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Environment International 137 (2020) 105529

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

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ARTICLE INFO

Handling Editor: Da Chen

Keywords:
Food safety
Infants and young children
Pesticide residues
Total diet study
Exposure assessment
Risk characterization

ABSTRACT

A total diet study (TDS) was undertaken to estimate the chronic dietary exposure to pesticide residues and health risks for the French infants and young children below 3 years old. As a whole, 516 pesticides and metabolites were analysed in 309 food composite samples including 219 manufactured baby foods and 90 common foods, which cover 97% of infants and young children's diet. These composite samples were prepared using 5,484 food products purchased during all seasons from 2011 to 2012 and processed as consumed. Pesticide residues were detected in 67% of the samples and quantified in 27% of the baby food samples and in 60% of the common foods. Seventy-eight different pesticides were detected and 37 of these quantified at levels ranging from 0.02 to 594 μg/kg. The most frequently detected pesticides (greater than 5% samples) were (1) the fungicides 2-phenylphenol, azoxystrobin, boscalid, captan and its metabolite tetrahydrophthalimide, carbendazim, cyprodinil, difenoconazole, dodine, imazalil, metalaxyl, tebuconazole, thiabendazole, (2) the insecticides acetamiprid, pirimiphos-methyl and thiacloprid, (3) the herbicide metribuzin and (4) the synergist piperonyl butoxide. Dietary intakes were estimated for each of the 705 individuals studied and for 431 pesticides incl. 281 with a toxicological reference value (TRV). In the lower-bound scenario, which tends to underestimate the exposure, the TRV were never exceeded. In the upper-bound scenario that overestimates exposure, the estimated intakes exceeded the TRV for dieldrin and lindane (two persistent organic pollutants) and propylene thiourea, a metabolite of propineb. For these three substances, more sensitive analyses are needed to refine the assessment. For 17 other detected and/or prioritised pesticides, the risk could not be characterised due to the lack of a valid TRV, of certain food analyses or the absence of analytical standards for their metabolites.

Abbreviations: ADI, Acceptable daily intake; ANSES, French Agency for Food, Environmental and Occupational Health & Safety; ATDS, Australian Total Diet Study; ATSDR, Agency for Toxic Substances and Disease Registry; BAC, Benzalkonium chloride; CI, Confidence interval; CRA, Cumulative risk assessment; CV, Coefficient of variation; DDAC, Didecyldimethylammonium chloride; DNT, Developmental Neurotoxicity; EC, European Commission; EFSA, European Food Safety Authority; EOGRTS, Extended One-Generation Reproductive Toxicity Study; EU, European Union; GEMS/Food, Global Environment Monitoring System - Food Contamination Monitoring and Assessment Program (WHO); iTDS, Infant Total Diet Study; JMPR, Joint FAO/WHO Meeting on Pesticide Residues; LB, Lower-bound scenario; LOD, Limit of detection; LOQ, Limit of quantification; MRL, Maximum residue level; NZTDS, New Zealand Total Diet Study; P90, 90th percentile; PBO, Piperonyl butoxide; POP, Persistent organic pollutant; PTDI, Provisional tolerable daily intake; RD-Mo, Residue definition for the monitoring; RD-RA, Residue definition for dietary risk assessment; TDS, Total diet study; TDS2, Second French Total Diet Study; THPI, Tetrahydrophthalimide; TRV, Toxicological reference value; UB, Upper-bound scenario; US-EPA, United States Environmental Protection Agency; WHO, World Health Organization

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https://doi.org/10.1016/j.envint.2020.105529
Received 23 August 2019; Received in revised form 24 December 2019; Accepted 25 January 2020
Available online 08 February 2020

1. Introduction

Improving knowledge on the dietary risk of chemical substances is one of the major challenges to public health, especially for a vulnerable population such as infants and young children under 3 years of age. This specific age group is more sensitive to several chemicals due to their high food intake/body weight ratio and to the immaturity of their defence systems against chemical stressors. Particularly in infants below 16 weeks, the enzymes involved in the metabolism of xenobiotics are not as efficient as in adults. Development processes during these periods are also more easily disturbed (Diamanti-Kandarakis et al., 2009; EFSA PPR Panel et al., 2018; EFSA Scientific Committee et al., 2017; Landrigan et al., 2004; Makri et al., 2004; NAS, 1993; Sly and Flack, 2008). Thus, foods for infants and young children i.e. infant formulae, follow-on formulae, processed cereal-based food and other baby foods, follow specific regulations for marketing and monitoring of chemicals with legal limits to ensure their safety (Commission Directive 2006/125/EC; Commission Directive 2006/141/EC; Regulation (EU) No 609/2013).

Pesticides are used to keep crops healthy and prevent them from being destroyed by disease and infestation. The marketing and use of pesticides are regulated in the European Union (EU) by the Regulation (EC) No 1107/2009. Pesticides products cannot be placed on the market and used without prior authorisation by the EU Member States. Before a pesticide active substance can be used within a plant protection product, it must be approved by the European Commission (EC) following an intensive evaluation led by the European Food Safety Authority (EFSA) in close cooperation with EU Member States. This evaluation includes health and environmental risk assessments. All matters related to legal limits for pesticide residues in common food and feed and their monitoring in the food chain are covered by the Regulation (EC) No 396/2005.

An assessment of the dietary exposure and risk to pesticide residues is also performed at post-marketing level. Each year, EFSA publishes a report on the results of the EU Member States' monitoring of pesticide residues in food that includes a section on baby foods (EFSA, 2019a). The annual assessment of dietary exposure to pesticide residues is incomplete for infants and young children, mainly because consumption data for these age groups are reported by a limited number of countries in the current system (EFSA PPR Panel et al., 2018; EFSA, 2007). Recent solutions were proposed to tackle this issue such as reporting and using more adequate consumption surveys in the EFSA Comprehensive European Food Consumption Database to better assess the exposure of infants and young children (EFSA PPR Panel et al., 2018; EFSA, 2011b).

In France, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) has developed and implemented a method for the monitoring of dietary exposure to pesticide residues that includes two complementary approaches: (1) quantitative dietary risk assessment based on the results of the monitoring programmes, regularly updated (Nougadère, 2014) and (2) multi-year total diet studies (TDS) such as the second French total diet study (TDS2) (ANSES, 2011). These two approaches enable the prioritisation of risk for more than 500 pesticides and 300 foods. This method has many advantages e.g. analysis of the whole diet including tap water, identification of the highest exposed individuals based on recent individual consumption data. However, until now, it has only covered adults and children above 3 years of age.

Therefore, between 2010 and 2016, ANSES conducted this infant total diet study (iTDS) on French infants and young children (under 3 years of age) in which concentration data were collected for 516 pesticides and their metabolites in 309 composite food samples including 219 foods for infants and young children (hereafter "baby foods") and 90 common foods (Hulin, 2014). The iTDS follows the TDS2 carried out between 2006 and 2011 that focused on 445 substances including 283 pesticides (ANSES, 2011; Nougadère, 2012).

TDSs are national monitoring studies on food chemical occurrence and dietary exposure, based on a standardised method recommended by international agencies (EFSA-FAO-WHO, 2011; WHO, 2005). They are implemented worldwide to complement the national monitoring programmes on chemicals in raw agricultural commodities, through the analysis of food processed as consumed at home (table-ready) incl. peeling, washing, heating, etc. After food sampling and analysis of the samples, the exposure is estimated by combining food consumption data and contamination data from food sample analysis. This approach provides the basis for realistic estimates of the total dietary exposure to various chemical substances.

To the best of our knowledge, the French infant TDS is the only TDS specifically designed for assessing dietary exposure to pesticide residues for all infants and young children under the age of 3 years. Some TDSs have focused on pesticides for limited age groups of infants e.g. 6–12 months in the New Zealand TDSs (MAF, 2011; MPI, 2018) and infants of 9 months in the Australia TDS (FSANZ, 2011).

In the iTDS reported here, the analyses of pesticide residues in foods were conducted with the best possible analytical performances needed to assess the most realistic levels of exposure for infants and young children. Analytical method developments were necessary to achieve detection and quantification limits lower than requested in the monitoring programs and previous TDSs. The results of the iTDS were recently published for trace elements (Sirot et al., 2018), cadmium (Jean et al., 2018), acrylamide, furan and polycyclic aromatic hydrocarbons (Sirot et al., 2019), perfluoroalkyl acids and brominated flame retardants (Rivière et al., 2019).

This study aims at measuring the concentrations of pesticide residues in food as consumed by French infants and young children and estimating dietary exposure and risk levels. Recommendations are provided to guide (1) the risk managers in the development of their monitoring programmes and preventive and corrective measures and (2) the risk assessors for their research and expertise in analytical chemistry, toxicology and exposure assessment.

2. Materials and method

2.1. Population studied and food consumption data

Different terminologies can be used to define the two main groups of population under consideration. In the present paper, the term "infants" refers to the infants under 1 year old while the term "young children" refers to the children aged between 1 and 3 years old in accordance with the EU legislation (EFSA PPR Panel et al., 2018; Regulation (EU) No 609/2013).

Consumption data of 705 infants and young children under 3 years of age were obtained from the most recent cross-sectional survey on individual dietary consumption of infants and young children conducted in 2005 (Fantino and Gourmet, 2008; Fantino, 2005). The recruitment of these individuals was based on proportionate quota sampling to be representative of infants and young children in France. The population has been categorised into four age groups to take into account the dietary diversification periods of the French infants and young children: 1–4 months (n = 124 individuals), 5–6 months (n = 127), 7–12 months (n = 195) and 13–36 months (n = 259). Breastfed children, even partially, were not included in the survey that focused only on the consumption of baby foods. Food and beverage consumption including water has been recorded through a 3-consecutive-days record describing foods, quantities and portion sizes. Body weights were also measured.

2.2. Food sampling and preparation

The sampling plan has been fully described in a previous paper (Hulin, 2014). Briefly, the consumption survey described previously guided the selection of the most consumed foods in terms of quantity and/or consumer rates, or foods known to contribute to the exposure to

one of the studied chemicals. The food list covered more than 97% of the children's diet. Between July 2011 and July 2012, 5,484 food products were purchased in 128 different stores and prepared "as consumed" by the population (i.e. peeled, cooked etc.). Foods included common foods such as vegetables, fruit or cakes as well as specific ready prepared/manufactured baby foods such as infant formulae. The food preparation practices were collected through a 2011 specific online survey on a representative sample of 429 parents living in metropolitan France and with at least one child under 3 years old (Hulin, 2014).

In total, 309 food composite samples (hereafter "samples") were prepared, each being a pool of 12 subsamples of the same food from different brands, places of purchase and modes of preparation. For each sample, the 12 subsamples collected (one per month during one year) were prepared, then grouped, homogenised and frozen (- 18 °C) before analysis. This number of subsamples was considered adequate by the experts in charge of defining standardized protocols for sampling and implementing TDSs, considering satisfactory confidence intervals (CI 95%) associated with the mean estimated concentrations in composite sample in pilot studies (Jensen et al., 2011). The 309 food items analysed included 219 baby foods (e.g. infant formulae, growing-up milk, apple puree) and 90 common foods (e.g. fresh apples, pasta, fried breaded fish…) and bottled water. These food items and their corresponding food groups were previously detailed (Hulin, 2014). Five groups of baby foods were considered, as for related Regulation (EU) No 609/2013: infant formulae, follow-on formulae, processed cereal-based foods and other baby foods (e.g. baby jars of fruits, vegetables, meat and/or fish).

Since tap water was not sampled in the iTDS, the results of the national monitoring programmes of pesticide residues in tap water, implemented by the French Ministry of Health, were used at individual level (Rety et al., 2012). Concentration in tap water of a given residue was estimated as the mean individual concentration at French department level. When certain *residue-French department* pairs were not available in the national database, the regional average (bigger administrative area than the department) concentration was used.

2.3. Pesticide residues and foods analysed

In this study, "pesticide residues" are considered as defined by the Regulation (EC) 396/2005: *"active substances, metabolites and/or breakdown or reaction products of active substances currently or formerly used in plant protection products […] which are present in or on the food products covered by Annex I, including those which may arise as a result of use in plant protection, veterinary medicine and as biocide"*.

The pesticides covered by the iTDS are mainly considered in the scope of the Regulation (EC) No 1107/2009, and the ones listed in its Annex 1 are approved (authorised) in the EU. The regulatory status (approved or not approved) of each pesticide is updated in real time in the *EU Pesticides database* (European Commission, 2019). Of the pesticides studied, 51% were approved during the sampling period and 47% were no longer approved but could also be detected in certain foods imported from countries outside the EU where they could be authorised. Other substances sought in the study (2%) are either persistent organic pollutants (POPs) that can still be found in the food chain due to historical uses and their persistence in the environment, or other substances not considered in the Regulation /1107, 2009 e.g. benoxacor, cloquintocet-mexyl, mefenpyr and piperonyl butoxide (PBO). PBO is a synergist of pyrethrins and pyrethroids without intrinsic insecticidal activity and is not considered as a pesticide active substance in the EU (European Commission, 2019).

Taken together, 516 parent pesticide active substances and their metabolites were analysed and then aggregated into 469 pesticides according to their residue definition described in Section 2.4 (Table 1 and Supplementary Tables S1 and S2).

Out of these pesticides, 84 had been prioritised ("priority pesticides") during the planning phase of the study, based on their toxicological profile and theoretical exposure (Hulin, 2014). Prioritised pesticides were (1) 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 (European Commission, 2019), or (2) considered as potential endocrine disruptors (European Commission, 2013) or (3) with a theoretical dietary exposure exceeding the TRV or (4) included in the national biomonitoring strategy (Fréry et al., 2013) and/or (5) exceeded the European Union maximum residue levels (MRLs) for baby foods (EFSA, 2011a). Commission Directives 2006/125/EC and 2006/141/EC set a default MRL of 0.01 mg/kg per individual pesticide in baby foods, except for five pesticides no longer approved in the EU (cadusafos, demeton-S-methyl, ethoprophos, fipronil and propineb) with MRLs ranging from 0.004 to 0.008 mg/kg.

All 516 compounds were sought in as many samples as possible, via multi-residue and single residue methods, and at least in all foods in which it is expected to be present on the basis of the EU pre-marketing assessment (EFSA, 2019f). For example, 113 residues were analysed in all 309 foods and 265 pesticides were sought in more than 150 foods (Table S2). The analysis of the banned organochlorine pesticides considered as POPs by the Stockholm Convention was only requested in food from animal origin and mixed matrices (animal and plants) in view of assessing the exposure (except dieldrin in cucurbits in which it is expected). All residues were sought in infants and follow-on formulae, mixed matrices considering that their proteins could come from vegetal (e.g. soya) and/or animal origin (e.g. cow milk).

The analytical methods and internal quality control are described in supplementary data (Appendix). The limits of detection (LOD) and limits of quantification (LOQ) are both considered in the two scenarios of the iTDS (see Section 2.5), for the management of left-censored data i.e. non-detected or non-quantified results. The LOD values depended on the substance, the matrix (food) and the method used (Appendix, Tables S1 and S2).

2.4. Processing of analytical results and concentration scenarios

The verification of the overall quality control results led to 1.5% of the test results (1537 substance-matrix combinations) submitted by laboratories being excluded. Only analytical results associated with a variation coefficient (CV) lower than 35% were kept and used (SANCO, 2013). Non quantified results with recovery levels lower than 45% or higher than 160% were excluded. Quantified values with recovery levels higher than 160% were also excluded. Quantified results with recovery levels outside the recommended range (70% to 120%) were corrected (SANCO, 2013). Quantified values with recoveries between 45% and 70% were adjusted from the actual recovery level to the minimal requested recovery level of 70%. Following this approach, quantified values with a recovery level ranging from 120 and 160% were adjusted to 120%.

In order to manage the results reported below the analytical limits, two concentration scenarios were assumed as recommended by international guidelines (GEMS/Food-EURO, 1995; WHO, 2013): the lower-bound (LB) scenario and the upper-bound (UB) scenario. Under the LB scenario, undetected results (below the LOD) were set to zero and unquantified results (detected between the LOD and the LOQ) to the LOD value. Under the UB scenario, undetected results and unquantified results were respectively set to the LOD and the LOQ.

Before calculating the mean concentration of each pesticide in a food (used later for the estimation of the exposure), the estimated concentrations of different compounds from a given multi-component residue definition were added per sample (e.g. aldrin and dieldrin concentrations summed and expressed as dieldrin) under LB and UB, to take into account the residue definitions (EFSA, 2016; OECD, 2009). The residue definitions for the monitoring (RD-Mo) and for risk assessment (RD-RA) are respectively mentioned in the *EU Pesticides*

Table 1
Number of samples and pesticides after aggregation and adjustment.

Food type	Number of food samples[1]	Number of pesticides analysed[2]	Number of analyses[2]
Food for infants and young children (baby foods)	219	352	60,415
Common foods incl. water	90	415	22,956
TOTAL	**309**	**469**	**83,371**

[1] The number of food samples analysed is equal to the number of food items, i.e. there is one composite sample per food item.
[2] After aggregation of active substances and/or metabolites according to the RD-RA. Adjustments have been made with mass ratios for molecular weight, and in some cases with conversion factors and toxicity equivalent factors **(Table S3)**. The number of analytes sought per sample varied according to the food samples (see Section 2.3).

Database and in the EFSA conclusions on the peer review of pesticide risk assessment (EFSA, 2019f; European Commission, 2019; Regulation (EC) No 396/ (2005). The RD-Mo can be the same than the RD-RA or can be restricted to the active substance and/or the relevant metabolites (main markers). The RD-RA was considered in this study except for some cases for which only the compounds of the RD-Mo could be analysed (lack of analytical methods or standards for the other compounds of the RD-RA). In this case, conversion factors, when available in the EFSA conclusions, were applied to the analysed markers' levels of the RD-Mo to convert them into toxicologically relevant levels, e.g. for tau-fluvalinate (Table S3) (Commission of the European Communities, 1997). Other adjustments were made with mass ratios to take into account the compounds' molecular weight. In addition, toxicity equivalent factors were applied for two cases (dimethoate/omethoate and carbendazim/thiophanate-methyl) as indicated in the EFSA outputs (Commission of the European Communities, 1997; EFSA, 2006; EFSA, 2009b). These different aggregations and adjustments of the analytical results were done with SAS software (9.3.) and are detailed in Table S3.

The substances had to be sufficiently stable during the storage period before their analysis, according to the conclusions of the EU evaluations (EFSA, 2019f), i.e. recovery of at least 70% of the quantities tested according to official standards after one year of storage at −18 °C, in order to limit the possible losses during storage (European Commission, 1997). For 10 prioritised pesticides, the exposure was not estimated because the stability was not reported or was insufficient: diazinon, dicofol, dithianon, etridiazole, forchlorfenuron, methidathion, permethrin, pymetrozine, pyrethrins, vinclozolin. These pesticides were included in the analysis, but not detected (Table S2).

2.5. Dietary exposure assessment and risk characterisation

The chronic dietary exposure was calculated with SAS software 9.3. for each pesticide and for each individual of the consumption survey, under LB and UB scenarios (cf. Section 2.4), as follows:

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

$E_{i,j}$ estimated daily exposure to pesticide j for individual i (μg/kg bw/day)
n number of foods in the diet of individual i
$C_{i,k}$ mean daily consumption of food k by individual i (g/day)
$L_{k,j}$ concentration of pesticide j in food k (mg/kg)
BW_i body weight of individual i (kg)

The exposure is expressed in micrograms of pesticide per kilogram of body weight per day (μg/kg bw/d). After assessing the individual exposures, the mean and the 90th percentile (P90) of exposure were calculated for each age group. Considering the number of individuals in each age group (see Section 2.1), the highest percentile of exposure considered as statistically robust was the P90 (EFSA, 2009a; Kroes et al., 2002). For each pesticide and each age group, the probability that the exposure exceeds the TRV was estimated as the percentage of individuals with an exposure exceeding the TRV, with a 95% confidence interval ($CI_{95\%}$). Pesticides for which this percentage of individuals was significantly different from zero, were considered as presenting a potential dietary risk for the age group. For each pesticide, the contribution of each food or food group to the total dietary intake was calculated as a percentage of the total exposure.

The chronic exposure was assessed for 431 pesticides for which it was possible to assess the coverage level of the diet potentially contributing to pesticide intake (contributing diet) for the 4 age groups. The contributing diet was calculated for each pesticide as the mean consumption (g/day/pers) of all theoretical contributors to pesticide intake (Nougadère, 2012). For a pesticide, the theoretical contributors were defined as all food commodities for which MRLs are not equal to the default MRL (0.01 mg/kg) or with authorised uses at the moment of the sampling (European Commission, 2019). The coverage level of the contributing diet corresponds to the ratio between the contributing diet covered by the iTDS sampling plan (i.e. all foods analysed) and the total contributing diet. A coverage level higher than 70% of the total contributing diet was considered to be acceptable, i.e. the uncertainty of the assessment is low.

Then, the risk was characterised for 281 pesticides with an acceptable coverage level and with a chronic TRV approved at national, European or international level. For 150 other pesticides, the risk could not be characterised because of an insufficient coverage level (<70%) and/or the lack of a valid TRV. Of these 150 pesticides, only 17 were considered relevant for the exposure assessment because they were detected in this study and/or considered priority pesticide (see Section 2.3). For the other ones, it is recommended to expand the analyses to other foods in order to increase the coverage level of the contributing diet.

For chronic risk, the TRV is most often an acceptable daily intake (ADI) for the pesticides in the scope of the regulation (EC) 1107/2009, but can also be a provisional tolerable daily intake (PTDI) such as for dieldrin (FAO/WHO, 1995) or hexachlorobenzene (WHO/IPCS, 1997). The selected TRVs mainly came from the *EU Pesticides database* (European Commission, 2019) and the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) (WHO, 2009; WHO, 2015). They were defined by EFSA, JMPR or other international bodies and safety agencies e.g. ANSES, Agency for Toxic Substances and Disease Registry (ATSDR), United States Environmental Protection Agency (US-EPA) (Table S3) and most have been validated by the European Commission following the European process of pesticide peer review at pre-marketing level under Regulation (EC) /1107, 2009. These TRVs have been considered applicable for the infants and young children by the *ad hoc* ANSES working group of toxicologists set specifically for this study. In particular, the toxicological studies required for the pre-marketing assessment by Regulation (EC) No 283/2013, including multigenerational studies and developmental toxicity studies, have been checked. A complementary literature search was undertaken to assess the existence of epidemiological studies or of more recent toxicological studies that would not have been considered by the EU pre-marketing assessment.

Finally, out of 469 pesticides studied, the exposure could be estimated for 431 pesticides. Of the 38 other compounds (not detected), 10

have insufficient stability, 26 metabolites are not included in a residue definition and are toxicologically irrelevant, and chlordecone and mirex were only sought in water. And the risk could be characterised for 281 pesticides with an applicable TRV and a coverage level higher than 70% of the contributing diet.

3. Results and discussion

3.1. Substances detected and concentrations in composite samples

Out of the 309 composite samples analysed, 208 (67%) had at least one detected residue and 113 (37%) at least one quantified residue. The detections concerned 32 food groups and the quantification 27 food groups, over 38 groups analysed (Table S1).

Of the 208 samples in which one or more pesticide residues were detected, 35 (17%) contained only one residue, 127 (61%) from two to five residues and 46 (22%) contained more than 5 residues. A maximum of 20 pesticides were detected together in a composite sample of baby food jars of apples and strawberries.

Table S1 shows the frequencies of detection and quantification, the range of quantification levels and the analytical limits, for each food/pesticide combination with at least one detection (n = 233). Table S2 shows the analytical results for each pesticide sought.

In all, 78 residues (17% of the residues sought) were detected: 33 fungicides, 30 insecticides and/or acaricides, 12 herbicides, a synergist (PBO), a plant growth regulator (diphenylamine) and one metabolite (ethylenethiourea). Thirty-seven were quantified at levels ranging from 0.02 (fenuron in water) to 594 μg/kg (chlorpropham in potatoes).

The most frequently detected pesticides (in more than 5% samples) were the fungicides 2-phenylphenol, azoxystrobin, boscalid, captan and its metabolite tetrahydrophthalimide (THPI), carbendazim, cyprodinil, difenoconazole, dodine, imazalil, metalaxyl, tebuconazole, thiabendazole, the insecticides acetamiprid, pirimiphos-methyl and thiacloprid, the herbicide metribuzin and the synergist PBO. Among these pesticides, metribuzin and 2-phenylphenol (18% of the samples), carbendazim (14%), tebuconazole (12%), captan (11%), thiabendazole (7%), pirimiphos-methyl (7%) and imazalil (6%) had been defined as priority pesticides in terms of monitoring because of their toxicological profile (Hulin, 2014). These frequencies of detection were quite similar in the TDS2 for PBO (17%), pirimiphos-methyl, thiabendazole and imazalil, used for post-harvest treatments of cereal grains and citrus respectively (Nougadère, 2012). PBO was found in 21 foods, particularly in wheat-based products and cereals for infants (Table S1). All these pesticides were approved in the EU, except carbendazim that was not allowed in France during the sampling period but that is also a relevant metabolite of thiophanate-methyl that was authorised (Table S2).

No exceedance of MRLs was identified for any of the 309 samples analysed (see details below).

3.1.1. Foods for infants and young children

Out of 219 baby food composite samples analysed (11 food groups), 147 (67%, 9 groups) contained at least one detected residue and 59 (27%, 6 groups) at least one quantified residue. In baby foods, 67 pesticides (19%) were detected and 16 pesticides (5%) quantified (Fig. 1) (Table S1).

No exceedance of MRLs was identified. The maximum value measured of 6.5 μg/kg of captan (THPI) in baby food jars of fruits/vegetables did not exceed the default MRL of 10 μg/kg set for baby foods (see Section 2.3.) (Commission Directive 2006/125/EC; Commission Directive 2006/141/EC).

No residue has been detected in infant formulae (first age milk, until 6 months).

Out of 71 samples of **infant and follow-on formulae and growing-up milk**, only one sample of follow-on formulae (6–12 months) presented detected but not quantified ("traces") levels of 2-phenylphenol. 2-phenylphenol was approved in the EU (Regulation (EC) No 1107/2009) and authorised in France for the treatment of storage premises and materials as well as dairy equipment and livestock buildings. In addition, it is still used as a biocide and had also been used as a food additive (preservative E231) in the EU until 2004.

Out of 14 samples of **milk-based drinks and desserts**, 12 presented residues at unquantified levels. Biphenyl, former food additive (E230) and fungicide banned in Europe in 2004, was detected in 9 samples. Triazole fungicides (fenbuconazole, tebuconazole) authorized in Europe were detected in 2 samples. THPI, a metabolite of captan, an approved fungicide, was detected in 2 samples. PBO was detected in 2 milk-based drinks' samples containing cereals (Table S1). PBO is a synergistic adjuvant of pyrethroids and pyrethrins in insecticidal preparations used in particular for the post-harvest treatment of cereals.

All baby food **jars** of fruits, vegetables and vegetables/fish or meat and fruit juices for infants contained detected residues (102 samples), among which 53 samples with quantified residues at levels ranging from 0.9 and 9.9 μg/kg (THPI). The most frequently quantified residues are those of pesticides approved in Europe: THPI/captan (n = 23 samples of baby jars), herbicide metribuzin (n = 14) and fungicide tebuconazole (n = 8). Residues were also detected in all **fruit juices for infants and young children** analysed (n = 4): 2 samples contained captan residues (THPI) at levels ranging from 1 to 3 μg/kg and one sample contained carbendazim (2 μg/kg). Residues were detected in all **soups and purees for babies** (n = 11) and boscalid was quantified in one sample (1.4 μg/kg) (Table S1).

All 17 samples of **cereals for infants** contained detected residues, and 2 samples at least one quantified pesticide with levels ranging from 4 to 4.4 μg/kg (PBO). The most frequently detected pesticides were PBO, tebuconazole, pirimiphos-methyl, and the fungicides boscalid, tricyclazole, THPI, difenoconazole and azoxystrobin.

With the exception of biphenyl, these pesticides were approved in Europe during sampling. Carbendazim has not been approved since 2014 but is the relevant metabolite of thiophanate-methyl approved until 2019.

3.1.2. Common foods and water

Of 90 common food samples analysed (28 food groups), pesticides were detected in 61 samples (68%, 23 groups) and quantified in 54 samples (60%, 21 groups) (Fig. 2) (Table S1). Out of 414 pesticides sought, 32 (8%) were detected and 28 (7%) quantified at least one time. The levels varied between 0.02 μg/L (fenuron in bottled water) and 594 μg/kg (chlorpropham in fried potatoes) (Table S1). These concentrations remained below the corresponding MRLs (Regulation (EC) No 396/2005) and the quality limits (QL) for bottled water (Decree of 14 March 2007).

All **cereal products** (15 samples of various groups: biscuits, rice/durum wheat products, croissant-like pastries, breakfast cereals, bread, pasta and mixed dishes) presented at least one pesticide with measured levels ranging from 1 μg/kg (tebuconazole in bread) to 137 μg/kg (PBO in breakfast cereals). The most frequently quantified residues were the post-harvest insecticides for cereal grains pirimiphos-methyl and chlorpyrifos-methyl, and the synergist PBO. Pirimiphos-methyl's levels varied from 3 to 78 μg/kg in biscuits. PBO's concentrations were measured between 3 and 137 μg/kg in breakfast cereals (Table S1).

All **fruits and compotes** (8 samples) contained 11 quantified pesticides between 1 μg/kg (2,4-D in fresh oranges) and 133 μg/kg (imazalil in clementines). In citrus, 2,4-D, imazalil, prochloraz and thiabendazole were quantified from 1 μg/kg (2,4-D) to 133 μg/kg (imazalil). Imazalil, propargite and thiabendazole were quantified in fresh bananas at levels from 2.7 to 4.9 μg/kg. In fruit compotes, carbendazim, cyprodinil, diphenylamine, fludioxonyl, imazalil, pirimicarb and thiabendazole were quantified at levels ranging from 1.4 μg/kg (cyprodinil) and 23 μg/kg (diphenylamine). In kiwis, fenhexamide was quantified (4,4 μg.kg) (Table S1).

All **vegetables** (11 samples) contained detected residues. Eleven pesticides were quantified, at levels ranging from 1 μg/kg (linuron) to

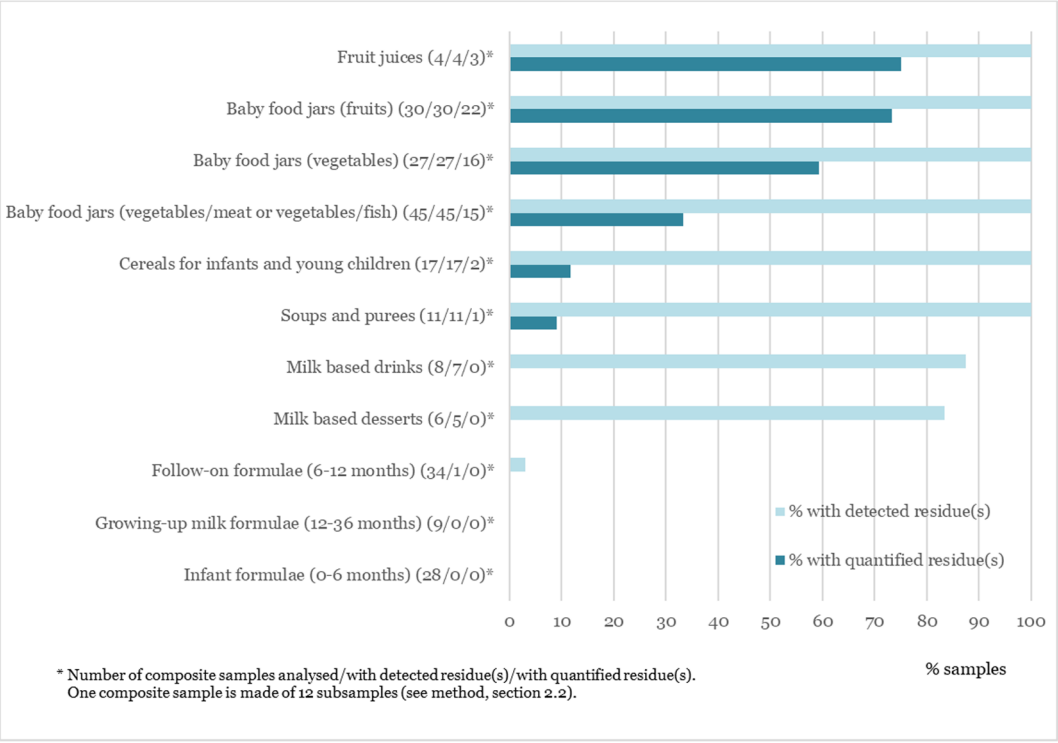

Fig. 1. Frequencies of detection and quantification per baby food group.

18 μg/kg (cyprodinil in beans). Prosulfocarb was quantified (5 μg/kg) in carrots. Lambda-cyhalothrin and metalaxyl were quantified in head cabbage, cauliflower and brocolis, from 2.4 (metalaxyl) to 18 μg/kg (cyprodinil). Dieldrin was quantified in courgettes (3,4 μg/kg). Carbendazim and cyprodinil were quantified in beans, at 1.2 and 18 μg/kg. Linuron and cyprodinil were quantified in mixed vegetables at 1 and 2,5 $\mu g.kg^{-1}$. Tebuconazole was quantified at 11 μg/kg in leeks. Azoxystrobin, cyprodinil, metalaxyl, and pyrimethanil were quantified in tomatoes from 1 to 3.4 μg/kg (Table S1).

Residues were detected in all three samples of **potatoes**. The quantified pesticides are the growth inhibitor chlorpropham (n = 3), the herbicide glufosinate (n = 1), PBO (n = 1) and pirimiphos-methyl (n = 1). Chlorpropham levels ranged from 91 (puree) to 594 μg/kg (French fries).

Regarding **dairy products** (17 samples) and chocolate (2 samples), 2-phenylphenol and PBO were detected in 10 samples, incl. 6 samples with 2-phenylphenol quantified at levels ranging from 6 to 29 μg/kg in cheese and butter.

Regarding the **other products of animal origin** including meat (4 samples of meat, poultry and game), fish (n = 1) and eggs (n = 2), quantified residues were found only in fish and eggs. Chlorpropham, PBO and pirimiphos-methyl were found in fried fish at levels ranging from 1.6 to 4.3 μg/kg. 2-phenylphenol was found in eggs (3.1 μg/kg).

In **bottled water** (13 samples), fenuron was quantified in 3 samples with levels between 0.02 and 0.06 μg/L. Other beverage, cacao hot drinks contained PBO and 2,4-D at 2.5 and 3.2 μg/kg (Table S1).

With the exception of dieldrin, fenuron and diphenylamine, pesticides found above in common food were authorised in the EU for agricultural uses during the sampling period. The presence of dieldrin in courgettes is also regularly observed in the results of the EU monitoring programmes (EFSA, 2018; EFSA, 2019a).

The mean number of quantified residues per sample was higher in common foods (2 residues per sample) than in baby foods (1 residue per sample).

3.1.3. Comparison with the literature

These results are consistent with the results of the TDS2 and the monitoring programmes of the EU's member states (ANSES, 2011; ANSES, 2014; EFSA, 2014; EFSA, 2019a). The pesticides the most frequently found in baby foods both in the iTDS and in the related 2012 EU monitoring programmes (EFSA, 2014) were: tebuconazole in 6 baby food groups, azoxystrobin in 5 baby food groups, pirimiphos-methyl in baby food cereals, carbendazim in baby food fruit juices, tebufenozide and spinosad in baby food jars of fruits, DDT in baby food jars of vegetables/meat or vegetables/fish. Other pesticides were only quantified in baby foods in the iTDS but not in the monitoring programmes of the EU member states: metribuzin, 2-phenylphenol, PBO, prosulfocarb, tau-fluvalinate and trifluralin (EFSA, 2014; EFSA, 2019a) (Table S1). Other pesticides in baby foods were only found in the EU monitoring programmes and not in the iTDS: chlorpyrifos-methyl, cyfluthrin, cypermethrin, methomyl, ethoprophos, phenthoate and hexachlorobenzene. The comparison of the mean concentrations between the iTDS and the monitoring programmes or other studies is not recommended, considering that the analytical limits (LOD and LOQ) are significantly better (i.e. 2 to 10 times lower) in the iTDS. Moreover, more pesticides have been analysed in the iTDS (n = 469) in comparison with the TDS2 (n = 283) (Nougadère, 2012).

Among the most recent TDSs, only the Australian and the New Zealand TDSs included the analysis of pesticides in food for infants and young children in view of estimating their dietary exposure. Since the grouping of baby foods for these TDSs is not the same as for the iTDS, no comparison is possible, and the following description is only indicative. In the 23th Australian TDS (ATDS), there were no detections of pesticides in any baby food (FSANZ, 2011). This is possibly due to LOD values more than 10 times higher in the ATDS than in the iTDS, i.e. ranging from 5 to 100 μg/L in the ATDS *vs* 0.1 μg/L to 0.3 μg/L in the iTDS for most of the analytes (see Section 2.3 and Appendix). In the 20th ATDS, residues of pirimiphos-methyl were found in two composite samples of infant cereals, such as in the iTDS. In the two last New Zealand TDSs (2009 and 2016 NZTDS), such as in the iTDS, no pesticide was detected in infant and follow-on formulae (MAF, 2011; MPI, 2018).

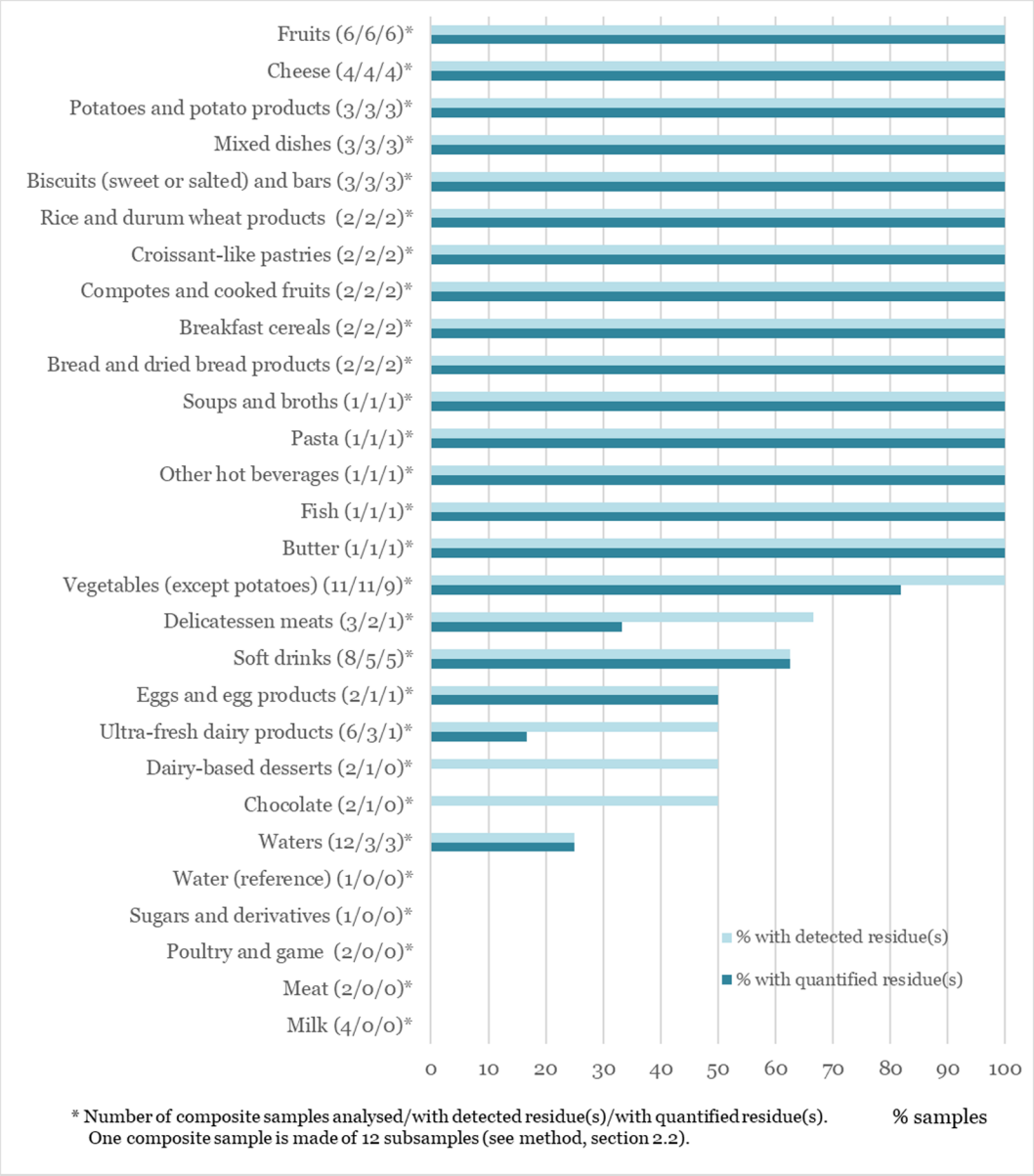

Fig. 2. Frequencies of detection and quantification for each common food group.

In the 2016 NZTDS, residues of bifenthrin, diphenylamine, fludioxonil, imazalil, iprodione, PBO, propargite and propiconazole were found in different infant weaning foods (MPI, 2018). All these residues were also detected in the iTDS (Table S1), except propargite and iprodione, no longer authorised in the EU. In the 2012 USFDA TDS, 97 pesticides were detected in 39 different baby foods including infant formulae: chlorpyrifos-methyl was quantified in a sample of milk-based infant formula and PBO in a soy-based sample (US FDA, 2019).

3.2. Dietary exposure and risk characterisation

Table S3 presents the exposure levels and the probability of infants and young children exceeding the TRV.

Under the LB scenario, which tends to underestimate exposure levels, no exceedance of TRV was identified for any age group. For infants until 4 months, the P90 reached 0.01% of the TRV for difenoconazole. For infants between 5 and 6 months, the P90 reached 3% TRV for dieldrin. For infants aged 7–12 months, the P90 was 5% TRV for dieldrin. For children aged 12–36 months, the P90 reached 6% TRV for pirimiphos-methyl.

Under the UB scenario that overestimates contamination and exposure levels, the P90 of exposure exceeded 10% of the TRV for various age groups (Fig. 3) and 36 pesticides among which only 3 were detected: chlorpyrifos-ethyl (2.6% of the samples), dieldrin (one sample of courgettes) and dimethoate (one sample of infant fruit juice). In the 23rd Australian TDS, the highest dietary exposures (P90) exceeding 10% of the TRV (P90) were also found for chlorpyrifos-ethyl and dieldrin for children aged 2–5 years (FSANZ, 2011).

In general, the contribution of common foods to the total exposure is much higher than that from baby foods. Because of the increased intake of common foods by young children, these have the highest exposure to pesticides, whereas infants have generally lower exposure. Infant formulae (first age milk) contribute to more than 80% of the total exposure of infants aged 1 to 4 months for all pesticides under the UB scenario. The contribution varies according to the pesticides studied.

3.2.1. Pesticides with a risk considered acceptable or tolerable (N = 278)

Out of 281 pesticides for which the risk could be characterised, the probability of exceeding the TRV was nil or insignificant for 278 pesticides, for all age groups and under the two scenarios considered (LB

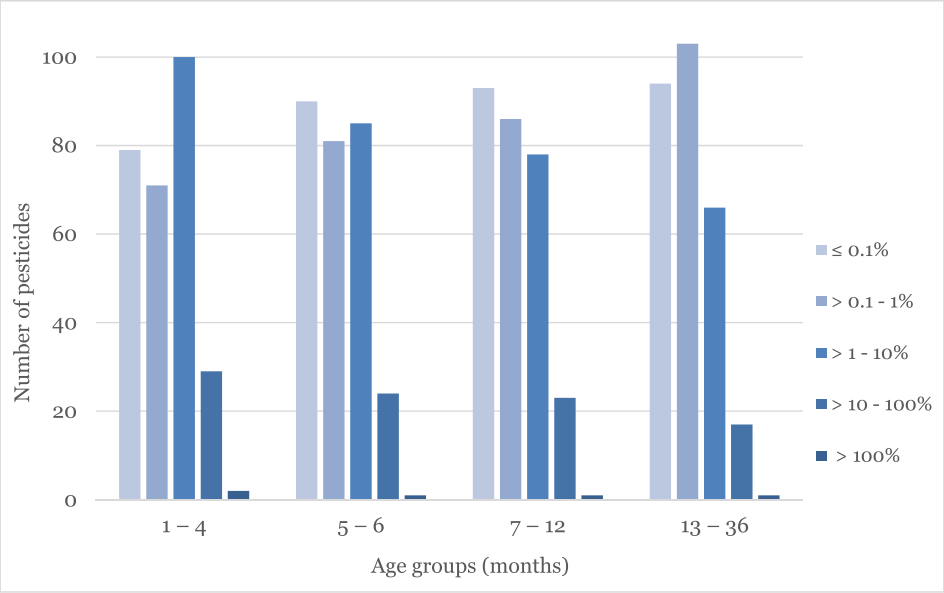

Fig. 3. Number of pesticides per range of exposure (% TRV, UB scenario, P90) and per age group.

and UB) (Table S3). The coverage level of the contributing diet is very good for these substances, ranging between 70 and 100%.

For the most frequently detected priority pesticides (>5% of the samples) (see Section 3.1), no exceedance of TRV was identified under the 2 scenarios, with a maximal estimated exposure (P90, UB) of 7% ADI for pirimiphos-methyl for young children (13–36 months) and 2% ADI for carbendazim for infants below 4 months.

In order to assess the food contributors of each of these pesticides frequently detected, the scenario LB is more realistic because it only reflects actual levels measured in food. The following percentages of food contribution to the total exposure is therefore based on the LB scenario.

For 2-phenylphenol, the follow-on formulae, ultra-fresh dairy products and baby jars (fruits) contribute to 85% of the mean dietary exposure of infants aged 5–6 months, and the ultra-fresh dairy products contribute to 47% of the exposure for the 7–12 months and 33% for the 13–36 months age group.

For carbendazim, fruits (baby jars, juices for infants) and vegetables contribute to 81% of the exposure of infants aged 5–6 months; for infants aged 7–12 months, the compotes and cooked fruits, baby jars (fruits) and vegetables contribute to 86% of the exposure; for the age group 13–36 months, the compotes and cooked fruits, fruits juices and vegetables contribute to 88% of the exposure.

For imazalil and thiabendazole, fruits (fresh, baby jars and compotes) contribute respectively to 99% and 99.8% of the exposure of infants aged 5–6 months, to 76% and 99.9% of the exposure of infants for the 7–12 months and to 86% and 100% for the 13–36 months age group. For imazalil, orange juice is also a main contributor with 24% of the exposure for 7–12 months and 14% for the 13–36 months. These results are consistent with previous studies (TDS2, EU monitoring programs) considering that these fungicides are mainly detected in citrus fruits because of authorised uses for post-harvest treatments.

For pirimiphos-methyl, wheat and rice-based products such as bread, pasta, croissant-like pastries, sweet and savoury biscuits and bars, sandwiches, pastries, cakes, together with rice and cracked durum wheat products, contribute to more than 99% of the exposure for infants and young children aged 5–36 months. For example, sweet and savoury biscuits and bars contributed to 66%, 44% and 40% of the total intake of pirimiphos-methyl respectively for the 5–6 months, for the 7–12 months and for the 13–36 months age groups. Cereals for infants contribute to 64% of the total exposure of infants aged 1–4 months. These results are consistent considering that this organophosphate insecticide is approved in the EU and commonly used for post-harvest treatment of cereal grains (EFSA, 2014; EFSA, 2019a; Nougadère, 2012).

Further studies are needed to assess the cumulative risk to pesticide residues in food by using the most recent methodologies (EFSA, 2019b; EFSA, 2019c; EFSA Scientific Committee et al., 2019).

3.2.2. *Pesticides for which a reassessment is needed (N = 3)*

Under the sole UB scenario, 3 pesticides presented a significant probability of exceeding the TRV for one or several age groups (Table S3): dieldrin (incl. aldrin), lindane (gamma-HCH) and propylene thiourea (PTU). Dieldrin was quantified in a composite sample of cooked courgettes and in 0.01% of tap water analyses. Lindane and PTU have not been detected in this study. This may be due either to very low background levels in composite samples (lower than the LOD) or the actual absence of these residues in the samples.

For these substances, the risk cannot be totally ruled out, due to exceedances of TRV under the sole UB scenario that overestimates actual exposure and risk. This overestimation of the risk under UB is linked to LODs that were too high with respect to the low TRVs, despite having considered for the exposure calculation of these 3 pesticides only theoretical food contributors. To confirm the absence of risk, it is recommended to re-evaluate the exposure from new analyses –with lower target LODs– of the main food contributors: animal products for dieldrin and lindane, cucurbits for dieldrin, fresh and processed fruits and vegetables for PTU.

For dieldrin, the PTDI of 0.1 μg/kg bw/day is based on hepatic effects observed in a 2-years study in rats (FAO/WHO, 1995). For lindane, the TRV of 0.01 μg/kg bw/day selected by the ANSES' Experts Committee was based on immunotoxicity observed in mice in a study of 24 weeks (ATSDR, 2005). No exceedances of the ADI of 5 μg/kg bw/day set by the JMPR (FAO/WHO, 2002) was reported but this ADI was not considered sufficiently protective for infants and young children, by the Experts Committee.

Dieldrin and lindane were used as pesticides in the EU until the nineties before being classified as POPs and banned at international level by the Stockholm Convention respectively in 2004 and 2009. Nevertheless, these contaminants are still widely found in the food chain in the annual monitoring programmes because of their high persistence and capacity of dispersion in the environment (ANSES,

2014; EFSA, 2019a). PTU is a metabolite of the dithiocarbamate fungicide propineb, no longer approved in the EU since 2018 but widely used during the study particularly in fruit crops.

In comparison, in the TDS2, dieldrin was not detected, lindane was quantified in roasted chicken (40 µg/kg) and detected in boiled eggs and roast pork and PTU was not analysed (Nougadère, 2012). In the French monitoring programmes conducted in 2011 and 2012, dieldrin was detected in freshwater and sea products (15% of samples), eggs (2%), meat (1%), lindane was detected in milk, eggs and chicken (3%) and in sea products (5%) and PTU was not analysed (ANSES, 2014; Nougadère, 2014).

These results for dieldrin are consistent with the Australian TDS (FSANZ, 2011) and the New-Zealand TDS (MPI, 2018), in which dieldrin was part of the substances with the highest exposure. In the NZTDS and ATDS, lindane was not detected and PTU was not analysed.

3.2.3. Relevant pesticides for which the risk cannot be characterised (N = 17)

The risk could not be characterised for 188 pesticides including 171 neither detected nor prioritised pesticides (of no concern) and 17 detected and/or defined as priority pesticides ("relevant pesticides") **(**Tables S1 and S2**)**. For these 17 relevant pesticides, the reasons were:

1) the absence of a valid TRV for fenuron, metolcarb, propargite and tricyclazole, for which further analyses and toxicological studies should be undertaken to set a valid TRV. For fenuron, herbicide banned in 2002 in the EU and rarely detected in France, it was recommended to carry out new analyses of the three natural mineral waters brands with residues detected, to confirm its presence before recommending the setting of a TRV;
2) an insufficient coverage (<70%) of the diet theoretically contributing to the exposure for biphenyl, chlorantraniliprole, dodine, flucythrinate, oxyfluorfen, pyridaben, tolfenpyrad and triflumizole. It is recommended to extend the surveillance to all contributing diet to increase the quality of the estimation;
3) the absence on the market of analytical standards of metabolites included in the RD-RA of chlorothalonil, chlorpropham, fenpropimorph, flusilazole and tepraloxydim. Moreover, conversion factors were not available and could not be estimated because of lack of information in the EU evaluation reports. It is therefore necessary to make available on the market these reference substances for the metabolites.

New analyses are therefore recommended for active substances (and their metabolites):

- still approved in the EU: chlorantraniliprole, dodine, oxyfluorfen, pyridaben and triflumizole.

- no longer approved in the EU: biphenyl, chlorothalonil, chlorpropham, fenpropimorph, fenuron, flucythrinate, flusilazole, metolcarb, propargite, tepraloxydim, tolfenpyrad and tricyclazole.

3.3. Limitations and uncertainties

Despite the advantages and performances of the iTDS, some limitations inherent to the study or TDSs in general and uncertainties should be underlined, along with the recommendations provided below.

As a first limitation, breastfed infants were not included in this study. In France, 70% of infants are breastfed at birth, with a median duration of 17 weeks for any breastfeeding and 7 weeks for predominant breastfeeding, and only 19% of infants still received breastmilk at 6 months (Wagner et al., 2015). Nevertheless, only the breastfed infants at the time of the recruitment were excluded from the study, but young children recruited in older age groups (7 to 36 months) can have been breastfed when being younger.

The number of consumers in each age group was not enough to derive a 95th percentile of exposure sufficiently robust for 2 age groups. Consequently, a statistically robust 90th percentile of exposure was estimated for each age group (see Section 2.5.) and was considered appropriate by the ANSES experts for this study (EFSA, 2009a; Kroes et al., 2002).

A TDS is not designed to assess intakes due to special situations such as contamination of foods by the local environment or by special diets such as organic diets or diets with major home consumption.

Copper, chlorates, benzalkonium chloride (BAC) and didecyldimethylammonium chloride (DDAC), that are not only pesticides, were not sought in this study; however, these compounds are very frequently detected in baby foods by the EU member states (EFSA, 2014; EFSA, 2019a). Copper is approved as a baby food nutrient. Chlorates are by-products of chlorine solutions used as disinfection agents in the food industry and as biocides. BAC and DDAC are also widely used as biocides.

Another limitation is that TDSs generally address risk assessment chemical by chemical. Therefore, possible cumulative and synergistic effects of exposure to multiple residues was not assessed. The question of which substances should be assessed together remains a challenge due to the complexity of the mixtures, particularly when all chemicals in food are considered. A recent EFSA guidance will support the assessment of cumulative risks (EFSA Scientific Committee et al., 2019). Recent EFSA outputs were published on cumulative assessment groups, probabilistic exposure and cumulative risk assessment (CRA) for the thyroid and nervous system (EFSA, 2019b; EFSA, 2019c; EFSA, 2019d; EFSA, 2019e). Previous works in this area focused on the cumulative exposure of substances with the same mechanism of action to express their cumulative effects using relative potency factors regarding an index compound (EFSA PPR Panel, 2008; EFSA PPR Panel, 2009; EFSA PPR Panel, 2013; FQPA, 1996). Further work is in progress in France to identify to which mixtures of substances infants and young children are exposed through their diet, as already performed for children over 3 years (Traoré et al., 2016) and for two cohorts of pregnant women including CRA (De Gavelle, 2016; Traoré, 2018). The mixtures identified may be used in epidemiological analyses to better explain the associations between exposure to mixtures and health effects (Sirot et al., 2018).

Uncertainties are present at the different steps of the risk assessment and may lead to the risks being overestimated or underestimated (EFSA Scientific Committee et al., 2018).

Concerning consumption data, they have been collected in 2005 and food habits may have changed. Nevertheless, the list of purchased products was updated just before the sampling to take into account the changes in terms of availability of baby foods on the market (Hulin, 2014). Moreover, only 3 days of consumption were reported and variance reduction methods were not used, which may lead to an overestimation of the 90th percentile of exposure (Mancini et al., 2015), but not the average.

Despite a good level of coverage of the diet potentially contributing to exposure for the majority of pesticides **(**Tables S1 and S2**)**, one uncertainty in this study is the absence of sampling of fresh strawberries, grape, melon and cucumber, considering the recruitment period of the consumption survey used. The actual consumption of these fruits and vegetables was only considered for the related processed products. Therefore, it is recommended to include these fruits and vegetables in a future similar study.

As the LB scenario tends to underestimate exposure levels, WHO recommends the use of two scenarios LB and UB to manage left-censored data (GEMS/Food-EURO, 1995; WHO, 2013). The uncertainty related to UB results was only identified for dieldrin, lindane and PTU in the iTDS, compared to 25 pesticides in the TDS2. This underlines the progress achieved for more accurate exposure estimates following the improvements in analytical methods in the iTDS. In order to further refine the exposure assessment, analytical improvements are recommended, i.e. lowering LODs. In a previous paper, it was indicated

that some statistical approaches proposed for the management of left-censored data are difficult to implement in TDSs (Nougadère, 2012). These methods depend on the sample size and the percentage of left-censored results (EFSA, 2010).

Early stages of life correspond to periods of high susceptibility. Therefore, before characterising the health risk, the appropriateness of the TRV for infants and young children have been carefully checked for each pesticide, taking into account data related to multigenerational and reproductive studies as suggested by the most recent guidelines and recommendations (Commission Regulation (EU) No 283/2013; EFSA PPR Panel et al., 2018). Nevertheless, recently, EFSA concluded that the established approach for setting TRV for pesticides "may not be appropriate for infants below 16 weeks of age", and recommended in some cases for the animal toxicity studies an extended one-generation reproductive toxicity study (EOGRTS, OECD TG443) and to screen pesticides for developmental neurotoxicity (DNT) properties in a DNT *in vitro* testing battery to be developed (EFSA PPR Panel et al., 2018; EFSA Scientific Committee et al., 2017; OECD, 2018). EFSA also concluded that the particular appropriateness of existing residue definitions for monitoring to cover processed food, both intended for infants and young children as well as conventional food, is questionable (EFSA PPR Panel et al., 2018).

4. Conclusions and perspectives

This study is the first TDS specifically designed for assessing the chronic dietary exposure of infants and young children to pesticide residues. This infant TDS is characterised by better analytical performances compared to both, the monitoring programmes and to the previous French TDS on pesticide residues (TDS2), with LOD values two to ten times lower than in the TDS2. As a consequence of the target analytical limits requested by ANSES to the participating laboratories, the uncertainty associated with the exposure estimation was reduced and more realistic results were obtained under the UB scenario in the iTDS.

Finally, the exposure estimates are below the toxicological reference values under the two scenarios for 278 pesticides. For 20 others, ANSES recommended to reassess the dietary exposure after having developed very sensitive analytical methods (dieldrin, lindane and PTU), to conduct broader analyses in other foods (8 pesticides), complementary toxicological studies to set a TRV (4 pesticides) or to make available reference standards of certain metabolites to be sought (5 pesticides).

This infant TDS, by providing the actual residue levels in baby foods, can also be useful to the risk managers in the context of possible upcoming revisions of the default MRL for certain pesticides in baby foods. Indeed, EFSA recently concluded that for infants below 16 weeks of age, lower MRLs than the current default MRL of 0.01 mg/kg for food for infants and young children are recommended for pesticide active substances with a TRV below 2.6 μg/kg bw/day (EFSA PPR Panel et al., 2018).

For infants and young children, there is also a need of new consumption surveys in order to support the assessment of dietary exposure to pesticide residues (EFSA PPR Panel et al., 2018).

In order to study pesticides mixtures and their potential effect on health for all groups of population, it is recommended to use the recent EFSA methodologies for assessing the risk of combined exposure to multiple chemicals (EFSA Scientific Committee et al., 2019) and for cumulative risk assessment of pesticide residues in food (EFSA, 2019b; EFSA, 2019c; EFSA, 2019d; EFSA, 2019e). This additional work would help to conclude in a holistic way and to propose more relevant risk management measures in order to ensure the safety of foods for infants and young children.

5. Disclaimer

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the organisms of affiliation. The authors declare they have no conflict of interests.

6. Authors' contributions

AN, VS and MH: coordination of the infant TDS, conceptualization, study design, methodology, software programming, data collection and data analysis, coordination of ANSES expertise and interpretation of the results. AN: coordination of the pesticide analyses, pesticide exposure/risk assessment, drafting, review and editing of this paper. JPC, PV and CF: study design, methodology and interpretation of the results within various ANSES experts' committees incl. the infant TDS scientific committee. RF and RH: chemical analyses and writing of the appendix "pesticide analyses and analytical methods". JCL: conceptualization, contribution to study design and funding acquisition. JJ, GR, XS and MM: coordination of ANSES experts' committees and contributing staff, scientific and technical inputs.

All authors revised the manuscript critically for important intellectual content and approved of the version to be published.

Declaration of Competing Interest

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.

Acknowledgments

The infant TDS was supported by the French Ministry for food, agriculture and fisheries, the French Ministry for health, the French Ministry for ecology and sustainable development and ANSES.

The authors would like to thank the ANSES expert committees in charge of assessing the chemical risk in food and the experts from the infant TDS scientific committee, namely: Claude Atgié, Pierre-Marie Badot, Jacques Bélégaud, Catherine Bennetau-Pelissero, Valérie Camel, Martine Clauw, Guillaume Duflos, Camille Dumat, Jérôme Gay-Queheillard, Philippe Glorennec, Michel Guerbet, Thierry Guérin, Laurence Guldner, Nicole Hagen-Picard, Laïla Lakhal, Claude Lambré, Bruno Le Bizec, Raphaëlle Le Garrec, Catherine Leclerc, Eric Marchioni, César Mattéi, André Mazur, Sakina Mhaouty-Kodja, Fabrice Nesslany, Alain Périquet, Alain-Claude Roudot, Patrick Sauvegrain, Rémy Slama, Karine Tack, Eric Verdon and Jean-Paul Vernoux.

The authors also gratefully acknowledge the contribution of their numerous ANSES colleagues in particular Frédéric Hommet, Chanthadary Inthavong, Stéphane Leconte, Josselin Réty, Elise Bracq, Nina Le Dreau and Gaëlle Vial, together with members of the ANSES Expert Committee (CES) on "plant protection products: chemical substances and preparations" for their contribution to this study.

The authors also thank Florianne Queiroga (La Drome Laboratoire) and Michael Hetmanski (Fera) who contributed to the chemical analyses of pesticide residues.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.105529.

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