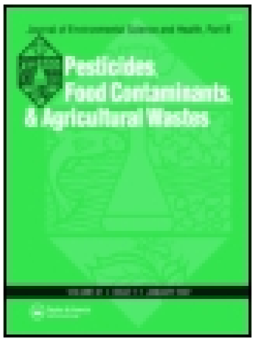

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Comprehensive estimate of the theoretical maximum daily intake of pesticide residues for chronic dietary risk assessment in Argentina

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ABSTRACT

A chronic dietary risk assessment for pesticide residues was conducted for four age groups of the Argentinian population following the procedure recommended by the WHO. The National Theoretical Maximum Daily Intake (NTMDI) for 308 pesticides was calculated for the first time, using the Maximum Residue Limits (MRLs) from several Argentinean regulations and food consumption data from a comprehensive National Nutrition and Health Survey. The risk was estimated by comparing the TMDI with the Acceptable Daily Intakes (ADI) identified by various sources. Furthermore, for each of the compounds with a TMDI >65% of the ADI, a probabilistic analysis was conducted to quantify the probability of exceeding the ADI. In this study 27, 22, 10, and 6 active ingredients (a.i.) were estimated to exceed the 100% of the ADI for the different population groups: 6–23 month-old children, 2–5 year-old children, pregnant women, and 10–49 year-old women, respectively. Some of these ADI-exceeding compounds (carbofuran, diazinon, dichlorvos, dimethoate, oxydemeton-methyl and methyl bromide) were found in all four of these groups. Milk, apples, potatoes, and tomatoes were the foods that contributed most to the intake of these pesticides. The study is of primary importance for the improvement of risk assessment, regulations, and monitoring activities.

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Pesticides; MRL; TMDI; dietary risk assessment; food consumption

Introduction

Argentina is a major agricultural producer of soybeans, corn, wheat, sunflowers and sorghum, among other extensive crops. In the last two decades, many different transgenic crops have been introduced, with a total currently surpassing 30 million hectares cultivated under no tillage, which has led to a steady increase in the use of pesticides.[1] As of December 2015, approximately 410 active ingredients (a.i.) and more than 4400 formulated products were registered in the country.[2] This situation can lead to the presence of pesticide residues in the treated commodities and their derivative food products, which are therefore important sources of pesticide exposure, although not the only sources. The exposures and effects resulting from the residues in food are several times higher than those effects induced by other sources such as inhalation or consumption of drinking water.[3,4]

Exposure to pesticides is linked to various adverse health effects including cancer, reproductive problems, neurotoxic effects, and endocrine disruption, among others.[5–8] However, a relationship between long-term exposures to repeated low doses of pesticides and their effects on human health is difficult to prove because the effects can appear many years after the contact.[9] In addition, toxicological studies have many other sources of uncertainty associated with the difficulties of studying extremely low amounts of the substances and the extrapolation of the effects from animal models to humans.[10]

In this context, the regulatory process has become increasingly responsive to scientific research. The assessment of consumer exposure is one of the most advanced areas. New goals have been set, and tools, such as probabilistic analysis and other techniques, have been developed. The importance of evaluating chronic exposures as well as acute and cumulative risk assessments has grown and has become a high priority in recent decades.[11,12] The consumer exposure methodology has evolved to address separate calculations (long-term and short-term exposures) and to modify the overly conservative initial approaches by introducing monitoring and supervised trial assays to collect actual residue data, as well as total diet surveys and other experimental approaches to address the evaluation of food intake exposure.[13–18] However, it is currently recognized that sufficient data and resources are not yet available to carry out such assessments routinely in many countries at the international level.[11,19] Thus, it is still a very useful first-stage approach to estimate ingestion of pesticide residues from the diet and to determine the Theoretical Maximum Daily Intake (TMDI) especially at national level (NTMDI) based on the MRL data.[14] This parameter (TMDI) leads to overestimated theoretical predictions because its assumptions are very

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conservative, on the basis that it considers that the residues in all food consumed daily are always present at MRL concentrations and no modification of the pesticide levels occurs during the history before consumption (storing, processing, cooking, etc.).[20] However, the TMDI provides a simple way to obtain the information that is necessary at the early stages of risk assessment to upgrade the regulations and to improve the monitoring and enforcement plans.

In Argentina, scientific evidence regarding the impact of the agricultural use of pesticides on health and the environment is growing rapidly.[21] The regulatory framework for food safety control has been improved by updated legislation. In 2010, a specific resolution established, for the first time, a list of national Maximum Residue Limits (MRLs) for a large group of foods. This list was supplemented in 2012 by documents that included several minor and unprotected crops.[22,23] Concomitant regulation by other governmental agencies such as the National Health Ministry [24] currently in place but are not fully harmonized with the other sources. However, the current monitoring and enforcement programs as well as research studies have not provided sufficient information on pesticide occurrence: only limited data representative of the large amounts of the currently regulated food/a.i. combinations are available.

The aims of the present study were to evaluate, for the first time and in a comprehensive way, the theoretical maximum daily intake (TMDI) at the national level for most of the regulated pesticides for four age groups of the Argentinian population following the WHO procedure, to compare the values obtained with the acceptable daily intake (ADI), to assess the status of the list of established MRLs and to obtain a classification based on the risk for the 308 compounds evaluated pesticides. To calculate the probability of exceeding the ADI, a probabilistic analysis was conducted using the food consumption distributions for the group of pesticides for which the TMDI exceeded the selected threshold of 65% of the ADI in at least one of the four studied population groups.

Methodology

Food consumption data

The data used in this work were obtained from the National Nutrition and Health Survey conducted by the National Health Ministry of Argentina in 2004–2005 and issued in 2007 and 2012.[25,26] The main purpose of the ENNyS survey was to produce information on the nutrition and health of the populations of mother and children at the national level. The survey was conducted for each of the 23 provinces of Argentina. The methodology used to collect food consumption data was the 24-hour recall. All food intake during the day before the survey, including drinks (except water and infusions) was recorded. The primary data recorded included: the food type, the number of individuals who reported consuming each food, the statistical median and average consumption (in grams or cubic centimeters) and their standard deviations, and the frequency of consumption. A total of 409,360 responses requested nationally from 311,182 homes were classified into four clusters: 6–23 month-old children and 2–5 year-old children (total of both clusters was 105,153 participants); 10–49 year-old women and pregnant women (294,655 and 9552 participants, respectively).

Table 1. Identification of the 97 significant food items from a total of 372 food types from the ENNyS survey distributed into 5 representative groups.

Food groups	n	Selected food items
Meat and meat products	4	Bovine meat, bovine fat, pig fat, egg.
Milk and dairy products	9	Fluid equivalent cattle milk (whole, low-fat, skim), cheese (whole, low-fat, skim), ricotta, butter, milk cream.
Fruits	22	Pineapple, banana, cherry, plum (plum, prune), apricot, peach, strawberry, kiwi, lemon, mandarin, apple (apple, peeled apple), melon, papaya fruit, quince, orange, raisin, grape, pear, grapefruit, watermelon.
Vegetables	28	Swiss chard, chicory, chili pepper (red and green), artichoke, celery, sweet potato, eggplant, watercress, broccoli, onion, cauliflower, escarole, asparagus, spinach, fennel, lettuce, potato, cucumber, leek, chicory–radicchio, beets, Brussel sprouts, cabbage, tomato, carrot, globe squash, squash.
Other (miscellaneous)	35	Vegetable oil mixture, sunflower oil, corn oil, olive oil, soybean oil, green olive, almond, corn (corn starch, corn flour, corn, corncob), white rice, rice (brown rice, rice flour), pea (fresh pea, dried pea), hazelnut, sugar (white sugar, brown sugar), cocoa, chickpea, broad bean, soy (soy flour, soybean), wheat flour, whole wheat flour, lentil, peanut, walnut, avocado, bean, wheat bran, wheat, green bean, honey.

The daily intakes declared by the various groups within the survey included a total of 372 forms of processed and unprocessed foods, which closely represent the dietary habits from all regions of the country. For our study, a careful selection of the items in this panel was performed based on the expectation of increased exposure to pesticide residues among the various regulated food/active ingredient pairs. Thus, a group of fruits, vegetables, vegetable oils, meats, milk and dairy products, and other miscellaneous foods were selected and distributed into five representative groups. As a result, a list of 145 relevant foods (39.2% of the total of 372), grouped into 97 "food items," was included in the present study (Table 1). These "food items" were grouped by similar foods that also had the same MRL to facilitate the handling of this large amount of information.

Maximum residue limits (MRLs)

The Maximum Residue Limits (MRLs) were obtained from the various resolutions of the National Food Safety and Quality Service (SENASA) and the Argentinean Food Codex (C.A.A.) on the basis of the publically available information from those organizations. The SENASA resolution N° 934,[22] issued in 2010, established its own requirements for the consumed domestic agricultural products and the foods derived from them. The resolution included more than 300 a.i. for a list of 227 vegetables (and other products) for a total of 2805 MRL/food combinations (Fig. 1). Other MRLs for vegetables were extracted from SENASA resolution N° 608,[23] published in 2012, which provides limits for several minor vegetables, also

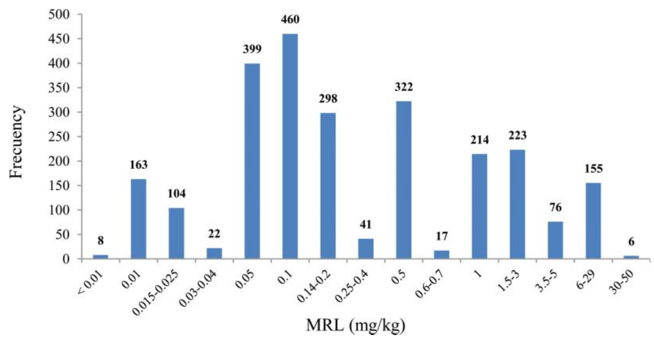

Figure 1. MRL (mg/kg) profile of the food item frequency (feed excluded) from resolution 934/2010 SENASA.

called "unprotected crops." The source for the meat and animal fat MRLs was SENASA resolution N° 511,[27] whereas for milk, the MRLs were extracted from Chapter 8 (dairy products) of the Argentinian Food Codex (C.A.A.), and also from the previously mentioned resolution N° 511. In this manner, a complete review of the Argentinian regulations was carried out to obtain a comprehensive list of the maximum residue limits for the pesticide residues in food currently authorized in the country.

Acceptable daily intake (ADI) sources

The Acceptable Daily Intake is a parameter that is extensively used to determine whether there is a chronic health risk to the population due to dietary exposure to pesticide residues. To estimate whether there is a potential risk to the health of a population, the daily intake of a pesticide is compared against this parameter. For this work, different sources of the ADIs were considered. The data from the Federal Institute for Risk Assessment (BfR) from Germany, the European Food Safety Agency (EFSA) and the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) were extracted from the EURL pesticides database.[28] The data from the IUPAC Pesticide Properties Database (PPDB),[29] the United States Environmental Protection Agency (US EPA),[30] and the Australian and Chinese governments [31,32] were also consulted. The difficulties in evaluating this parameter on an experimental basis are well established in the literature. In addition, harmonization of the values provided by different sources is challenging because there are major differences among them, for example, in the cases of procymidone (0.0028 EFSA – 0.1 JMPR), lambda-cyhalothrin (0.0025 EFSA – 0.02 JMPR), dichlorvos (0.00008 EFSA – 0.001 BfR), and diazinon (0.0002 EFSA – 0.005 BfR). In the present work, the lowest ADI value available for each pesticide was used.

Body weight data

In general, for the purpose of dietary risk assessment estimates, the food consumption data should be indexed to the individual consumer body weight. If individual data are not available, the average body weights for the target population should be used. Values of 60 kg and 15 kg for adults and children, respectively, are assumed for most populations in the world. However, for certain regions, the average body weight of the population may differ significantly.[33] In this study, for the groups of pregnant women and 10–49 year-old women, body weights of 60 kg were assumed, whereas for the 6–23 month-old children and the 2–5 year-old children, 10.2 kg and 15.4 kg, respectively, were used. The children's body weights were estimated using the guidelines for the evaluation of growth.[34]

Estimation of exposure

The calculation of the deterministic (point estimates) chronic exposure to pesticides was conducted according to the procedure established by the World Health Organization in the Guidelines for predicting dietary intake of pesticide residues, as revised in 1997.[14] As a screening method for assessing exposure, the NTMDI is compared with the established ADI for each pesticide. If the NTMDI value exceeded the ADI, it was necessary to apply factors to refine the intake to reach a conclusion on the acceptability of proposed MRLs and the underlying Good Agricultural Practices (GAP) from a public health point of view.[14] The following calculations were used for these parameters:

$$\text{NTMDI} = \sum_{i=1}^{n} \text{MRL}_i \times F_i$$

$$\%\ \text{ADI} = \frac{\text{NTMDI} \times 100}{\text{ADI} \times \text{BW}}$$

NTMDI: National Theoretical Maximum Daily Intake (mg/day).
MRL: Maximum Residue Limit (mg/kg).
F: Food consumption data (kg/day).
ADI: Acceptable Daily Intake (mg/kg bodyweight/day).
BW: Body weight (kg).

In a second stage, a more detailed evaluation of the exposure to a group of pesticides was performed using a probabilistic approach. Because the screening technique is known to significantly overestimate exposure, it is generally unnecessary to perform a probabilistic analysis when the screening calculations show exposures or risks to be clearly below levels of concern.[35] Therefore, for those pesticides that exceeded 65% of the ADI, a quantitative risk assessment was performed. The model was created using the software package @Risk (version 4.0, Palisade Corporation, Ithaca, NY, USA). The main output of the model was the probability that the exposure to a pesticide exceeded the ADI. This probability was estimated through 5000 iterations with Latin hypercube sampling. This number of iterations provided adequate convergence of the simulation statistics ($<1\%$). The mean and standard deviation of the consumption of each food were properly adjusted to a lognormal distribution. The consumption frequency was also taken into account in the input of the model. In this manner, a probability distribution for each pesticide–food combination was produced as the model output, from which the probability of occurrence values greater than 100% of the ADI was obtained.

Results and discussion

Of all of the pesticide compounds registered in the country for agricultural use through 2015, 308 a.i. were evaluated in this study, including 119 herbicides (38.5%), 109 insecticides (35.3%) and 80 fungicides (25.9%). Figure 1 displays the profile

Table 2. List of the 308 active ingredients evaluated and their % of the ADI for 2–5 years old children cluster.

%ADI	*n*	Pesticide type	Active substance
0–0.9	81	Herbicides	2,4-DB, 6-Benzyladenine, acifluorfen-sodium, aclonifen, aminopyralid, asulam, benazolin-ethyl, bispyribac-sodium, butralin, butroxydim, chloridazon, chlorimuron-ethyl, chlorsulfuron, clomazone, clopyralid, cloquintocet-mexyl, cloransulam-methyl, cyhalofop-butyl, dicamba, dichlorprop, diclosulam, dimethenamid, dinitramine, flucarbazone, flufenacet, flumetsulam, flumiclorac-pentyl, flumioxazin, fluoroglycofen, fluroxypyr, fomesafen, foramsulfuron, gibberellins A4 and A7, glufosinate-ammonium, halosulfuron, hexazinone, imazamox, imazapic, imazapyr, imazaquin, imazethapyr, iodosulfuron-methyl-sodium, ioxynil octanoate, isoxaflutole, lactofen, lenacil, mepiquat chloride, mesotrione, metolachlor, metsulfuron-methyl, molinate, napropamide, naptalam, nicosulfuron, oxadiazon, oxasulfuron, paclobutrazol, pendimethalin, phenmedipham, picloram, pinoxaden, primisulfuron, profoxydim, propaquizafop, propyzamide, prosulfuron, pyraflufen-ethyl, pyroxsulam, quinclorac, quizalofop-ethyl, quizalofop-p-tefuryl, sodium naphthalene-1-acetate, sulfentrazone, tebuthiuron, terbacil, terbutryn, topramezone, tralkoxydim, triasulfuron, trifloxysulfuron, trinexapac-ethyl
	18	Fungicides	Anilazine, cyazofamid, cyproconazole, dimethomorph, dimoxystrobin, fenarimol, fenhexamid, fluopicolide, fluoxastrobin, fluquinconazole, fosetyl-aluminium, kasugamycin, kresoxim-methyl, mandipropamid, metconazole, picoxystrobin, quinoxyfen, triadimenol
	21	Insecticides	Acrinathrin, beta-cyfluthrin, carbosulfan, cartap, chlorantraniliprole, chlordane, chlorfenapyr, coumaphos, DDT, fenpropathrin, fenthion, flonicamid, hexythiazox, lufenuron, methiocarb, methoprene, piperonyl butoxide, pyriproxyfen, thiodicarb, triflumuron, zeta-cypermethrin
1–4.9	16	Herbicides	Acetochlor, alachlor, ametryn, bentazone, bromoxynil, chloromequat, dalapon, flurochloridone, gibberellic acid, glyphosate, M.C.P.A, methabenzthiazuron, oxyfluorfen, prometryn, terbuthylazine, trifluralin
	22	Fungicides	Azoxystrobin, benalaxyl, boscalid, bupirimate, chinomethionat, cymoxanil, cyprodinil, epoxiconazole, fenbuconazole, flutolanil, flutriafol, hexaconazole, iprovalicarb, metalaxyl-M, metiram, metominostrobin, penconazole, propamocarb hydrochloride, sodium orthophenyl phenol, thiophanate-methyl, tolyfluanid, triforine
	20	Insecticides	Acequinocyl, acetamiprid, benfuracarb, buprofezin, chlorfluazuron, cyhalothrin, cyromazine, emamectin benzoate, fenpyroximate, fluazuron, flufenoxuron, flumethrin, methoxyfenozide, phosphine, pymetrozine, pyrethrin, spinetoram, spirodiclofen, tefluthrin, thiamethoxam
5–49.9	17	Herbicides	Aminoethoxyvinylglycine, atrazine, clethodim, clodinafop-propargyl, diclofop methyl, diquat, diquat dibromide, diuron, ethephon, fenoxaprop-ethyl, fluazifop-P-butyl, haloxyfop-R-methyl ester, metribuzin, paraquat, propanil, sethoxydim, simazine
	30	Fungicides	Benomyl, copper hydroxide, copper oxychloride, copper sulfate pentahydrate, cuprous oxide, difenoconazole, diphenylamine, dithianon, dithiocarbamates, fluazinam, fludioxonil, flusilazole, folpet, imazalil, iprodione, mancozeb, myclobutanil, propiconazole, pyraclostrobin, pyrimethanil, tebuconazole, tetraconazole, tetra copper tricalcium sulfate, thiabendazole, tin triphenyl acetate, triadimefon, tribasic copper sulfate, trifloxystrobin, vinclozolin, zineb
	46	Insecticides	Abamectin, acephate, aldicarb, alpha-cypermethrin, amitraz, bendiocarb, beta-cypermethrin, bifenazate, bifenthrin, bromopropylate, chlorpyrifos, chlorpyrifos-methyl, clofentezine, cyfluthrin, cyhalothrin (sum), cypermethrin, deltamethrin, diflubenzuron, esfenvalerate, ethion, ethoprop, fenazaquin, fenbutatin oxide, fenitrothion, fenvalerate, formetanate, imidacloprid, lambda-cyhalothrin, malathion, mecarbam, methidathion, methomyl, novaluron, permethrin, phenthoate, pirimicarb, profenofos, propoxur, pyridaben, tebufenozide, teflubenzuron, terbufos, tetradifon, thiacloprid, triazophos, trichlorfon
50–99.9	4	Herbicides	2,4-D, linuron, maleic hydrazide, methylarsonic acid (M.S.M.A.)
	5	Fungicides	Bitertanol, captan, carbendazim, chlorothalonil, thiram
	6	Insecticides	Azinphos-methyl, disulfoton, endosulfan, methamidophos, propargite, pyridafenthion
$\geq$100	1	Herbicides	Paraquat dichloride
	5	Fungicides	Ferbam, prochloraz, procymidone, propineb, ziram
	16	Insecticides	Azocyclotin, carbaryl, carbofuran, cyhexatin, diazinon, dichlorvos, dicofol, dimethoate, fenamiphos, fipronil, methyl bromide, oxydemeton-methyl, phorate, phosmet, pirimiphos-methyl, spinosad

for the most important MRL regulation that was consulted.[22] This graph shows a high prevalence of low concentration values for MRLs, ranging between 0.01 and 1 mg/kg. A few cases with values $\geq$ 30 mg/kg correspond to special situations. This is the case of methyl bromide, for which high MRLs remain after postharvest treatment for four fruits (citrus, kiwi, avocado, and table grapes). Other cases are carbendazim (dried hops) and maleic hydrazide (potato), which also have exceptionally high MRL values.

The numbers of pesticides that were evaluated in the four age clusters were slightly different because there were some differences in food consumption among these age groups. Thus, a total of 308 a.i. were included in the study for the groups of children aged 6–23 months and 2–5 years, while for women aged 10–49 years and pregnant women 307 and 306 a.i., respectively, were considered. Table 2 shows the compounds classified according their application as herbicides, fungicides, and insecticides and the %ADI calculated for the group of children aged 2–5 years. Of the compounds evaluated for this group, 271 (88%) had a %ADI $<$ 50. Fifteen compounds (4.9%) had a %ADI between 50 and 99. Finally, 22 compounds (7.1%) exceeded 100% of the ADI. The remaining three age clusters showed very similar patterns (Fig. 2). The complete data are presented in Tables A1, A2, and A3 in the Appendix.

The consumption of the wide range in the types of food declared by the four clusters contributed very differently to the intake of each evaluated pesticide. Some of these differences were shown to be very significant, for example, the consumption of tomatoes explains 83% of total methyl bromide intake for the adult cluster (women aged 10–49 years). In contrast, the contribution of peaches to the intake of diazinon did not exceed 1% of the total intake. Therefore, twenty-four foods were identified as major contributors to the TMDI from the list of compounds in Table 3. Citrus (oranges and tangerines) and other fruits (apples, pears, bananas, peaches, and table grapes); leafy vegetables (chard, spinach, and lettuce) and other vegetables (tomatoes, potatoes, carrots, onions, squash, and zucchini); cereals (rice, corn, and wheat flour) and sugar cane, made the greatest contributions. Within the group of animal-origin foods, milk, egg, meat, and bovine fat were the main contributors to the intake.

Over 87% of the active ingredients that were evaluated (269 of a total 308) showed values below 65% of the ADI. It can be

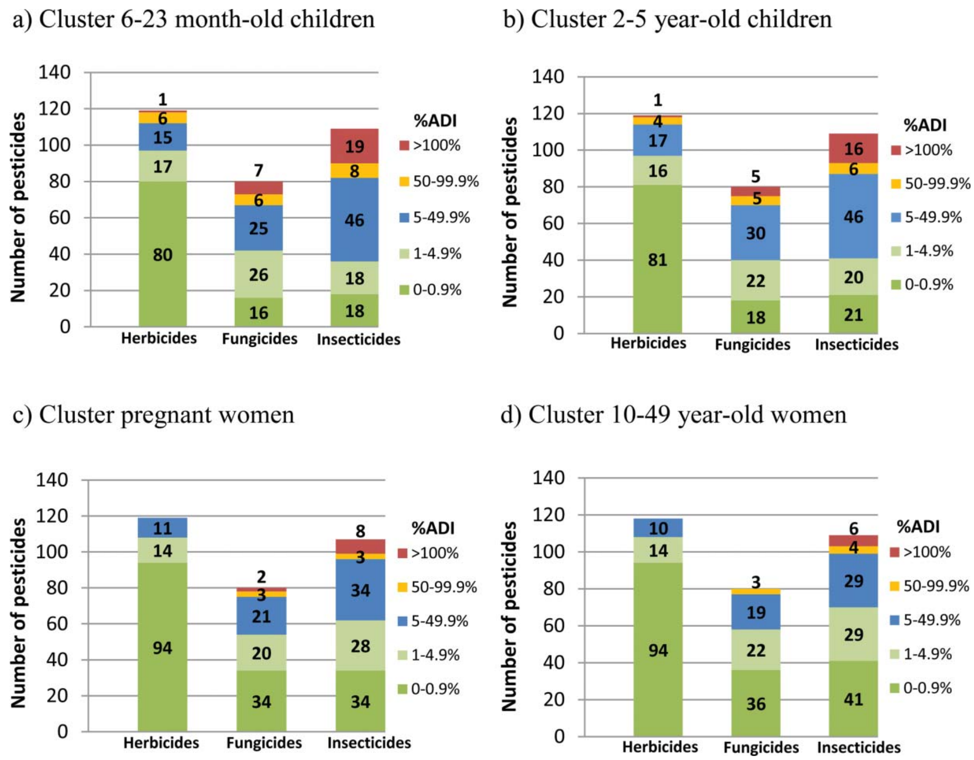

Figure 2. Distribution of total compounds in each sub-population presented as the %ADI profiles in five categories (>100%; 50–99.9%; 5–49.9%; 1–4.9%; 0–0.9%) and three pesticide groups (herbicides, fungicides, insecticides). (a) 6–23 month-old children; (b) 2–5 year-old children; (c) pregnant women; and (d) 10–49 year-old women.

assumed that this major group of compounds implies a low health risk for population, considering that our risk assessment at this level provides an overestimate of the actual dietary exposure on the basis of the conservative criteria used. In a subsequent stage, a probabilistic analysis was conducted to detect and hierarchically classify the compounds that are most likely to exceed the ADI. Thus, the remaining 39 compounds (23 insecticides, 11 fungicides and 5 herbicides) that exceeded 65% of the ADI and possessed a quantifiable probability of exceeding 100% ADI were evaluated as potentially high-risk compounds (Table 3). The TMDI values for this group of compounds in general were in the range of 67–3049% ADI. An overview of these compounds indicates the existence of three groups of compounds. First, there was a group of 12 compounds with TMDI values in the range of 67–97% ADI, including chlorothalonil, carbendazim, pyridaphenthion, dithiocarbamates, 2,4-D and amitraz. A second group of 21 compounds, including several that are currently banned in Argentina (endosulfan, disulfoton, phorate), or whose use is severely restricted (methamidophos), exceeded 100% ADI in at least one of the four age clusters. Finally, the six pesticides of most concern on the basis of exceeding 100% ADI in the four age clusters, as indicated by the deterministic approach, were mainly acetyl cholinesterase inhibitors from the organophosphate and carbamate insecticide families: diazinon, dichlorvos, dimethoate, oxydemeton-methyl, and carbofuran. In this same group was methyl bromide, a pesticide with multiple restricted uses.

Organophosphate pesticides (OPPs) were the family of compounds with the widest implications in the study, which showed that 13 compounds exceeded the 65% ADI threshold. As previously mentioned, among the active ingredients with the highest TMDI values were diazinon and dichlorvos, two compounds that are not approved for use in the EU, as well as dimethoate and oxydemeton-methyl for which improvement in the existing knowledge regarding concerns about the toxicity of certain metabolites have been actively recommended.[36] In Argentina, MRLs have been designated for diazinon in fruits, vegetables, meat and dairy, and for dichlorvos, some agricultural uses related to stored grains, meat and milk production are authorized. Dimethoate is authorized for several uses with MRLs ranging from 0.02 mg/kg for table grapes up to 2 mg/kg for cabbage. Oxydemeton-methyl is authorized for a various types of fruits, with limits up to 0.7 mg/kg, and for others vegetables and cereals with a maximum of 0.2 mg/kg. Six other organophosphorus compounds (pirimiphos-methyl, phosmet, phorate, methamidophos, fenamiphos, and disulfoton) with relatively high TMDI values in at least one cluster presented probabilities of exceeding the ADI ranging from 38 to 100%. Finally, three compounds of this family (azinphos-methyl, pyridafenthion, terbufos) showed probabilities of exceeding the ADI ranging between 13 and 29%.

Some restrictions on the use of organophosphorus compounds have been adopted in this country. Specifically, azinphos-methyl was banned for vegetable and fruit crops in 1991, and methamidophos was banned for use in pome fruit in 1998. In addition, prohibitions for disulfoton were adopted in 2010 and for 25 more compounds including coumaphos, mecarbam, phorate, triazophos, and terbufos, in 2011. Regarding these regulations, the lack of harmonization among the MRL lists from different sources and the failures to upgrade them are also remarkable. In particular, the C.A.A. MRLs for milk should be upgraded, taking into account the prohibitions and current status of some pesticides.

The systemic *N*-methyl carbamate carbofuran is not authorized in the EU, but there are established MRLs for this agent

Table 3. Active ingredients with at least 65% of the ADI in each cluster and probability (%) of exceeding 100% ADI threshold.

	Children 6–23 mos.		Children 2–5 y.o.		Pregnant women		Women 10–49 y.o.	
Active substance	%ADI	%Prob.	%ADI	%Prob.	%ADI	%Prob.	%ADI	%Prob.
2,4-D	68.7	11.3	—	—	—	—	—	—
Amitraz	67.6	7.1	—	—	—	—	—	—
Azinphos methyl	77.2	12.9	—	—	—	—	—	—
Azocyclotin	364.2	100	292.4	100	118.1	62.5	—	—
Bitertanol	109.0	49.7	74.1	14.1	—	—	—	—
Captan	126.3	72.8	98.0	38.0	—	—	—	—
Carbaryl	259.9	100	172.6	95.0	—	—	—	—
Carbendazim	89.4	24.4	67.9	4.6	—	—	—	—
Carbofuran	3049.5	100	2219.4	100	516.0	100	386.2	99.9
Chlorothalonil	97.2	37.3	70.2	13.3	—	—	—	—
Cyhexatin	264.1	100	169.0	98.1	—	—	—	—
Diazinon	605.3	100	508.8	100	197.3	100	152.6	98.9
Dichlorvos	1430.2	100	967.0	100	160.5	98.5	127.6	83.3
Dicofol	209.9	99.2	196.8	98.4	81.0	18.7	—	—
Dimethoate	353.2	100	324.5	100	141.7	79.6	114.7	54.6
Disulfoton	163.6	95.1	96.6	38.2	—	—	—	—
Dithiocarbamates	81.8	18.9	—	—	—	—	—	—
Endosulfan	119.4	62.6	76.8	12.7	—	—	—	—
Fenamiphos	163.5	84.0	149.4	77.6	—	—	—	—
Ferbam	281.2	99.9	237.1	99.6	101.6	41.8	75.5	17.6
Fipronil	523.4	100	333.8	100	—	—	—	—
Linuron	74.2	13.2	—	—	—	—	—	—
Maleic hydrazide	76.1	22.4	68.6	18.1	—	—	—	—
Methamidophos	145.1	79.0	74.9	12.8	—	—	—	—
Methyl bromide	1845.8	100	2509.0	100	1325.6	100	1083.8	100
M.S.M.A.	77.4	22.7	74.0	20.5	—	—	—	—
Oxydemeton methyl	1004.8	100	755.1	100	277.4	100	185.4	98.9
Paraquat dichloride	134.5	62.8	124.4	60.6	—	—	—	—
Phorate	350.5	100	207.1	99.6	—	—	—	—
Phosmet	568.0	100	392.7	100	156.6	93.7	87.1	24.9
Pirimiphos-methyl	196.6	99.3	163.7	96.3	—	—	—	—
Pyridaphenthion	87.9	29.2	—	—	—	—	—	—
Prochloraz	129.4	73.2	128.1	68.1	—	—	—	—
Procymidone	286.2	99.3	195.5	93.9	94.8	34.9	97.4	37.3
Propineb	126.2	69.5	114.5	58.4	—	—	—	—
Spinosad	262.6	100	159.7	96.7	—	—	—	—
Terbufos	81.8	18.9	—	—	—	—	—	—
Thiram	88.5	28.1	80.5	18.6	—	—	—	—
Ziram	359.4	100	298.8	100	131.4	79.0	96	34.1

in Argentina for various crops. However, its use is prohibited for pears and apples, mainly due to export requirements. There are concerns regarding the environmental impact of methyl bromide, another compound found to be critically important, but it is still authorized in Argentina for agricultural use with severe restrictions. Formulations containing more than 70% methyl bromide as an active principle are not allowed.[37] The main agricultural authorizations of methyl bromide are for soil treatment (no fixed MRL) and post-harvest treatment of cereals, citrus, almonds, and some other vegetables, such as tomatoes, avocados, grapes, and peppers. The high MRL values (20–50 mg/kg) adopted for most crops and the relatively low ADI value (0.001 mg/kg), could explain the high TMDI values observed in the four age clusters.

A high incidence of MRL violations in other countries has been reported for the dithiocarbamates, a fungicide group that is widely used in Argentina.[38] This chemical family was analyzed as the group of "dithiocarbamates" in milk, according to Argentinean Food Codex [24] and as single compounds in vegetables. Among these compounds, ferbam (which is not authorized in the EU), propineb, thiram and ziram, joined the list of compounds of concern. Ferbam, propineb, and ziram demonstrated values in excess of the ADI, while thiram and the whole group of "dithiocarbamates" (with contributions only from milk and dairy products) did not exceed the ADI values in any cluster. The dithiocarbamates are also a group of compounds for which improved attention with respect to the regulations and controls in the country is required.

Organochlorine pesticides (OCPs) were banned entirely in Argentina in previous decades and are currently only of concern with respect to the environment. However, two insecticides, endosulfan (completely prohibited in 2013) and dicofol (authorized for plant products and as well as for milk) were of concern with respect to the ADI thresholds for the clusters of children.

Herbicides constituted the largest number of compounds in the study and in general did not present a great risk concern. Only a few compounds were shown to be more critical. In the deterministic approach, paraquat-dichloride exceeded the 100% ADI in both groups of children. Also linuron, 2,4-D, maleic hydrazide, and M.S.M.A., which showed the highest TMDI values, were shown to have a probability of 11–23% of exceeding the 100% ADI (Table 3). Glyphosate and atrazine, the most used herbicides in the country, demonstrated very low values in the four clusters (0.7–2.9% and 3.6–10.7% ADI, respectively). The general situation observed for most herbicides could be due to the relatively higher ADI values possessed by these compounds compared to those values for the insecticides and fungicides.

The methodology used to assess risks from chronic dietary intake of pesticide residues should reflect the reality as closely as possible, using the most representative data available to estimate exposures. Often this cannot be achieved due to the absence or deficiency in the available information, principally regarding the data for food consumption as well as the actual food pesticide concentrations. For this reason, reliable conclusions from the risk assessment process require consideration of the limitations and characteristics of the information. Argentina runs a national monitoring and enforcement plan for pesticide residues and other contaminants in food from animal and vegetable origins (CREHA Plan). The monitoring and enforcement is conducted annually and analyses meat, milk, eggs, honey, fruits and vegetables for certain selected or representative pesticide residues. However, this plan does not provide concentration data for the complete list of regulated pesticides from all consumed foods. There are also no data available in the country on the residue concentrations in processed or ready-to-eat foods. The use of the MRL data for the pesticide concentrations in food is therefore a unique approach to a comprehensive screening of the national situation. While the exposures posited by this model are unlikely to occur, the use of MRLs is a valid technique for the first level of the risk assessment process.[14]

Food consumption data should ideally reflect the dietary habits of the groups within a population.[39] Four different types of data are the primary sources of information to assess food consumption: (i) food supply data (basket); (ii) data from household surveys of consumption; (iii) data from dietary surveys among individuals through several techniques (food records, 24-hour recall method, food frequency method, dietary history method, and current use); and (iv) the collection of duplicate diets. In general, to characterize the average usual intake of a group, a 24-hour recall or 1-day food record method is appropriate, provided that the sample is representative of the population under study and all days of the week are equally represented.[40] Selection of the most suitable method must take into account some aspects related to the purpose of the study including the foods of primary interest, the need to gather group data versus individual data, the population characteristics (age, sex, education, and cultural diversity), the level of specificity required in the description of food, and the resources available, among others.[41] When short surveys are used, the foods that are consumed less frequently are often underestimated whereas the amounts of the most frequently consumed foods are overestimated.[42] These factors contribute to uncertainty in the results and should be taken into account when interpreting the results and drawing conclusions.

According to some authors, the ADI does not apply to children under 12 weeks of age, mainly due to the lack of maturity of the organs and metabolic system.[43] European Commission recommended a special evaluation of the ADI for use in children up to 16 weeks of age.[44] Other authors from ILSI (1998) have not reached a full consensus regarding the age at which ADI values can be applied. They recommend case-by-case studies because various factors influence the derivation of the ADI, and therefore its application to a certain age range. Some members of this panel of researchers suggested that ADI should apply from 12 weeks of age or from 12 to 16 weeks of age.[45] Despite the discussions on the ADI applicability, it was considered useful to this work to include the youngest age group (6–23 months) in the evaluation. The application of ADI as a toxicological endpoint provided an appropriate tool to screen and compare the potential risk from the chronic dietary intake of pesticide residues for the four age clusters considered.

The difficulties and challenges found in present study and the main results presented here led to the formulation of several recommendations: (i) the need to harmonize the existing MRLs in the different regulations, and in particular, the set for milk in the Argentinean Food Codex (C.A.A.), given the discrepancies with SENASA regulation. (ii) To generate specific Food Consumption Data in a systematic manner that can be used for chronic, acute and cumulative risk assessment. (iii) To enhance the scope and improve the monitoring of pesticide residues and the enforcement systems that are applied to control the domestic consumption of these compounds in foods, considering the findings of the present study and subsequent refinements. (iv) To systematize and consolidate the risk assessment process as an important element of food safety management. (v) To improve the public access to updated information on each registered a.i., especially the MRLs, monitoring, field-supervised trials (STMR) and highest reference value (HR) data. (vi) To obtain information regarding the processing factors, variability, and other factors closely related to the residue levels that are potentially found in consumed food.

Conclusions

This work constitutes the first approach to the theoretical chronic dietary risk assessment of pesticide residues in Argentina. The results address and extend the existing data, regarding both the representative consumption data and the great scope of pesticides involved. The achieved classifications were based on deterministic and probabilistic analyses of the complete list of pesticides, which permitted a good evaluation of the whole status of the MRL regulations in the country. Specifically, a list of 39 compounds and a group of 24 food items with greater risk implications were defined. The methodology applied generally overestimates the true exposure to pesticide residues, and it should therefore not be concluded that the proposed MRLs in these critical cases are unacceptable or that there is a risk to the health of the population when the TMDI exceeds the ADI. Further studies to quantify the levels of the residues through observational and experimental means and to consider additional factors including the residues in the edible portions of the foods and processing factors are necessary to obtain a more refined characterization of the dietary exposure to those pesticides. However, the findings of the present work are a relevant contribution that is necessary for the revision of the current status of the regulations, for the implementation of improved monitoring and enforcement plans, and for continuity of further relevant stages of the dietary risk assessment process in the country.

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Appendix

Table A1. List of the 307 active ingredients evaluated and their % of the ADI for 10–49 year-old women.

%ADI	*n*	Pesticide type	Active substance
0–0.9	94	Herbicides	2,4-DB, 6-Benzyladenine, acetochlor, acifluorfen-sodium, aclonifen, ametryn, aminopyralid, asulam, benazolin ethyl, bentazone, bispyribac-sodium, butralin, butroxydim, chloridazon, chlorimuron-ethyl, chlorsulfuron, clomazone, clopyralid, cloquintocet-mexyl, cloransulam-methyl, cyhalofop-butyl, dalapon, dicamba, dichlorprop, diclosulam, dimethenamid, dinitramine, diquat, flucarbazone, flufenacet, flumetsulam, flumiclorac-pentyl, flumioxazin, fluoroglycofen, flurochloridone, fluroxypyr, fomesafen, foramsulfuron, gibberellic acid, gibberellins A4 and A7, glyphosate, glufosinate-ammonium, halosulfuron, hexazinone, imazamox, imazapic, imazapyr, imazaquin, imazethapyr, iodosulfuron-methyl-sodium, ioxynil octanoate, isoxaflutole, lactofen, lenacil, mepiquat chloride, mesotrione, methabenzthiazuron, metolachlor, metsulfuron-methyl, molinate, napropamide, naptalam, nicosulfuron, oxadiazon, oxasulfuron, oxyfluorfen, paclobutrazol, paraquat, pendimethalin, phenmedipham, picloram, pinoxaden, primisulfuron, profoxydim, propaquizafop, propyzamide, prosulfuron, pyraflufen-ethyl, pyroxsulam, quinclorac, quizalofop-ethyl, quizalofop-p-tefuryl, sodium naphthalene-1-acetate, sulfentrazone, tebuthiuron, terbacil, terbuthylazine, terbutryn, topramezone, tralkoxydim, triasulfuron, trifloxysulfuron, trifluralin, trinexapac-ethyl
	36	Fungicides	Anilazine, benalaxyl, bupirimate, chinomethionat, cyazofamid, cymoxanil, cyproconazole, dimethomorph, dimoxystrobin, epoxiconazole, fenarimol, fenbuconazole, fenhexamid, fluopicolide, fluoxastrobin, fluquinconazole, flutolanil, fosetyl-aluminium, hexaconazole, iprovalicarb, kasugamycin, kresoxim-methyl, mandipropamid, metalaxyl-M, metconazole, metiram, metominostrobin, penconazole, picoxystrobin, propamocarb hydrochloride, quinoxyfen, sodium orthophenyl phenol, thiophanate-methyl, tolyfluanid, triadimenol, triforine
	41	Insecticides	Acequinocyl, acetamiprid, acrinathrin, benfuracarb, beta-cyfluthrin, carbosulfan, cartap, chlorantraniliprole, chlordane, chlorfenapyr, chlorfluazuron, coumaphos, cyhalothrin, cyromazine, DDT, fenbutatin oxide, fenpropathrin, fenpyroximate, fenthion, flonicamid, fluazuron, flufenoxuron, flumethrin, hexythiazox, lufenuron, mecarbam, methiocarb, methoprene, methoxyfenozide, phosphine, piperonyl butoxide, profenofos, propoxur, pymetrozine, pyriproxyfen, spinetoram, spirodiclofen, tefluthrin, thiodicarb, triflumuron, zeta-cypermethrin
1–4.9	14	Herbicides	Atrazine, bromoxynil, clethodim, clodinafop-propargyl, chloromequat, diclofop methyl, fenoxaprop-ethyl, fluazifop-p-butyl, haloxyfop-R-methyl ester, M.C.P.A, metribuzin, prometryn, propanil, simazine
	22	Fungicides	Azoxystrobin, boscalid, copper hydroxide, cyprodinil, difenoconazole, dithiocarbamates, diphenylamine, fluazinam, fludioxonil, flusilazole, flutriafol, imazalil, iprodione, myclobutanil, propiconazole, pyraclostrobin, pyrimethanil, tebuconazole, tetraconazole, triadimefon, trifloxystrobin, vinclozolin
	29	Insecticides	Acephate, aldicarb, alpha-cypermethrin, bendiocarb, beta-cypermethrin, bifenazate, bromopropylate, buprofezin, cypermethrin, diflubenzuron, emamectin benzoate, esfenvalerate, ethion, ethoprop, fenazaquin, fenvalerate, formetanate, imidacloprid, permethrin, pirimicarb, pyrethrin, pyridaben, tebufenozide, terbufos, tetradifon, thiacloprid, thiamethoxam, triazophos, trichlorfon
5–49.9	10	Herbicides	2,4-D, aminoethoxyvinylglycine, diquat dibromide, diuron, ethephon, linuron, maleic hydrazide, methylarsonic acid (M.S.M.A.), paraquat dichloride, sethoxydim
	19	Fungicides	Benomyl, bitertanol, captan, carbendazim, chlorothalonil, copper oxychloride, copper sulfate pentahydrate, cuprous oxide, dithianon, folpet, mancozeb, prochloraz, propineb, tetra copper tricalcium sulfate, thiabendazole, thiram, tin triphenyl acetate, tribasic copper sulfate, zineb
	29	Insecticides	Abamectin, amitraz, azinphos-methyl, bifenthrin, chlorpyrifos, chlorpyrifos-methyl, clofentezine, cyfluthrin, cyhalothrin (sum), cyhexatin, deltamethrin, disulfoton, endosulfan, fenamiphos, fenitrothion, fipronil, lambda-cyhalothrin, malathion, methamidophos, methidathion, methomyl, novaluron, phenthoate, phorate, pirimiphos-methyl, propargite, pyridafenthion, spinosad, teflubenzuron
50–99.9	3	Fungicides	Ferbam, procymidone, ziram
	4	Insecticides	Azocyclotin, carbaryl, dicofol, phosmet
≥100	6	Insecticides	Carbofuran, diazinon, dichlorvos, dimethoate, methyl bromide, oxydemeton-methyl

Table A2. List of the 306 active ingredients evaluated and their % of the ADI for pregnant women cluster.

%ADI	*n*	Pesticide type	Active substance
0–0.9	94	Herbicides	2,4-DB, 6-Benzyladenine, acetochlor, acifluorfen-sodium, aclonifen, alachlor, ametryn, aminopyralid, asulam, benazolin ethyl, bentazone, bispyribac-sodium, butralin, butroxydim, chloridazon, chlorimuron-ethyl, chlorsulfuron, clomazone, clopyralid, cloquintocet-mexyl, cloransulam-methyl, cyhalofop-butyl, dalapon, dicamba, dichlorprop, diclosulam, dimethenamid, dinitramine, flucarbazone, flufenacet, flumetsulam, flumiclorac-pentyl, flumioxazin, fluoroglycofen, flurochloridone, fluroxypyr, fomesafen, foramsulfuron, gibberellic acid, gibberellins A4 and A7, glyphosate, glufosinate-ammonium, halosulfuron, hexazinone, imazamox, imazapic, imazapyr, imazaquin, imazethapyr, iodosulfuron-methyl-sodium, ioxynil octanoate, isoxaflutole, lactofen, lenacil, mepiquat chloride, mesotrione, methabenzthiazuron, metolachlor, metsulfuron-methyl, molinate, napropamide, naptalam, nicosulfuron, oxadiazon, oxasulfuron, oxyfluorfen, paclobutrazol, paraquat, pendimethalin, phenmedipham, picloram, pinoxaden, primisulfuron, profoxydim, propaquizafop, propyzamide, prosulfuron, pyraflufen-ethyl, pyroxsulam, quinclorac, quizalofop-ethyl, quizalofop-p-tefuryl, sodium naphthalene-1-acetate, sulfentrazone, tebuthiuron, terbacil, terbuthylazine, terbutryn, topramezone, tralkoxydim, triasulfuron, trifloxysulfuron, trifluralin, trinexapac-ethyl
	34	Fungicides	Anilazine, benalaxyl, bupirimate, chinomethionat, cyazofamid, cymoxanil, cyproconazole, dimethomorph, dimoxystrobin, epoxiconazole, fenarimol, fenbuconazole, fenhexamid, fluopicolide, fluoxastrobin, fluquinconazole, flutolanil, fosetyl-aluminium, hexaconazole, kasugamycin, kresoxim-methyl, mandipropamid, metalaxyl-M, metconazole, metiram, metominostrobin, penconazole, picoxystrobin, propamocarb hydrochloride, quinoxyfen, sodium orthophenyl phenol, tolyfluanid, triadimenol, triforine
	33	Insecticides	Acetamiprid, acrinathrin, benfuracarb, beta-cyfluthrin, carbosulfan, cartap, chlorantraniliprole, chlordane, chlorfenapyr, chlorfluazuron, cyhalothrin, cyromazine, DDT, fenpropathrin, fenthion, flonicamid, fluazuron, flumethrin, hexythiazox, lufenuron, methiocarb, methoprene, methoxyfenozide, phosphine, piperonyl butoxide, profenofos, propoxur, pymetrozine, pyriproxyfen, spinetoram, thiodicarb, triflumuron, zeta-cypermethrin
1–4.9	14	Herbicides	Atrazine, bromoxynil, clethodim, chloromequat, clodinafop-propargyl, diclofop methyl, diquat, fenoxaprop-ethyl, fluazifop-p-butyl, haloxyfop-R-methyl ester, M.C.P.A, metribuzin, prometryn, simazine
	20	Fungicides	Azoxystrobin, boscalid, copper hydroxide, cyprodinil, difenoconazole, diphenylamine, fluazinam, fludioxonil, flutriafol, iprovalicarb, myclobutanil, propiconazole, pyraclostrobin, pyrimethanil, tebuconazole, tetraconazole, thiophanate-methyl, triadimefon, trifloxystrobin, vinclozolin
	29	Insecticides	Acephate, acequinocyl, aldicarb, alpha-cypermethrin, bendiocarb, beta-cypermethrin, buprofezin, cypermethrin, emamectin benzoate, esfenvalerate, ethoprop, fenazaquin, fenbutatin oxyde, fenpyroximate, fenvalerate, flufenoxuron, formetanate, imidacloprid, mecarbam, permethrin, pirimicarb, pyrethrin, pyridaben, spirodiclofen, tebufenozide, tefluthrin, thiamethoxam, triazophos, trichlorfon
5–49.9	11	Herbicides	2,4-D, aminoethoxyvinylglycine, diquat dibromide, diuron, ethephon, linuron, maleic hydrazide, methylarsonic acid (M.S.M.A.), paraquat dichloride, propanil, sethoxydim
	23	Fungicides	Benomyl, bitertanol, captan, carbendazim, chlorothalonil, copper oxychloride, copper sulfate pentahydrate, cuprous oxide, dithianon, dithiocarbamates, flusilazole, folpet, imazalil, iprodione, mancozeb, prochloraz, propineb, tetra copper tricalcium sulfate, thiabendazole, thiram, tin triphenyl acetate, tribasic copper sulfate, zineb
	35	Insecticides	Abamectin, amitraz, azinphos-methyl, bifenazate, bifenthrin, bromopropylate, clofentezine, chlorpyrifos, chlorpyrifos-methyl, cyfluthrin, cyhalothrin (sum), cyhexatin, deltamethrin, disulfoton, endosulfan, ethion, fenamiphos, fenitrothion, fipronil, lambda-cyhalothrin, malathion, methamidophos, methidathion, methomyl, novaluron, phenthoate, phorate, pirimiphos-methyl, propargite, pyridafenthion, spinosad, teflubenzuron, terbufos, tetradifon, thiacloprid
50–99.9	3	Fungicides	Ferbam, procymidone, ziram
	4	Insecticides	Azocyclotin, carbaryl, dicofol, phosmet
≥100	6	Insecticides	Carbofuran, diazinon, dichlorvos, dimethoate, methyl bromide, oxydemeton-methyl

Table A3. List of the 308 active ingredients evaluated and their % of the ADI for 6–23 month-old children cluster.

%ADI	*n*	Pesticide type	Active substance
0–0.9	80	Herbicides	2,4-DB, 6-Benzyladenine, acifluorfen-sodium, aclonifen, aminopyralid, asulam, benazolin ethyl, bispyribac-sodium, butralin, butroxydim, chloridazon, chlorimuron-ethyl, chlorsulfuron, clomazone, clopyralid, cloquintocet-mexyl, cloransulam-methyl, cyhalofop-butyl, dicamba, dichlorprop, diclosulam, dimethenamid, dinitramine, flucarbazone, flufenacet, flumetsulam, flumiclorac-pentyl, flumioxazin, fluoroglycofen, fluroxypyr, fomesafen, foramsulfuron, gibberellins A4 and A7, glufosinate-ammonium, halosulfuron, hexazinone, imazamox, imazapic, imazapyr, imazaquin, imazethapyr, iodosulfuron-methyl-sodium, ioxynil octanoate, isoxaflutole, lactofen, lenacil, mepiquat chloride, mesotrione, metolachlor, metsulfuron-methyl, napropamide, naptalam, nicosulfuron, oxadiazon, oxasulfuron, paclobutrazol, pendimethalin, phenmedipham, picloram, pinoxaden, primisulfuron, profoxydim, propaquizafop, propyzamide, prosulfuron, pyraflufen-ethyl, pyroxsulam, quinclorac, quizalofop-ethyl, quizalofop-p-tefuryl, sodium naphthalene-1-acetate, sulfentrazone, tebuthiuron, terbacil, terbutryn, topramezone, tralkoxydim, triasulfuron, trifloxysulfuron, trinexapac-ethyl
	16	Fungicides	Anilazine, cyazofamid, cyproconazole, dimethomorph, fenarimol, fenhexamid, fluopicolide, fluoxastrobin, fluquinconazole, fosetyl-aluminium, kasugamycin, kresoxim-methyl, mandipropamid, metconazole, picoxystrobin, quinoxyfen
	18	Insecticides	Beta-cyfluthrin, cartap, chlorantraniliprole, chlordane, chlorfenapyr, coumaphos, DDT, fenpropathrin, flonicamid, lufenuron, methiocarb, methoprene, phosphine, piperonyl butoxide, pyriproxyfen, thiodicarb, triflumuron, zeta-cypermethrin
1–4.9	17	Herbicides	Acetochlor, alachlor, ametryn, bentazone, bromoxynil, chloromequat, dalapon, diclofop-methyl, flurochloridone, gibberellic acid, glyphosate, M.C.P.A, methabenzthiazuron, oxyfluorfen, prometryn, terbuthylazine, trifluralin
	26	Fungicides	Azoxystrobin, benalaxyl, boscalid, bupirimate, cymoxanil, cyprodinil, dimoxystrobin, epoxiconazole, fenbuconazole, fluazinam, flutolanil, flutriafol, hexaconazole, iprovalicarb, metalaxyl-M, metiram, metominostrobin, penconazole, propamocarb hydrochloride, pyrimethanil, sodium orthophenyl phenol, tetraconazole, thiophanate-methyl, tolyfluanid, triadimenol, triforine
	18	Insecticides	Acequinocyl, acetamiprid, acrinathrin, benfuracarb, buprofezin, carbosulfan, chlorfluazuron, cyromazine, ethion, fenthion, fluazuron, flumethrin, hexytiazox, methoxyfenozide, pymetrozine, pyrethrin, spinetoram, tefluthrin

(*Continued on next page*)

Table A3. (*Continued*)

%ADI	*n*	Pesticide type	Active substance
5–49.9	15	Herbicides	Atrazine, clethodim, clodinafop-propargyl, diquat, diquat dibromide, diuron, ethephon, fenoxaprop-ethyl, fluazifop-p-butyl, haloxyfop-R-methyl ester, metribuzin, molinate, paraquat, propanil, simazine
	25	Fungicides	Benomyl, chinomethionat, copper hydroxide, copper sulfate pentahydrate, cuprous oxide, difenoconazole, diphenylamine, fludioxonil, flusilazole, folpet, imazalil, iprodione, mancozeb, myclobutanil, propiconazole, pyraclostrobin, tebuconazole, tetra copper tricalcium sulfate, thiabendazole, tin triphenyl acetate, triadimefon, tribasic copper sulfate, trifloxystrobin, vinclozolin, zineb
	46	Insecticides	Abamectin, acephate, aldicarb, alpha-cypermethrin, beta-cypermethrin, bifenazate, bifenthrin, bromopropylate, chlorpyrifos, chlorpyrifos-methyl, clofentezine, cyfluthrin, cyhalothrin, cyhalothrin (sum), cypermethrin, deltamethrin, diflubenzuron, emamectin benzoate, esfenvalerate, ethoprop, fenazaquin, fenbutatin oxide, fenpyroximate, phenthoate, fenvalerate, flufenoxuron, formetanate, imidacloprid, lambda-cyhalothrin, malathion, mecarbam, methidathion, methomyl, permethrin, pirimicarb, profenofos, propoxur, pyridaben, spirodiclofen, tebufenozide, teflubenzuron, tetradifon, thiacloprid, thiamethoxam, triazophos, trichlorfon
50–99.9	6	Herbicides	2,4-D, aminoethoxyvinylglycine, linuron, maleic hydrazide, methylarsonic acid (M.S.M.A.), sethoxydim
	6	Fungicides	Carbendazim, chlorothalonil, copper oxychloride, dithianon, dithiocarbamates, thiram
	8	Insecticides	Amitraz, azinphos-methyl, bendiocarb, fenitrothion, novaluron, propargite, pyridafenthion, terbufos
≥100	1	Herbicides	Paraquat dichloride
	7	Fungicides	Bitertanol, captan, ferbam, prochloraz, procymidone, propineb, ziram
	19	Insecticides	Azocyclotin, carbaryl, carbofuran, cyhexatin, diazinon, dichlorvos, dicofol, dimethoate, disulfoton, endosulfan, fenamiphos, fipronil, methamidophos, methyl bromide, oxydemeton-methyl, phorate, phosmet, pirimiphos-methyl, spinosad