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Germán Cano-Sancho, A.J. Ramos, S. Marin, V. Sanchis

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Fumonisin in Catalonia (Spain) and exposure assessment of special population groups.

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Methods/Techniques:	Chromatography - HPLC, Risk assessment - modelling
Additives/Contaminants:	Fumonisin, Mycotoxins - fumonisin
Food Types:	Baby food, Beer
Abstract:	Fumonisin B1 (FB1) and B2 (FB2) are mycotoxins produced by <i>F. verticillioides</i> and <i>F. proliferatum</i> that commonly contaminate corn. The objectives of this study were, in one hand, to study the occurrence of fumonisin in Catalonia (north-eastern region of Spain), and, in the other hand, to assess the exposure of Catalanian population to these mycotoxins. Contamination data was provided by a wide survey, where 928 individual samples were pooled to analyze 370 composite samples. Fumonisin were extracted and purified using immunoaffinity columns, and determined by means of HPLC with fluorescence detector. The raw consumption data came from a nutritional study specifically designed to assess the dietary intake of the main foodstuffs related to fumonisin contamination for all population age groups. In addition, two special groups were selected to be specially related with maize consumption: immigrants and celiac sufferers. Contamination and consumption data were combined by simulation using an essentially parametric (P-P) method. The P-P method draws sampling values from distribution functions fitted to consumption and contamination datasets. Moreover, to quantify the accuracy and reliability of the statistics estimates, we built the related confidence intervals using a Pseudo-Parametric bootstrap method. Considering the results from this study, fumonisin can be commonly found in some commodities from Catalanian market, such as beer, corn snacks or ethnic foods, however, in any case these values exceed the maximum EU

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	levels. The most exposed group should be expected to be infants followed by immigrants, but in all cases, they were far from the TDI of 2 µg/ kg bw/day.

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3 **Fumonisin in Catalonia (Spain) and exposure assessment of special**
4 **population groups**
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11 Cano-Sancho*, G., Ramos A.J., Marín S. and Sanchis V

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16 Applied Mycology Unit, Food Technology Department, University of Lleida, XaRTA-
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18 UTPV, Rovira Roure 191, 25198, Lleida, Spain.
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23 *Corresponding author: German Cano-Sancho. Telephone number: (+0034) 973702670.

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25 Fax number: (+0034) 973702596. E-mail address: gcano@tecal.udl.cat
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32 **Abstract**
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34
35 Fumonisin B₁ (FB₁) and B₂ (FB₂) are mycotoxins produced by *F. verticillioides* and *F.*
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37 *proliferatum* that commonly contaminate corn. The objectives of this study were, on the
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39 one hand, to study the occurrence of fumonisins in Catalonia (north-eastern region of
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47 purified using immunoaffinity columns, and determined by means of HPLC with
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49 fluorescence detection. The raw consumption data came from a nutritional study
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51 specifically designed to assess the dietary intake of the main foodstuffs related to
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53 fumonisins contamination for all population age groups. In addition, two special groups
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3 were selected to be specially related with maize consumption: immigrants and celiac
4 sufferers. Contamination and consumption data were combined by simulation using an
5 essentially parametric (*P-P*) method. The *P-P* method draws sampling values from
6 distribution functions fitted to consumption and contamination datasets. Moreover, to
7 quantify the accuracy and reliability of the statistical estimates, we built the related
8 confidence intervals using a Pseudo-Parametric bootstrap method. Considering the results
9 from this study, fumonisins can be commonly found in some commodities from the
10 Catalonian market, such as beer, corn snacks and ethnic foods, however, in any case these
11 values were well below the maximum EU levels. The most exposed group should be
12 expected to be infants followed by immigrants, but in all cases, they were far from the
13 TDI of 2 µg/ kg bw/day.
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32 **Keywords:-** Occurrence, exposure assessment, fumonisins, cereal food, gluten-free
33 products, ethnic food
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39 **Introduction**

40 Fumonisin B₁ (FB₁) and B₂ (FB₂) are mycotoxins mainly produced by *Fusarium*
41 *verticillioides* and *F. proliferatum* that commonly contaminate corn (Nelson et al. 1992).
42 Fumonisin B₁ (FB₁) and B₂ (FB₂) are mycotoxins mainly produced by *Fusarium*
43 *verticillioides* and *F. proliferatum* that commonly contaminate corn (Nelson et al. 1992).
44 Fumonisin B₁ (FB₁) and B₂ (FB₂) are mycotoxins mainly produced by *Fusarium*
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60 Fumonisin B₁ (FB₁) and B₂ (FB₂) are mycotoxins mainly produced by *Fusarium*
verticillioides and *F. proliferatum* that commonly contaminate corn (Nelson et al. 1992).
Shephard et al. 1996; Visconti et al. 1996; WHO 2001).

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FBs have a remarkable structural similarity to sphingolipids (Merrill and Sweeley 1996; Riley et al. 2001). This group of mycotoxins, especially FB₁, potently inhibit the enzyme ceramide (CER) synthase which catalyzes the acylation of sphinganine (Sa) and reacylation of sphingosine (So). The inhibition of CER synthase by FBs increases the intracellular Sa concentration, main contributor to the toxicity and carcinogenicity of FB₁ (Wang et al. 1991; Merrill et al. 1993; Yoo et al. 1996; Riley et al. 2001). Based on this biological perturbation, elevation of Sa to So, or Sa 1-phosphate to So 1-phosphate, ratios in tissues, urine and blood, have been proposed as potential biomarkers of fumonisin exposure in various animal species (Wang et al. 1992; Riley et al. 1993; Wang et al. 1999; Van der Westhuizen et al. 2001; Kim et al. 2006; Tran et al. 2006; Cai et al. 2007; Cano-Sancho et al. 2011b).

Human exposure to fumonisin contaminated commodities has been linked to oesophageal and liver cancer in South Africa and China (Sydenham et al. 1990; Yoshizawa et al. 1994). Acute and chronic toxicity of FBs has been largely demonstrated in several animal species, including carcinogenicity and cardiovascular toxic effects (Gelderblom et al. 1988, 1991). FB₁ is a cancer promoter, but a poor cancer initiator. It is not genotoxic because FB₁ does not induce unscheduled DNA synthesis in primary rat hepatocytes (Norred et al. 1992).

Based on toxicological evidence, the International Agency for Research on Cancer (IARC) has classified FB₁ as possibly carcinogenic (group 2B) to humans (IARC 2006). The Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated FBs and

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3 allocated a provisional maximum tolerable daily intake (PMTDI) of 2 µg/kg body
4 weight/day to FBs on the basis of the non observed effect level (NOEL) of 0.2 mg/kg
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6 body weight/day and a safety factor of 100 (WHO 2001). This PMTDI for FBs has
7
8 recently been confirmed by the Scientific Committee on Food (SCF 2003).
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15 The European Commission established a maximum FBs levels of 1000 µg/kg in maize
16 and maize-based food intended for human consumption, 800 µg/kg in maize-based
17 breakfast cereals and snacks and 200 µg/kg in maize-based infant food (European
18 Commission 2006b, 2007).
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28 In the Mediterranean countries, maize is more widely used for animal nutrition than for
29 human consumption, but some countries traditionally use the maize in regional cooking
30 as *broa* (maize-based bread from Portugal) and polenta (from Italy). As a consequence of
31 the use of maize grits as adjunct in brewing process, aflatoxins and FBs can be also found
32 in beer (Torres et al. 1998; Pietri et al. 2009). The natural occurrence of FBs in corn or
33 corn-based foods has been studied largely (Sydenham et al. 1991; Shephard et al. 1996;
34 SCOOP 2003; Castelo et al. 1998; Hlywka et al. 1999), and surveys have been conducted
35 in several cases in corn-based products marketed in Spain (Sanchis et al. 1994, 1995;
36 Torres et al. 1998; Castellá et al. 1999; Velluti et al. 2001). Dietary intake of FBs has
37 been previously assessed in population from France, USA, Netherlands, Canada or South
38 Africa (Kuiper-Goodman et al. 1996; De Nijs et al. 1998; Humphreys et al. 2001;
39 Leblanc et al. 2005; Shephard et al. 2007).
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3 In the framework of the Project to Assess the Exposure of Catalonian Population to the
4 Mycotoxins, and following the line of our previous studies (Cano-Sancho et al. 2009,
5 2010, 2011c), the objectives of this study were, on the one hand, to study the occurrence
6 of FBs in Catalonia (north-eastern region of Spain), and, on the other hand, to assess the
7 exposure of Catalonian population to these mycotoxins.
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14 **Materials and methods**

15 *Fumonisin analysis*

16 *Samples*

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18 During 2008 and 2009, 185 samples of sweet-corn, 216 samples of corn-based snacks,
19 216 beer samples, 168 corn flakes, 90 baby food samples were obtained in six
20 hypermarkets and supermarkets from twelve main cities (Tortosa, Tarragona, Reus,
21 Vilanova i la Geltrú, l'Hospitalet de Llobregat, Barcelona, Terrassa, Sabadell, Mataró,
22 Girona, Manresa and Lleida) of Catalonia, representative of 72 % of the population. From
23 each supermarket or hypermarket, 3 samples (if present) of each product were randomly
24 taken. The level of FB₁ and FB₂ was determined in a total of 72 composite samples of
25 each category by equally pooling the 2 or 3 items taken from each store (depending of
26 availability) to obtain an analytical sample or “*composite*”: 12 cities x 6 stores/city = 72
27 samples/category. However, in some cases, 3 items or any items were not available in the
28 store, thus, less than 72 composites could be obtained. Additionally, 18 gluten-free
29 food samples (mainly maize-based bread and pasta) and 35 ethnic food samples, such as
30 Mexican tortillas, corn flour or cuscus, were purchased in specialised stores to be
31 analysed individually. Regarding brands, thirty-one sweet corn, seventy-nine corn-based
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3 snacks, sixty-four beers, thirty-two corn flakes different brands were purchased, which
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5 can be considered the majority of market share in Catalonia of these products, as well as
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7 in the rest of Spanish market. The samples were transported and stored under suitable
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9 conditions until analysis.
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12 13 14 15 *Analytical procedure*

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17 Fumoniprep[®] immunoaffinity cleanup columns (IAC) (R-Biopharm, Rhône Ltd Glasgow,
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19 UK) were used to extract FB₁ and FB₂ from beer samples. A volume of 5 mL of beer
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21 previously degassed in ultrasonic bath during 40 minutes was mixed with 15 mL of
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23 phosphate buffer solution (PBS; 0.8 % NaCl, 0.12% Na₂HPO₄, 0.02% KH₂PO₄, 0.02%
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25 KCl) and drained through the IAC. The column was washed with 20 mL of PBS solution
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27 and FBs were eluted with 1.5 mL of methanol grade HPLC and 1.5 mL of milli-Q water.
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29 Regarding solid maize-based samples, 10 g of ground sample composite was mixed with
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31 1 g NaCl, and 50 mL of extract solution (50% water, 25% methanol, 25% acetonitrile) for
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33 20 minutes and filtered. 10 mL of filtrate was diluted with 40 mL of PBS and drained
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35 through the IAC and follows as described previously.
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44 Fluorescent derivatives of FB₁ and FB₂ were obtained using pre-column derivatisation
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46 with an *o*-phthaldialdehyde (OPA) solution prepared diluting 40 mg of *o*-
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48 phthaldialdehyde with 1 mL of methanol HPLC grade and mixed with 5 mL of
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50 Na₂B₄O₇·10H₂O (0.1M) and 50 µL de 2-mercaptoethanol. Derivatisation was conducted
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52 mixing 200 µL of eluate with 200 µL of OPA solution for 30 seconds in vortex.
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55 Chromatography equipment: Separations Module Alliance 2695 Waters®, analytical
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3 column Waters Spherisorb® 5µm ODS2, 4.6 x 150 mm, Multi λ Fluorescence Detector
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5 Waters 2475® , kept at 35 °C and a flow-rate maintained at 1 mL/min. Injection volume
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7 was 100 µl. Mobile phase was based on a methanol and 0.1M sodium dihydrogen
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9 phosphate (77:23, v/v) solution. Excitation and emission wavelength were 335 nm and
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11 440 nm, respectively.
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18 The analytical method used for FBs was assessed for selectivity, linearity, and precision.
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20 Selectivity was checked by injecting 100 µl of mycotoxin standard solution three times
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22 before injecting extracted samples and comparing the peak retention times and the
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24 fluorescence spectra of the substances that produced these peaks. Standard curves were
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26 generated by linear regression of peak areas against concentrations.
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32 Precision and recovery were established by determination of FB₁ and FB₂ levels, spiked
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34 in each food categories by triplicate. The concentrations of fumonisins fortified in tested
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36 samples were ranged from 25 µg/kg to 660 µg/kg. Recovery was determined by
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38 comparing the absolute responses of FBs, with the absolute responses of calibration
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40 standards. The limit of detection (LOD) was considered to be three fold the signal of
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42 blank noise, and the limit of quantification (LOQ) was considered equal to 3×LOD.
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46 Recovery ranges were 76.5 ± 11.5 - 109.7±12.3 % in corn snacks; 101.5±11.8 -
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48 104.0±7.3 % in sweet corn; 91.6±8.4 - 107.5±5.0 in corn flakes, 93.0±14.0 - 108.0±10.0
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50 % in beer and 90.7±15.1 - 115.5±27.9 % in baby food. Repeatability was expressed as
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52 relative standard deviation (RSDr), it ranged between 11.3 and 15.0 % in corn snacks;
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54 between 7.0 and 11.6 % in sweet corn; between 4.6 and 9.1 % in corn flakes; between
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3 10.0 and 15.0 % in beer; between 16.6 and 24.1 % in baby food. The mean limit of
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6 detection (LOD) was 3.9 µg/kg in beer and 5.2 in solid based foods. These values were in
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8 accordance to performance criteria established by Commission Regulation (EC) N°
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10 401/2006 (European Commission 2006a).
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12 13 14 15 *Fumonisin dietary intake assessment* 16

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18 The main problem in assessing the intake of mycotoxins is related to few representative
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20 available dietary data regarding foods contaminated with mycotoxins. There are some
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22 methods developed to assess dietary intake overall known as market basket, 24-hour
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24 dietary recall and food record methods, food-frequency methods or dietary history. Given
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26 that corn-based products consumption is considered as sporadic or casual among
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28 Catalonian population, food-frequency methods should be chosen because it may be
29
30 advantageous to sacrifice precise intake measurements in exchange for more crude
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32 information related to an extended period of time (Walter 1998). In this study, food
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34 dietary intake was assessed through a specific Food Frequency Questionnaire (FFQ)
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36 developed for Catalonian population including those foods typically consumed in the
37
38 region which may be potentially contaminated with these mycotoxins. According to
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40 World Health Organization advices, studies to assess dietary intake of chemical
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42 contaminants, should show the significant intake among standard population, with all
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44 population groups that could have different dietary patterns. Therefore, five different
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46 population groups were considered: infants (0-3 years), children (4-9), adolescents (10-19
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48 years), adults (20-65 years) and elders (> 65 years). Moreover, adult celiac sufferers and
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50 adults with ethnic dietary pattern were included in the nutritional study, and studied
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3 separately. FFQ consisted of 38 items of specific foods worldwide known to be the most
4 important food contaminated by mycotoxins studied, excluding those foods not consumed
5 in the region. Concerning frequency of consumption, 5 response options ranging from
6 never to annually, were considered. Quantities were assessed by portion size with the aid
7 of a series of colour photograph models. Finally, 76 seniors, 720 adults, 235 adolescents,
8 69 parents of children, 164 parents of infants, 70 adult celiac sufferers and 56 adults with
9 ethnic dietary pattern were interviewed in 2008-2009 by trained interviewers. In the
10 present study, the adults were treated separately according to their sex, with a major
11 population group of 336 adult males and another of 384 adult females. Individuals were
12 from 89 cities and towns from Catalonia. Study level, dietary habits, sex, age, ethnics and
13 anthropometric data were considered in the questionnaire.
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32 Exposure Assessment through Direct Approach

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34 If we assume independency between consumption ($C_{\pi,j}$) and contamination (T_j), as well
35 as between their products, we can estimate the mean exposure of the population π with
36 the population sample π_0 as follows:
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$$40 \hat{E}_{\pi_0} = \sum_{j=1}^p \bar{C}_{\pi_0,j} \bar{T}_j$$

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42 Where $\bar{C}_{\pi_0,j}$ is the arithmetical mean of the normalised consumption of the foodstuff j in
43 the population group π_0 , and \bar{T}_j is the arithmetical mean of the available contamination
44 data of the related food. We could consider this approach to be a theoretical approach, but
45 it would have to be a (very) simplified theoretical approach. For example, this simplified
46 approach does not enable us to calculate complicated statistics such as high quantiles.
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48 Simulation methods would therefore be required to obtain estimates of these statistics.
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Finally, we will consider this approach to be a direct approach. Left-censored data (those samples below LOQ) was substituted by LOD/2 in order to calculate the mean toxin level used in the exposure assessment model.

Exposure Assessment through Stochastic Approach

Stochastic procedure used is based on the Parametric-Parametric (P-P) method reported extensively in Gauchi and Leblanc (2002) and Cano-Sancho et al. (2011b). In brief, for each consumption and contamination dataset, the gamma *pdf* was fitted with the method of maximum likelihood using the CAPABILITY procedure of SAS software (SAS 2010). The appearance of the histograms was continuous and only one distribution was considered pooling all age groups data, fitting all data to gamma *pdf*. In case of gluten-free foods and sweet-corn, the mean contamination was used in the simulations because not enough data were available for computations. Left-censored was treated as the previous section, replacing non quantified samples by 0.5xLOD.

The *P-P* method used to estimate the normalised exposure k of the S simulation set was built as follows:

$$\hat{E}_k^{(P-P)} = \sum_{j=1}^p \tilde{c}_{i(j)} \tilde{t}_j$$

where $\tilde{c}_{i(j)}$ is a random normalised consumption i for the foodstuff j , drawn from \hat{C}_j , the corresponding adjusted gamma *pdf*, and \tilde{t}_j is a random contamination for the foodstuff j , drawn from \hat{T}_j , the corresponding adjusted gamma *pdf*.

The mean of normalised exposures over the simulation set S was then estimated using the following equation, where n was the number of random deviates drawn (10,000 in the present study):

$$\hat{E}_S^{[P-P]} = \frac{1}{n} \sum_{k=1}^n \hat{E}_k^{[P-P]}$$

Other statistics were directly computed on the histogram built with the simulations of the S set, and statistics were also estimated from the lognormal and gamma fitted *pdfs* (results not shown).

Pseudo-parametric bootstrap confidence intervals were built as reported by Gauchi and Leblanc (2002), by randomly drawing B samples of size n_{π_0} in the exposure simulation set S (being B equal to 10,000). The boundaries of the 95% confidence interval are calculated taking the 0.025th and 0.975th empirical quantiles of the final bootstrap distribution.

Results

Occurrence of total fumonisins in food

FB₁ was the major fumonisin found in all food categories. In beer and corn snacks both mycotoxins were present simultaneously, and the mean ratios FB₁/FB₂ were 2.3 and 1.9, respectively. According to Table 1 and Figure 1, highest occurrence of total fumonisins (FB₁+FB₂) was found in beer samples with 90 % of positive samples, followed by corn snacks (61 %), ethnic foods (51 %) and corn flakes (39 %). Baby foods and gluten-free foods showed low levels of positive samples (23.3 and 5.6 %, respectively) and they were not detected in sweet corn. Positive samples of corn snacks and corn flakes presented moderated mean values (119.1±83.1 µg/kg and 78.9±27.9 µg/kg, respectively). The highest values were found in ethnic food samples, with a mean of 196.7 ± 191.8 and a maximum level of 682.2 µg/kg. Despite the high maximum value, no sample exceeded

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3 the limit established by EU (European Commission 2007). The gluten-free foods and
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5 baby food showed the lowest mean levels of positive samples.
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10 *Place Table 1 about here and Figure 1 about here.*
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13 ***Fumonisin dietary intake assessment*** 14

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16 Through the specific nutritional study performed with a sample of Catalonian inhabitants
17 during 2008 and 2009 we could better estimate the dietary patterns of those commodities
18 related with fumonisin contamination. As shown in Table 2, the corn flakes and corn
19 snacks were mainly consumed by children and adolescents, while beer was most widely
20 consumed by immigrants and adult males. Celiac sufferers commonly consumed gluten-
21 free products as bread and pasta, and other maize based food as breakfast cereals and
22 corn snacks. Most of immigrants consumed food products imported from their origin
23 countries, becoming a staple food in their current diet.
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39 *Place Table 2 about here.*
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43 Fumonisin dietary intake of the Catalonian population sample was assessed through a
44 direct method and by means of the simulation method described above. The mean and
45 variance of fumonisin dietary intake estimated through the direct approach for all
46 population groups are presented in table 3.
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3 Considering these estimates, the most exposed population group was the infants, followed
4 by immigrants, children and adult males. Differences were found between adult males
5 and females.
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12 Concerning the dietary intake estimated through the simulation procedure, mean values
13 were commonly higher than those calculated using the direct method, with the exception
14 of celiac sufferers (See Table 4 and Figure 2). Stochastic method was not applied to
15 elders because few consumers of each item was found in this group and commonly those
16 consumers reported a low level of consumption in each category.
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32 The highest means were estimated for infants, followed by the immigrants and adults.
33 Celiac sufferers showed the lowest exposure estimates. Pseudo-parametric bootstrap
34 confidence intervals permitted to assess the reliability and accuracy of the computations.
35 We observed that these intervals decreased when we estimated the highest quantiles.
36 Extremely wide confidence intervals were built for the 95th and 99th quantiles, especially
37 for immigrants and children. It is an accepted fact that it is very difficult to obtain good
38 accuracy for the 99th-quantile, in particular (Breiman et al. 1990).
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51 All estimates were far from the TDI of 2000 ng/kg body weight/day, including the
52 highest quantiles of immigrants and infants (the most exposed groups).
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Discussion

Occurrence of total fumonisins in corn-based food

This is the first study conducted in Spain with a highly representative sampling method, using a high number of individual samples of the main corn-based food categories collected around the Catalonian geography to assess a wide pool of analytical samples, including baby foods, ethnic foods or gluten-free foods not reported until now. Although our study was conducted in Catalonia, the main brands marketed in Spain have been purchased and analysed, therefore, results from our study could be extrapolated to the Spanish market.

A previous study conducted in Spain showed smaller concentrations than our study for corn snacks and corn flakes but the authors found contaminated samples of sweet corn with respective mean values of 46.27, 17.03 and 55.96 $\mu\text{g}/\text{kg}$, all of them determined by HPLC (Velluti et al. 2001). D'Arco et al. (2007) compared organic and conventional maize-based food and they found higher percentage of contaminated samples in organic commodities (78 %) than in conventional food (16 %), moreover, the maximum and highest mean was found in the organic category (235 vs 51 $\mu\text{g}/\text{kg}$). In the present study, we analyzed mainly conventional food because the consumption of organic maize foods is not widespread in Spain, and these products are supplied by a little number of retail stores. Regarding beer samples from Spain, a previous study performed by ELISA kit, showed similar values to our study in the range $85.53 \pm 0.34 - 4.76 \pm 1.21$ $\mu\text{g}/\text{kg}$ (Torres et al. 1998).

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3 Previous studies carried out with corn-flakes, reported mean levels of contamination
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5 closest to our mean value of 78.9 ± 27.9 $\mu\text{g}/\text{kg}$, being those means 76.0 $\mu\text{g}/\text{kg}$ in France,
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8 79.3 and 129.0 $\mu\text{g}/\text{kg}$ in Canada (Kim et al. 2003; Molinié et al. 2005; Roscoe et al.
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10 2008); however Martins et al. (2008) did not found any sample from Portugal exceeding
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12 the detection level. Lombaert et al. (2003) showed mean levels of 33 and 14 $\mu\text{g}/\text{kg}$ for
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14 soy-based and multi-grain cereals for babies, respectively, in the line of our results.
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16 Moreover, FBs were previously analyzed in ethnic foods from United Kingdom, and only
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18 trace levels were found in cereal-based foods as noodles, rice, corn flour and pitta bread
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20 (Patel et al. 1996), quite different from our study where fumonisins were quantified in
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22 half of samples. In Spain, the ethnic food market started in the 90's, whilst the highest
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24 growth rates have occurred since 2000. Sales passed from 7.2 million dollars in 1999 to
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26 40.6 million dollars in 2004 (Camarena and Sanjuán 2008), therefore this commodities
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28 should be taken into account as potential mycotoxin carriers.
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37 In the present study only FB_1 and FB_2 were determined in food, however, it is a well
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39 known that FBs can be conjugated when food is thermally treated. These bound forms are
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41 not detectable using the conventional analytical techniques, but can be hydrolysed in the
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43 gastrointestinal tract and produce the toxic effect (Dall'Asta et al. 2009). Therefore, in
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45 future exposure assessment works, powerful techniques focused on direct or indirect
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47 analysis of conjugated forms should be used to improve the accuracy of the estimates.
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53 *Fumonisin dietary intake assessment*

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3 The lack of accurate and representative dietary data of corn-based food intake from
4 Spanish population was the main problem to assess the exposure of the population to
5 FBs. Through a specific FFQ administered to a population sample from the region, it has
6 been possible to obtain a more accurate approximation to dietary intake habits from each
7 population group.
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18 Despite experts have recommended the use of stochastic approaches to provide a more
19 realistic exposure assessment, to date, few studies have been published using this
20 methodology to assess the exposure of populations to mycotoxins (Kroes et al. 2002;
21 WHO 2005; EFSA 2006; Verger and Fabiansson 2008), the direct or deterministic
22 methods being the most commonly used.
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32 The results of exposure assessment obtained through the direct method showed infants as
33 the main risk group, followed by immigrants, male adults and children with respective
34 daily dietary intake of FBs of 0.156 ± 0.154 , 0.065 ± 0.069 and 0.063 ± 0.090 and
35 0.063 ± 0.064 $\mu\text{g}/\text{kg}$ body weight/day. A previous study conducted in Spain on dietary
36 intake of FBs was developed using corn dietary intake data of Spanish population
37 supplied by Food and Agriculture Organization (FAO) combined with FBs levels in non
38 processed corn obtained from their study (Ariño et al. 2007). Despite this fact could result
39 in overestimation of FBs intake, that study showed lower levels of exposure than our
40 results with mean intake for adults of 0.0038 $\mu\text{g}/\text{kg}$ body weight/day. Leblanc et al.
41 (2005) reported exposure of French population to FBs using dietary data from a strict
42 epidemiological work (n=3003), showing results in the line of our study with values of
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3 0.05 and 0.18 $\mu\text{g}/\text{kg}$ body weight/day for children mean and high consumers (percentile
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6 95) and 0.01 and 0.06 $\mu\text{g}/\text{kg}$ body weight/day for adults mean and high consumers,
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8 respectively, our combined values (males and females) being: 0.048 and 0.16 $\mu\text{g}/\text{kg}$ body
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10 weight/day for adult and baby means. Results from SCOOP (2003) showed variable
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12 levels, some of them slightly higher than our results, as for Italian consumers or
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14 Norwegian babies values of 0.52 and 0.86 $\mu\text{g}/\text{kg}$ body weight/day were reported,
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16 respectively, while other results were in the line with ours, as those for population from
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18 Austria, Germany, Belgium or Netherlands. In all cases, these values are far from those
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20 estimated in other regions highly exposed to FBs as South-Africa, where mean daily
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22 intake of FBs ranged from 3.43 ± 0.15 to 8.67 ± 0.18 $\mu\text{g}/\text{kg}$ body weight/day (Shephard et
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24 al. 2007).
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32 When we compared the direct method with stochastic method, we commonly found
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34 higher estimations through simulation. In the present study this was not crucial because in
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36 all cases the estimates were far from the safe level. However, this method can become
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38 mandatory in those cases when risk assessors need to accurately study the dietary intake
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40 of highly exposed populations.
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46 To our knowledge, this is the first study to assess the exposure of special population
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48 groups to FBs. The special groups selected in the present study had dietary habits
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50 markedly different from the general population. In one hand, celiac sufferers substitute
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52 the wheat-based food for other gluten free cereals, and in the other hand, some ethnic
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54 groups partially maintain the dietary patterns from their country of origin. In Catalonia
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3 during 2009, the immigrant population represented 15.9 % of the total population
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5 (Migracat 2010); therefore, their specificities should be taken into account to assess the
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7 exposure of this collective in other close regions.
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12 Considering our results, despite FBs being found regularly in Catalonian market,
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14 especially in ethnic food, beer and corn snacks, all levels remain far from EU maximum
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16 levels. Babies should be expected to be the main risk group to fumonisin intake; however
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18 these results suggest that no human risk derived from FBs should be expected in any
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20 Catalonian population group. The stochastic method provides more accurate estimations
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22 than the direct method, including the variability and uncertainties in the model, as well as
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24 the possibility to compute confidence intervals to validate the estimations.
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Table 1. Occurrence of total fumonisins (FB₁+FB₂) in corn-based food marketed in Catalonia

Food category	n	n	Positives	Mean± SD	Max
	Individual samples	“Composite”		µg/kg	µg/kg
Corn snacks	216	72	44	119.1 ± 83.1	475.5
Sweet corn	185	72	0	—	—
Corn Flakes	168	72	28	78.9 ± 27.9	139.5
Beer	216	72	64	36.9 ± 20.1	157.2
Baby foods	90	30	7	36.4 ± 8.5	50.7
Free-gluten food	18	18	1	22.5	22.5
Ethnic food	35	35	18	196.7 ± 191.8	682.2
Total	928	370	162		

Mean ± SD = Mean ± Standard Deviation

Review Only

Table 2. Normalised consumption of foodstuffs by Catalonian population (expressed in g / kg body weight/day) and percentage of consumers in each category (between parentheses, %)

	Corn flakes	Corn snacks	Beer	Sweet corn	Ethnic food	Gluten-free bread	Gluten-free pasta
<i>Elders</i>	0.01 (6.6)	0.00 (25)	0.53 (29)	0.00 (0)			
<i>Adult females</i>	0.19 (40)	0.02 (33)	0.76 (53)	0.19 (37)	-	-	-
<i>Adult males</i>	0.13 (33)	0.02 (32)	1.69 (73)	0.14 (39)	-	-	-
<i>Adolescents</i>	0.50 (65)	0.13 (82)	0.29 (25)	0.15 (45)	-	-	-
<i>Children</i>	1.41 (72)	0.18 (84)	0.00 (0)	0.33 (38)	-	-	-
<i>Immigrants</i>	0.23 (38)	0.11 (45)	2.27 (61)	0.14 (54)	0.39 (80)	-	-
<i>Celiac sufferers</i>	0.34 (64)	0.07 (72)	0.32 (40)	0.14 (52)	-	1.19 (94)	1.31 (96)

Table 3. Exposure of each population group to fumonisins (units in $\text{ng kg}^{-1} \text{bw day}^{-1}$) using the direct approach. Where \hat{E}_{π_0} is the exposure mean of the population π with the population sample π_0 and $\hat{V}(E_{\pi_0})$ the variance estimate.

	\hat{E}_{π_0}	$\hat{V}(E_{\pi_0})$
Celiac sufferers	40.9	$(35.0)^2$
Immigrants	65.1	$(69.0)^2$
Adults females	34.5	$(55.5)^2$
Adults males	63.2	$(90.3)^2$
Adolescents	36.7	$(44.3)^2$
Children	63.0	$(64.0)^2$
Infants	156.0	$(152.4)^2$

($\text{ng kg}^{-1} \text{bw day}^{-1}$)

Table 4. Results of exposure assessment ($\text{ng kg}^{-1} \text{bw day}^{-1}$) of the population groups from *P-P* simulation method. These results were obtained directly from the 10000 simulation outputs without *pdf* fittings. Bootstrap confidence intervals are presented between brackets (in $\text{ng kg}^{-1} \text{bw day}^{-1}$).

	<i>Adult females</i>	<i>Adult males</i>	<i>Immigrants</i>	<i>Celiac sufferers</i>
Mean	103.02 [91.84 - 115.27]	100.41 [88.62 – 113.33]	130.99 [71.64 – 221.57]	33.16 [20.13 - 52.18]
SD	116.47 [91.82 - 147.31]	114.21 [89.78 – 143.31]	291.26 [106.22 – 548.57]	61.62 [24.78 - 125.43]
Skewness	3.55	3.28	7.97	6.16
Kurtosis	22.52	17.59	135.88	68.44
Median	66.97 [58.92 - 76.33]	64.17 [55.99 – 73.87]	37.07 [18.35 – 66.20]	12.93 [8.19 - 19.66]
0.90 th quantile	226.73 [194.24 - 268.01]	225.48 [187.84 -264.92]	337.03 [171.85 – 631.48]	82.20 [43.72 - 153.27]
0.95 th quantile	320.76 [263.42 - 394.07]	313.33 [258.01 – 394.49]	560.64 [278.11 – 1264.82]	132.39 [68.71 - 276.57]
0.99 th quantile	563.08 [434.16 - 792.45]	577.19 [413.73 – 770.59]	1313.14 [479.93 – 3727.78]	294.88 [112.74 - 836.29]
	<i>Adolescents</i>	<i>Children</i>	<i>Infants</i>	
Mean	79.25 [69.01 – 90.36]	85.30 [59.30 - 119.96]	195.19 [168.91 – 223.68]	
SD	83.17 [64.81 – 103.93]	125.13 [62.71 - 250.98]	161.90 [130.01 – 201.47]	
Skewness	2.78	4.99	1.73	
Kurtosis	12.10	44.69	5.06	
Median	53.09 [44.45 – 61.61]	44.57 [30.66 – 63.69]	152.33 [125.27 - 185.52]	
0.90 th quantile	175.84 [143.52 – 211.80]	201.01 [128.33 – 314.25]	402.98 [335.03 – 484.66]	
0.95 th quantile	241.05 [191.29 – 295.83]	293.66 [172.74 - 489.71]	508.20 [410.86 - 650.41]	
0.99 th quantile	414.62 [282.63 – 559.11]	601.14 [280.30 – 1943.99]	748.56 [543.63 – 966.64]	

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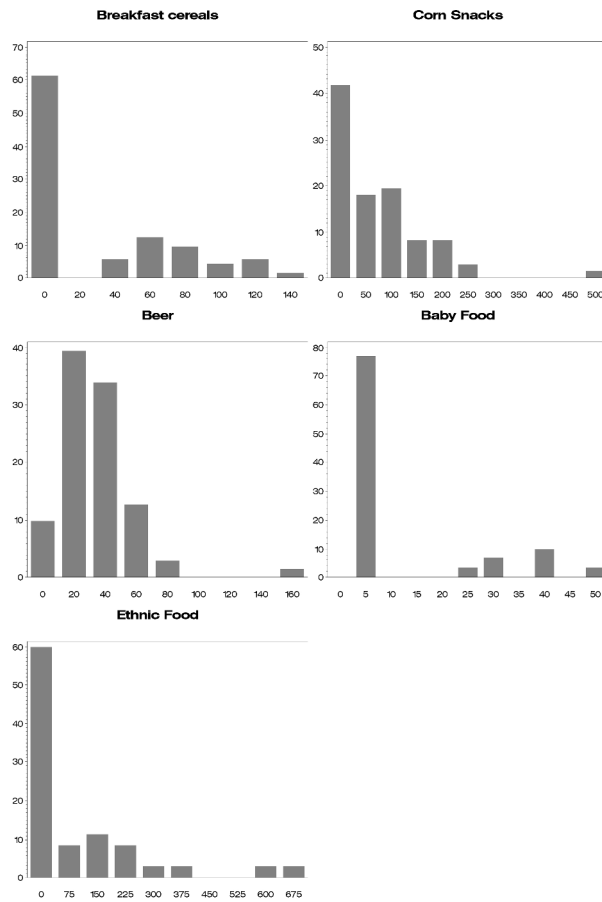


Figure 1. Contamination histograms (relative frequencies), in $\mu\text{g kg}^{-1}$ for each food
952x952mm (96 x 96 DPI)

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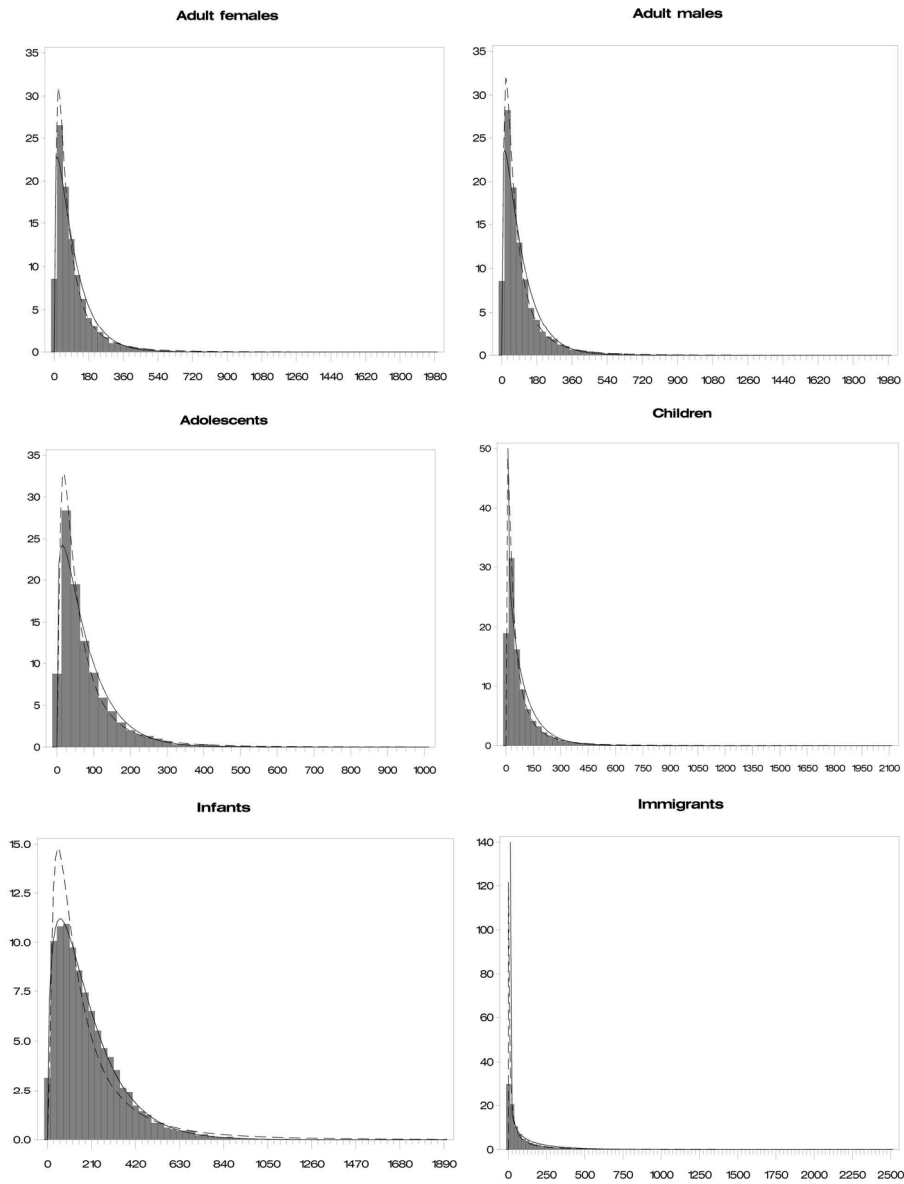


Figure 2. Fitted gamma (solid line) and lognormal (broken line) pdfs for the population groups with exception of celiac sufferers (relative frequencies). Exposure in $\text{ng kg}^{-1} \text{ bw day}^{-1}$.
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10 Figure 1. Contamination histograms (relative frequencies), in $\mu\text{g kg}^{-1}$ for each food
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15 Figure 2. Fitted gamma (solid line) and lognormal (broken line) *pdfs* for the population
16 groups with exception of celiac sufferers (relative frequencies). Exposure in ng kg^{-1} bw
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