                                                         |
| Phytoestrogens          | ×                                                        |                                                     |                               |基质：a-estradiol, b-estradiol, estrone Androgens: dihydrotestosterone, epitestosterone, 4-androstenedione, testosteron, 5b-dihydrotestosterone, androsterone, 5α-dihydrotestosterone, 17b-testosteron, 17α-testosteron, epiandrosteron, 5b-androstane-3one-17b-ol, etiocholanolone, DHEA Progestagens: progesteron |                                                                                         |
| Natural steroids        | ×                                                        |                                                     |                               | Minerals: calcium, sodium, magnesium, iron, zinc Toxic trace elements: aluminium, antimony, arsenic, cadmium, lead, mercury, tin, barium, strontium, gallium, silver, tellurium, germanium |                                                                                         |
| Inorganic contaminants  | ×                                                        | ×                                                   | ×                             | Dioxins and furans: PCDD: TCDD_2378, PCDD_12378, HCDD_123478, HCDD_123678, HCDD_123789, HCDD_1234678, OCDD PCDF: TCDF_2378, PCDF_12378, PCDF_23478, HCDF_123478, HCDF_123678, HCDF_1234678, HCDF_123789, HCDF_1234678, HCDF_1234789, OCDF |                                                                                         |
| PCBs                    | ×                                                        |                                                     |                               | PCB-NDL: PCB_28, PCB_52, PCB_101, PCB_138, PCB_153, PCB_180 |                                                                                         |
| Brominated flame retardants | ×                                                        |                                                     |                               | PBB: BB52, BB101, BB153 TBBPA |                                                                                         |
| Perfluorinated compounds | ×                                                        | ×                                                   | ×                             | PFOS, PFBS, PFHxS, PFHpS, PFDS PFOA, PFBA, FPFA, 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 |                                                                                         |

(continued)
Table 1. Continued.

| Groups                        | Origin                                      | Used in food contact materials | Used for technological or agricultural reasons or formed during food process | Substances or congeners                                                                 |
|-------------------------------|---------------------------------------------|---------------------------------|-----------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
|                               | Natural or environmental contamination of natural origin | Environmental contamination of anthropogenic origin |                                                                 |                                                                                          |
| Alkylphenols                  | ×                                           | ×                               | ×                                                                           | 4-tert-octylphenol and 4-nonylphenol mix isomers                                       |
| Nitrosamines                  | ×                                           | ×                               | ×                                                                           | NDBA, NDEA, NDMA, NDPhA, NDPA, NMEA, NMOR, NPIP, NPYR                                |
| Bisphenols                    | ×                                           | ×                               | ×                                                                           | BPA, BADGE                                                                              |
| Ink photo-initiators          | ×                                           | ×                               | ×                                                                           | 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, DhaiP, DbahP, Benzofluorene |
| Acrylamide                    | ×                                           | ×                               | ×                                                                           | Amide: propyzamide                                                                     |

Anilide: propanil
Anilinopyrimidine: mepanipyrim
Avermectin: abamectin, emamectin
Benzimidazole: carbendazim, thiabendazole
Benzoylphenyleurea: flufenoxuron
Carbamate: carbaryl, carbofuran, chlorpropham, methoxyl, oxamyl, thiophanate-methyl
Chloroacetamid: alachlor
Chloronitrile: chlorothalonil
Cyclohexene oxime: profloxycim, tepraloxydim
Dicarboximide: captan, cidim, flumioxazin, iprodione, procymidone
Dinitroaniline: trifluralin
Dithiocarbamates: dithiocarbamates
Glycine derivative: glyphosate
Hydroxybenzonitrile: bromoxynil, Ioxynil
Imidazole: imazalil, prochloraz
Isoxasole: isoxaflutole
Morpholine: fenpropimorph
Organochlorine: chlordan, DDT, dieldrin, endosulfan, endrin, HCH, heptachlor, hexachlorobenzene, lindane
Organophosphate: chlorpyrifos, chlorpyrifos-methyl, dimethoate, malathion, phosmet, pirimiphos-methyl
Phenol: 2-phenylphenol
Phenoxy herbicide: 2,4-D, 2,4-DB
Phenylpyrazole: fipronil
phenylurea: chlorotoluron, diuron, isoproturon, linuron
Phosphonic acid: glufosinate
Pyrethroid: acrinathrin, bifenthrin, cyfluthrin, deltamethrin, esfenvalerate, tau-fluvalinate
Pyridine: picloram
Quaternary ammonium: diquat
Spinosyn: spinosad
Strobilurin: dimoxystrobin, kresoxim-methyl
Sulfite ester: propargite

(continued)
Review of customary food preparation/cooking processes in common use and selection of process combinations to apply.

Determination of pooling level for foods.

Selection of representative food items from food consumption data

The consumption survey used to determine the food list was the last published French survey on individual dietary consumption in children under 3 years (Fantino 2005; Fantino & Gourmet 2008). This cross-sectional study was conducted from January to March 2005 for the French Association for Children’s Food (SFAE) (Fantino 2005).

Individual, consecutive 3-day weight food records were collected from a sample of 706 children selected through proportionate quota sampling based on the age of the children, the occupation of the mother and the family socio-economic category. Totally or partially breastfed infants (during the survey period) were excluded from the study for practical reasons. Because available infant foods on the market are constantly changing, infant products were updated before selecting foods. For some products only the name had been modified. However, when a product had been withdrawn from the market, it was replaced in the database with a product that would have probably been chosen by parents if the consumption survey had been conducted at the time of the selection step. The closest products, using the panel purchase for identification based on four criteria, were used: targeted age, brand, flavour, targeted meal (breakfast, lunch, dinner). Data from the 2009 Kantar World purchase panel were used (unpublished data). These data give the number of units, volume and price of each infant product bought by a marketing panel of 20,000 French households. Based on these data and the selection criteria, products similar to the ones indicated by consumption data were identified. If several products were identified, the one presenting the greatest number of criteria similar to the initial product and the highest number of units bought (based on the purchase panel data) was selected.

Because the water used for diluting powdered infant formula was not specified in the consumption survey, the type and brand of water consumed otherwise was considered to dilute powder. When water type or brand were not recorded, results from a study on food preparation/cooking processes by parents were used (see below): a random sample was drawn to select water according to age group and based on the percentage of children in the survey consuming each water type and brand.

The food list was based on two main criteria:

- The most consumed food in terms of quantity and/or percentage of consumers.
- Foods that are known or supposed to be the main contributors to the exposure to one or more substances of interest.

Different selection thresholds were followed for specific infant foods (jarred foods, infant formulae, etc.), as well as water, which represents an important food group for

| Origin | Natural or environmental contamination of natural origin | Environmental contamination of anthropogenic origin | Used in food contact materials | Used for technological or agricultural reasons or formed during food process | Substances or congeners |
|--------|--------------------------------------------------------|---------------------------------------------------|--------------------------------|--------------------------------------------------|------------------------|
| Groups |                                                        |                                                   |                                |                                                  | Tetronic acid: spirodiclofen |
|        |                                                        |                                                   |                                |                                                  | Thiocarbamate: molinate |
|        |                                                        |                                                   |                                |                                                  | Triazine: atrazine, simazine |
|        |                                                        |                                                   |                                |                                                  | Triazinone: metribuzin |
|        |                                                        |                                                   |                                |                                                  | Triazole: amitrole, cyproconazole, |
|        |                                                        |                                                   |                                |                                                  | epoxiconazole, fluquinconazole, flusilazole, |
|        |                                                        |                                                   |                                |                                                  | metconazole, myclobutanil, tebuconazole, |
|        |                                                        |                                                   |                                |                                                  | triadimenol |
|        |                                                        |                                                   |                                | ×                                                | Sodium acetate (E262) |
|        |                                                        |                                                   |                                |                                                  | Ascorbyle palmitate (E304) |
|        |                                                        |                                                   |                                |                                                  | Tartrates: tartric acid (E334), sodium tartrate (E335), potassium tartrate (E336), calcium tartrate (E354) |
|        |                                                        |                                                   |                                |                                                  | Phosphates: phosphoric acid (E338), sodium phosphates (E339), calcium phosphates (E341) |

Table 1. Continued.
newborns, and non-specific foods called “common foods” (meat, vegetables, etc.) in this study. In the previous French TDSs, numerous data have been collected on nutrients and food contaminants in common foods (ANSES 2011a, 2011b). Therefore, to maximise the cost-effectiveness of the study, the focus was re-centred on specific infant foods. The most consumed foods were identified using the average consumption for each age group in our study and calculated with the raw data of the SFAE’s survey. These groups were defined according to stages of food diversification, based on French national recommendations (INPES 2004). Four age groups were defined: 0–4, 5–6, 7–12 and 13–36 months. For infant foods, the most consumed foods, representing 90% of the total diet or eaten by at least 5% of consumers in at least one of the age groups, were selected. For common foods, the main contributors to exposure were identified using the results of the TDS2 (ANSES 2011a, 2011b) and added if they were consumed at a rate of more than 1 g day$^{-1}$. For substances from FCM, pesticides and additives, which were specific to this study, a specific food selection was made. For additives, the main contributors were identified according to legislation (Ministerial Order of 29 August 2011) that defines in which food categories they are authorised (unpublished data). For pesticides, the food commodities consumed at a rate of more than 1 g day$^{-1}$ and/or contributing to more than 2.5% of the ADI for priority pesticides were identified. For substances migrating from FCM, no specific contributors were identified, but analysis according to packaging was defined.

From this selection, food items were defined. For common foods, groupings were made according to the food items of the TDS2 (Sirot et al. 2009). Foods having similar nutritional composition or ingredients and/or preparation steps (which can lead to similar contamination levels) were pooled. For example, potato-based products were grouped according to how they are prepared because preparation practices can lead to differences in nutritional or contamination levels (Figure 1). For infant foods, similar criteria were used. However, similar products from different brands were not grouped when the information about the brand chosen by the parents was available in the consumption study. This approach was chosen to take into account, in the exposure assessment, parent and, thus, child brand loyalty. This was particularly valuable for assessing exposure via infant formula.

Review of customary food cooking processes and selection of food and process combinations

To prepare and cook foods as close as common home practices, a national study on parents’ food preparation/cooking processes was carried out by ANSES in June 2011. Households with at least one child under 3 years old were targeted. The population study included 429 parents living in metropolitan France. The sample was representative of families involved in the collection of food consumption (Fantino & Gourmet 2008), in terms of parent socio-professional categories and child age groups. The population included in this study was compared with that of the consumption survey based on socio-demographic characteristics (age, socio-professional category, child age and gender). The same proportion of children in each age group included in the consumption survey was used in the survey of home practices.

Information was collected via an online questionnaire submitted to the studied population and used to determine how to prepare subsamples. It included questions on:

- Cooking process: do parents heat foods or not? If so, what kind of cooking equipment is used (microwave, bottle warmer, pan)?

![Figure 1. Example of the establishment of a sampling plan from food list to food samples.](image-url)
Containers used during the cooking process: do parents heat the product directly in its packaging or in other containers; what kind of container and what is the container made out of?; Is the container closed?

Heating method: time and wattage.

These questions were asked for each food category given by parents to their children. An example of information collected for the preparation of infant formula is given in Figure 2. Eight food categories were identified:

- Specific infant foods: infant formulae, milk-based beverages for breakfast, snack or dinner, soups or purees and infant meals.
- Common foods: milk, meat, fish or eggs, vegetables or potatoes and starchy foods (rice, pasta, etc.).

For each food category, the percentage of the each type of preparation/cooking and heating processes was calculated. Based on these percentages, the number of subsamples to be prepared according to each practice was determined. Sampling was random and subsamples were then allocated to each practice.

More general questions were also asked on kitchenware and place settings or on the type of water used for diluting infant formula.

Determination of samples and pooling levels for foods

A sampling plan was defined from these food items. To take into account the potential variability of contamination arising from the use of different FCMs, specific samples were defined for the analysis of substances from FCMs if the food item in question was sold in different types of packaging. For common foods, a broader grouping was then used. For example, for potato-based products, “classic” food items were listed according to the type of preparation (mashed, boiled, fried), whereas for specific samples, groupings were based on packaging (fresh, plastic bags and individual packaging), as indicated in Figure 1.

For each food item identified, 12 subsamples of equal weight were analysed. One subsample was bought every month for one year to account for any potential seasonal variability. Instead of a mixed food approach, this approach led to individual food samples mixed together to include seasonal variability as well as different flavours, various ways of consuming or different cooking methods. According to the information available on consumption data, subsamples for common foods were identified on the basis of different levels of composition, as in the TDS2 (Sirot et al. 2009): quantity consumed, texture or manufacturing process, fat, salt or other component content, flavour and/or origin and product specifications. The subsamples were then chosen on the basis of market shares from available SECODIP-TNS or Kantar Worldpanel.

![Figure 2. Example of information and results given by the study on food preparation/cooking processes used by parents. The percentage of the population who declared using a given cooking practice the most often is given in parentheses; n is the number of subsamples prepared for each cooking practice.](image-url)
purchase surveys (unpublished data). Information on place of purchase, preservation method and varieties (for vegetables or fruits, for example) was used. For infant foods, identification of food samples depended on the type of item. For items with a specific product identified using the consumption data (brand, flavour, packaging, etc.), the 12 subsamples were similar. For items without information on brand, packaging or for which several flavours were grouped (e.g. for dairy drinks), subsamples were chosen according to market shares of infant foods from the 2009 SECODIP-TNS purchase survey. For each subsample, the way of cooking was then defined according to data collected on the preparation/cooking processes used by parents. The percentage of the different preparation/cooking processes per category was used to determine the number of subsamples prepared with each identified preparation/cooking and heating process. For the time and wattage of heating, the mean of each heating process was be traced to its FCM. Each subsample was kept at –18°C until all 12 subsamples had been prepared. After collecting the 12 subsamples, they were pooled together by cryogrinding and put in containers. Cryogrinding was performed in a specific room with air renewal provided by a central air handler and temperature regulation. Three different types of grinder were used according to the volume and quantity of samples. Volumes of the grinder cuvette ranged from 80 ml to 6.5 L and were all made of stainless steel. In order to limit potential migration of inorganic contaminants present in stainless steel like chromium, new cuvettes were bought for this study. Blades were made of stainless steel or steel covered with tungsten carbide. One of the grind covers made of polycarbonate was replaced by a cover of glass. Containers used for storage of samples and subsamples were checked beforehand for potential migration. Migration tests showed that the containers may release some alkylphenols; therefore, additional, specific samples were taken in glass containers. For practical reasons, this additional analysis consisted in collecting six subsamples over 2 months and pooling them together to obtain the composite samples, i.e. analytical samples. The different analytical portions were then sent to laboratories for analyses. Three analytical portions of each composite sample were reserved for possible further analyses.

**Method of food collection, preparation and transport**

Foods were sampled between July 2011 and July 2012. Sampling was carried out in only one region because most products were nationally distributed. Therefore, tap water was not sampled and results from other countrywide campaigns were used. Field staff bought the food products in different stores: each subsample of one food item was bought in different shops, except for store brands. It was possible to buy several subsamples of different food items in the same store but at least 10 different shops were visited per month. If the product was no longer available on the market during the sampling period, it was replaced by the most similar product among those present on the market using the same criteria as for updating the food consumption database.

All food products were then stored according to their storage conditions (frozen, room temperature, etc.) until preparation. For each subsample, detailed information was given for pre-cooking preparation, cooking with time and wattage when applicable and post-cooking preparation. Information on the quantity of salt to add, type of fat to use, and also type of water to use for dilution of milk powder was given. As in the TDS2, the common products used to prepare other products (e.g. milk, butter or oil) were chosen according to their market shares. For water used in food preparation, a specific brand conditioned in a glass bottle and used by laboratories as reference water was used. A similar quantity of every batch of water used for each subsample was kept to make a composite sample that was also analysed for the different substances considered in this study. Using an unique water for every product to be diluted give the possibility to compare results in terms of contamination of the product considered, without taking into consideration variation in water concentration. For exposure calculations, all possible associations between each product and each type of water really used by parents will be considered by adding contamination due to the water really used and subtracting the contamination of reference water. Regarding materials, all information was given to the field staff, including information on kitchen utensils (wood, metal, plastic, etc.) based on the results of the study on the food preparation/cooking processes used by parents (see below). New and used materials were employed and special attention was paid to feeding bottles. All materials that were used for preparation were recorded so that each subsample could be traced to its FCM. Each subsample was kept at –18°C until all 12 subsamples had been prepared. After collecting the 12 subsamples, they were pooled together by cryogrinding and put in containers. Cryogrinding was performed in a specific room with air renewal provided by a central air handler and temperature regulation. Three different types of grinder were used according to the volume and quantity of samples. Volumes of the grinder cuvette ranged from 80 ml to 6.5 L and were all made of stainless steel. In order to limit potential migration of inorganic contaminants present in stainless steel like chromium, new cuvettes were bought for this study. Blades were made of stainless steel or steel covered with tungsten carbide. One of the grind covers made of polycarbonate was replaced by a cover of glass. Containers used for storage of samples and subsamples were checked beforehand for potential migration. Migration tests showed that the containers may release some alkylphenols; therefore, additional, specific samples were taken in glass containers. For practical reasons, this additional analysis consisted in collecting six subsamples over 2 months and pooling them together to obtain the composite samples, i.e. analytical samples. The different analytical portions were then sent to laboratories for analyses. Three analytical portions of each composite sample were reserved for possible further analyses.

**Results and discussion**

**Food selection and food samples**

Based on consumption criteria, 287 food items were defined, including 219 infant foods and 68 common foods. In addition, 27 common foods were included as potential chemical substance contributors. Food items based on products of animal origin were added to measure the contribution of natural steroids, although few data are available on this subject. These items were chipolata-type sausages and other pork-based products, different kinds of
cheeses, “cordon bleu” and hake. Samples of meunière-style sole, poultry nuggets, goat milk and milk-based beverages with fruits were also considered for the analyses of POPs because they have not been sampled in previous TDSs. Among the 30 foods identified as the main contributors of pesticides, pineapple and tomatoes were also added to the sampling plan. Tomatoes were also included to measure Alternaria toxins. Lastly, two samples of sweet biscuits were added to measure acrylamide and two samples of soy-based products to measure phytoestrogens. For infant foods, 161 food items were identified by a specific brand, whereas 58 items were general food items. Among these food items, five main types of material packaging were identified: plastic, glass, tin cans, cardboard and paper. Specific samples were then defined when a food item had several types of packaging. The number of samples by food group and related consumption amounts are presented in Table 2. Quantity consumed and percentage of consumers per age group for the 314 food items are available in Supplemental Material online (Appendix 1).

In all, 5484 food products were purchased to make up 457 composite samples. For the specific sampling in glass, 195 samples were prepared. The list of the 457 composite samples and the 195 specific samples in glass are available in the Supplemental Material online (Appendix 2).

Selected food items covered between 95.3% and 98.2% of specific infant foods consumed according to the age group. Table 2 gives the total percentage of consumption according to food category and the related percentage of coverage. For specific infant foods, the least covered category was infant fruit juices with a coverage percentage of 54%, whereas infant formulae and growing-up milks were covered at almost 100%.

Although the coverage percentage of common foods was lower, it reached 82.8%–99.97%. This percentage was higher for substances already assessed in the TDS2, because its results were used. Therefore, results from the 1352 composite samples representing 212 food items increased the coverage percentage of consumption specifically for these substances. In this case, only two food groups were not covered (sandwiches and specific foods) and the coverage rate for common foods reached 96.7% and 99.9% according to age group.

Despite the good coverage in this study, sampling excluded breast milk. Information on consumption and samples of human milk is very difficult to obtain. In France, the breastfeeding rate is quite low compared with other Organisation for Economic Co-operation and Development (OECD) countries (OECD 2012): only two out of three newborns are breastfed immediately after birth and only 42% of these infants are still breastfed at the end of the fourth month (Bonet et al. 2013). However, it is now recognised that some contaminants, especially some POPs, can be found in high concentrations in human milk and lead to a potential risk for newborns (EFSA 2011b; Ulaszewska et al. 2011). Therefore, collecting data on breast milk contamination in France would be valuable for estimating exposure in this particular population.

Only a few other countries have included infant products in their TDSs to estimate exposure in infants and toddlers. Australia, New Zealand and the United States collected data on infant products for children above 6 months old and considered different contaminants among agricultural and veterinary compounds, minerals, trace elements and mycotoxins. In the American TDS, there were 57 infant food items (Egan et al. 2007). The Canadian TDS gave information on the exposure assessment of children from 0 to 3 years old and focused on a broad-spectrum of contaminants (Dabeka & Cao 2013). To our knowledge, in Europe, only the UK has considered exposure in infants from 1.5 years old, but only based on consumption of common foods because infant foods were not sampled (EFSA et al. 2011b). However, in the European Union-funded project Cascade (“Chemicals as Contaminants in the Food Chain”), a specific integrated study, has been conducted to assess exposure of infants to chemical contaminants through the analysis of European baby foods. This project focused on EDs and targeted BPA, vinclozolin, PCDD/Fs, PCBs, genistein, promicidone, iprodione and cadmium (Piccinelli et al. 2010). Food samples were selected using market baskets, as in the TDS approach. In all, 30 baskets for infant formula and 15 for solid foods and beverages were prepared to cover monthly diets of infants from the fifth to the ninth months. These products were purchased in eight different countries and then pooled according to food categories. Based on the number of food products purchased, composite samples prepared and components analysed, our TDS will be one of the largest studies on the contamination of infant products and on exposure in children under 3 years old.

**Food preparation and food collection**

The characteristics of the population included in the study on the food preparation/cooking processes used by parents are shown in Table 3. When compared with the characteristics of the consumption survey population, there were no differences in terms of infant gender (p = 0.5251) or region (p = 0.07). However, people who answered the preparation study questionnaire were older (32.0 versus 29.9 years, p < 0.0001) and belonged to a higher socio-professional category (p < 0.0001) than in the consumption survey population.

Results of the study showed that 54% of parents used mineral water for diluting powdered formula, whereas 35% used spring water and 9% tap water; 2% used either spring or mineral water. Distribution according to age group (Table 4) was used to determine the type of water used for diluting infant formula in the consumption study.
As described in the Methods section, the percentage of each process was calculated and used to determine the number of subsamples used to prepare using each process. Figure 2 shows the relative percentage of each practice, and the associated number of subsamples analysed with these practices (based on 12 subsamples). In the example,
two subsamples of each composite sample of infant formula were not heated, because 18% of parents did not heat milk for their children, six were heated by microwave, three in a bottle-warmer and one in a water bath. For the three that were heated in a bottle-warmer, two were in plastic feeding bottles (one open and one closed) and one in a closed glass feeding bottle.

With this approach, subsamples were prepared with different customary food preparation/cooking processes in common use as recommended. However, lesser-used processes that may lead to specific contamination were not considered, e.g. the use of a kettle – which may potentially contain BPA – to heat water. Pooling subsamples prepared in different ways precludes the study of the influence of preparation process on the exposure to contaminants. However, the aim of a TDS is to evaluate the exposure of the general population and not to focus on specific or particular “at-risk” food preparation methods. Therefore, it was decided to prepare foods with only commonly used methods. The French infant TDS will be one of the first studies to use information on FCMs, which can have a potential impact on contamination especially when considering substance migration.

The type of kitchen utensils or cooking practices can influence the concentration of substances in foods. For example, some substances can migrate from kitchen utensils, e.g. chromium from stainless-steel pans, perfluorooalkyl acids from the coating in non-stick pans or BPA from old baby bottles. Utensil wear and tear can influence BPA migration (Tan & Mustafa 2003). Cooking and heating process can also lead to variation in food contamination, in particular for heat-induced contaminants such as acrylamide (Tareke et al. 2002), furan (Crews et al. 2007) or polycyclic aromatic hydrocarbons (White et al. 2008). Some cooking practices or wear rates can also influence the migration of substances present in FCMs, such as phthalates or BPA (Startin et al. 1987; Brede et al. 2003). Therefore, knowing the actual cooking and heating process is absolutely necessary to prepare food as consumed by children and to obtain contamination data as reliable as possible.

### Food collection

Sampling was done in the region of Clermont-Ferrand in central France. Food products were mainly bought in hyper- and supermarkets (90%), followed by drugstores (for specific infant formula, 8%), but also in more specific distribution networks, including open-air markets, bakeries or grocer shops. In total, purchases were made in 127 different shops, with a mean of 26 different shops every month.

TDS plans are usually designed to cover at least one of the two main aspects of representativeness: seasonality and geographical variation. Seasonal variation in contamination was taken into account by sampling the products throughout the year and pooling them together. However, seasonal variation in consumption was not taken into account because the consumption data used for selecting the food items was recorded only between January and March. Therefore, focusing on only one season can lead to bias. This is the case, for example, when considering some vegetables and fruits, as strawberries, eaten mostly during one specific season. Moreover, sampling was only done in one region because most foods were processed foods. Therefore, they are expected to present homogeneous contamination levels in all regions (ANSES 2013). Regarding infant foods, one product is generally delivered across the country by only one factory of a specific manufacturer. For common foods which may show regional variation, such as meat, fish, fruit or vegetables, results of the TDS2 will be used for most of the substances. In TDS2, the products were sampled in different regions in France. For exposure assessment, data will be matched between the sampling region and the child’s region of residence.

### Table 3. Characteristics of the households and respondent population in the preparation study (n = 429).

| Characteristics                                    | Proportion/mean ± SD |
|----------------------------------------------------|----------------------|
| Proportion of women                                | 73%                  |
| Age of respondent (mean ± SD)                      | 32 ± 6 years         |
| Number of children in the household                |                      |
| One                                                | 40%                  |
| Two                                                | 38%                  |
| Three or more                                      | 22%                  |
| Socio-professional category (SPC) of head of the household |
| Upper SPC Farmers                                  | 0.9%                 |
| Craftsmen, tradesmen, company managers              | 4.7%                 |
| Managerial, intellectual professions               | 21.9%                |
| Middle level occupations                           | 19.6%                |
| Lower SPC Employees                                | 38.9%                |
| Workers                                            | 9.1%                 |
| Retired                                            | 0.2%                 |
| Other unemployed persons                           | 4.7%                 |

### Table 4. Type and brand of water used for diluting powdered formula.

| Age group (months) | 1–4      | 5–6      | 7–12     | 13–36    |
|--------------------|----------|----------|----------|----------|
| Mineral water      | 58.8     | 52.6     | 46.5     | 61.4     |
| Spring water       | 41.2     | 35.6     | 39.6     | 21.4     |
| Tap water          | 0.0      | 5.1      | 10.9     | 17.2     |
| Mineral or spring water | 0.0 | 6.8 | 3.0 | 0.0 |
Conclusions

A TDS produces representative and accurate estimates of the dietary exposure of the population to beneficial or harmful chemical substances. Performing a TDS specifically on the infant population arises from the need to have same method as the one used for the general population and therefore to be able to assess dietary exposure to a wide range of contaminants for the whole population, including sensitive populations such as children. Based on these data on chronic exposure, risk assessment will be done to identify substances for which a risk cannot be ruled out (due to values that exceed health guidance values or to the risk of inadequate nutritional intake compared with requirements) or food elements that contribute the most to dietary exposure. ANSES and its expert committees may therefore be able to use these results for issuing recommendations on food safety. Moreover, TDSs can be used by food risk managers to determine priorities for possible public and private interventions and for scientific research by identifying substances or food categories for which in-depth prospective food safety studies are needed. In particular, aggregated and/or combined exposure assessments are some of the new challenging issues in risk assessment.

Thus, the present infant TDS will provide new data on the chemical contamination of infant products by a large range of food chemicals. Given the targeted population and substances, some new methodological choices were made compared to the previous French TDSs. These new methods cover various aspects involving food preparation and home-cooking to mimic as much as possible the actual cooking practices used in the population, taking into account brand loyalty, packaging information – which can have an impact on contamination levels – traceability of every type of kitchen utensil, etc. Information on selecting the food items and data on food preparation are not often available. However, such choices are crucial elements for the establishment of a TDS sampling design. The design of the French infant TDS provides an example of the kind of relevant methodological choices that can be made to produce the most accurate assessment of dietary exposure to chemicals. From the 7th EU-PCRD research programme on the on-going European TDS-exposure project (2011–14; see http://www.tds-exposure.eu), common methodological choices, including developing a sampling plan according to the selected substances and populations, may be of use to help define and develop a European Union-harmonised approach for member states to use in their own TDS programmes. Harmonisation will ensure the best, most accurate and most comparable dietary exposure practices as technically achievable with the fewest sources of uncertainty for use in risk assessment.

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Supplemental data

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