JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Article

pubs.acs.org/JAFC

Residues in Beeswax: A Health Risk for the Consumer of Honey and Beeswax?

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ABSTRACT: A scenario analysis in regard to the risk of chronic exposure of consumers to residues through the consumption of contaminated honey and beeswax was conducted. Twenty-two plant protection products and veterinary substances of which residues have already been detected in beeswax in Europe were selected. The potential chronic exposure was assessed by applying a worst-case scenario based on the addition of a "maximum" daily intake through the consumption of honey and beeswax to the theoretical maximum daily intake through other foodstuffs. For each residue, the total exposure was finally compared to the acceptable daily intake. It is concluded that the food consumption of honey and beeswax contaminated with these residues considered separately does not compromise the consumer's health, provided proposed action limits are met. In regard to residues of flumethrin in honey and in beeswax, "zero tolerance" should be applied.

KEYWORDS: *beeswax, residue, honey, risk, consumer, plant protection product, veterinary substance, action limit, chronic exposure, scenario*

■ INTRODUCTION

Beeswax and honey can be contaminated by residues of plant protection products and veterinary substances through different pathways. Beekeepers can use chemical substances (e.g., veterinary substances, biocides) to treat beehives, notably to control the *Varroa destructor* mite,[1] a parasite of bees that causes bee varroosis. Applying varroacides in honeybee colonies leaves residues in bee products, especially in beeswax, in which they accumulate with years of treatment given that they are mostly fat-soluble and nonvolatile.[2] Veterinary substances can also be applied to honeybee colonies to control other bee

Received: June 23, 2016
Revised: October 11, 2016
Accepted: October 14, 2016

diseases, such as American foulbrood (*Paenibacillus larvae*), European foulbrood (*Melissococcus plutonius*), and nosemosis (*Nosema apis* and *Nosema ceranae*). Moreover, insect repellents can be used by the beekeeper against wax moths (*Achroia grisella* and *Galleria mellonella*) in stored combs. In Europe, the European Medicines Agency (EMA) provides the list of active substances and commercial products authorized in beekeeping,[3] per Member State. Bees themselves can also introduce residues of plant protection products into the hives. Residues from chemical treatment of bees and from the environment can end up in beeswax of the existing combs. Furthermore, commercially available beeswax from third countries may also be used. In those countries, chemical substances, such as antibiotics, not allowed under European legislation, are used in beekeeping[4] and/or in agriculture. Furthermore, after it has been used, beeswax is very often salvaged, remelted, and reused within the beekeeping sector. This practice may lead to accumulation of residues in beeswax.[5]

From a contaminated wax comb, residues can be transferred to stored honey,[2] as demonstrated, for example, by Reybroeck et al.[6] for sulfamethazine. This carry-over could lead to an exceeding of maximum limits, posing a health risk to consumers. Consumers can also be exposed to residues via the consumption of beeswax by itself, that is, through consumption of "comb honey" or "chunk honey or cut comb in honey" or as food additive E901.[7] The latter is used as a glazing agent in the preparation of pastries, for the treatment of some fruits, as a food supplement (capsules and tablets), and as a flavor carrier. There is currently no legal requirement concerning the possible presence of plant protection product and veterinary substance residues in beeswax, at either the European level or at the Belgian level.

To prevent and/or control these potential risks in the food chain, it is proposed to implement action limits for the presence of residues in beeswax. Beeswax exceeding those action limits should not be put on the market. To determine these action limits, a scenario analysis in regard to the risk of chronic exposure of consumers to residues of plant protection products and veterinary substances through the consumption of contaminated honey and beeswax was conducted.

For this purpose, the following assumptions were made. We considered beeswax as the most relevant bee product to be the starting point of our scenario analysis (i.e., the hazard identification step). This matrix can indeed accumulate residues, especially from acaricides,[2,8,9] unlike honey, in which residues levels are generally low.[9] We identified therefore residues that have already been found in beeswax and, as a worst-case scenario, we considered that these residues could also be present in honey, in the same concentrations in both matrices. The consumption of honey and beeswax only as foodstuffs was taken into account, not as cosmetics or pharmaceuticals. We considered the consumer as an adult of 60 kg body weight (bw). No residue breakdown in honey and beeswax over time was taken into account. Only the chronic toxicity of the selected substances was taken into account, not the acute one. Moreover, despite the fact that consumers could be exposed to residues of different chemical substances at the same time through the consumption of contaminated honey and beeswax and that adverse synergistic effects could occur, the hazard characterization is based on the toxicity of each substance considered separately.

MATERIALS AND METHODS

On the basis of scientific literature and analysis results from the Institute for Agricultural and Fisheries Research (ILVO), a list of plant protection products and veterinary substances of which residues have already been detected in beeswax in Europe was established (Table 1). For each of these chemical substances, corresponding acceptable daily intakes (ADIs), water solubilities, and octanol/water partition coefficients are summarized in Table 2.

From that list, plant protection products or veterinary substances were selected (see Hazard Characterization and Table 3) on the basis of their human toxicity, their water or fat solubility, and the fact that their use in beekeeping is authorized or that their use could theoretically be authorized via the "cascade[10] system" (veterinary substances).

Consumer's exposure to each of these selected residues, through honey and beeswax consumption, was assessed considering a "maximum level of contamination". This "maximum level of contamination" was defined as equal to an action limit to be achieved for honey and beeswax and which was determined as follows. If a maximum residue limit (MRL) was set for honey, based on veterinary use of the substance, this value was also selected as the action limit for beeswax. If no MRL was set out for honey based on a veterinary use of the substance but well based on a use of the substance as a plant protection product, that value was also selected as the action limit for beeswax. In all other cases, the default MRL corresponding to 10 μg/kg according to European Regulation (EC) 396/2005[11] was applied as the action limit for honey as well as for beeswax, except for cymiazole, for which this regulation does not apply. In this specific case (absence of MRL), "zero tolerance" (= prohibition of putting honey/beeswax on the market when the residue is detected) was considered.

According to EFSA,[7] the daily food consumption of beeswax is estimated to 1.29 g/person, that is, 0.022 g/kg bw for a 60 kg individual. This conservative assumption is based on the 95th percentile of consumption of foodstuffs containing beeswax, the beeswax being added at the highest proportions in those foodstuffs.

With regard to honey, food consumption data vary between 20 g per day and per person (EU Committee for Medicinal Products for Veterinary Use (CVMP))[12] and 50 g per day and per person (Joint FAO/WHO Expert Committee on Food Additives (JECFA)).[13] The value of 50 g honey per day and per person represents the acute daily intake (95th percentile) for an adult of 60 kg according to EFSA.[14] For Belgium, values of 50 and 67.2 g honey per day and per person are recorded as the 95th percentile, respectively, of the chronic daily intake (consumers only) and of the acute daily intake (consuming days only) for an adult according to the EFSA Comprehensive European Food Consumption Database (http://www.efsa.europa.eu/en/food-consumption/comprehensive-database).

The assessment of consumers' chronic exposure to the selected residues through the food consumption of honey and beeswax was based on a worst-case scenario. This consisted, for each residue and based on the "maximum level of contamination" (cf. above) for this residue, in adding the honey contribution (via the consumption of 50 g of honey/person/day) and the beeswax contribution (via the consumption of 1.29 g beeswax/person/day) to a theoretical maximum daily intake (TMDI) and in checking that the ADI value (Table 2) is not being exceeded. The contributions of honey and beeswax were calculated on the basis of a residue concentration equal to the MRL or to the action limit mentioned in Table 3. The TMDI values generally come from the EMA and take into account the residue intake via other foodstuffs (e.g., meat, milk, eggs), but sometimes via honey as well. The TMDI is, however, not always known. In that case, consumers' exposure through the consumption of honey and beeswax is compared to the ADI.

RESULTS AND DISCUSSION

Hazard Identification. The 68 residues found in beeswax in Europe according to the different references/sources mentioned in this section are reported in Table 1.

DOI: 10.1021/acs.jafc.6b02813
J. Agric. Food Chem. XXXX, XXX, XXX−XXX

In Belgium, Nguyen et al.[15] looked for the presence of 55 pesticide residues in 48 beeswax samples, collected between March 2004 and March 2005 and originating from 16 randomly selected apiaries in the Walloon region (southern Belgium); in each apiary three randomly selected beehives were sampled. The three most commonly found residues were flusilazole, bromopropylate, and coumaphos, with detection frequencies of 31.3, 25.0, and 25.0%, respectively. Simon-Delso et al.[16] looked for the presence of residues of 99 plant protection products in 54 beeswax samples, collected at the end of 2011 and originating from apiaries located in the northern Walloon region (southern Belgium) and in the Brussels-Capital region (central Belgium). τ-Fluvalinate, coumaphos, and boscalid were the three most commonly found residues, with detection frequencies of 40.7, 35.2, and 22.2%, respectively. Ravoet et al.[5] looked for the presence of residues of 293 organochlorine and organophosphorous compounds in 10 samples of beeswax combs, collected in the spring of 2012 and originating from apiaries in the Flemish region (northern Belgium). None of the samples was free of residues. τ-Fluvalinate, coumaphos, bromopropylate, and δ-hexachlorocyclohexane (HCH) were the four most commonly found residues, with detection frequencies of 100, 90, 70, and 70%, respectively. In addition, other data from analyses carried out between 2004 and 2014 are available at the Institute for Agricultural and Fisheries Research (ILVO). When considered separately, the analyses pertain only to a limited number of samples, and these results are therefore not published (Reybroeck, personal communication). During this period, 36 samples were analyzed for the presence of residues of veterinary substances, varroacides, and/or plant protection products. Different methods, with different scopes, were used to analyze these samples. The majority (20/36 = 55.6%) of these samples were beeswax from Belgium, the other ones (16/36 = 44.4%) were beeswax from India, China, Argentina, Poland, and Cameroon.

In France, Chauzat and colleagues[17,18] looked for the presence of residues of 44 plant protection products in 93 beeswax samples taken between September 2002 and October 2005. Five departments located in an area stretching from northern to southern France were selected, and in each of these departments five apiaries were chosen. Residues of plant protection products were not detectable in 33 samples (35.1%). In the other samples, τ-fluvalinate, coumaphos, and cypermethrin were the three most commonly found residues, with detection frequencies of 52.2, 46.7, and 16.1%, respectively.

In Germany, Wallner[2] showed for the year 1997 that German beeswax (number of samples = 226) was contaminated with residues of coumaphos, bromopropylate, and τ-fluvalinate with detection frequencies of 61.0, 54.9, and 37.2%, respectively. International beeswax (number of samples = 158) was contaminated with residues of τ-fluvalinate, bromopropylate, and coumaphos with detection frequencies of 55.1, 20.9, and 19.0%, respectively.

In Spain, Serra-Bonvehí and Orantes-Bermejo[19] looked for the presence of residues of 11 acaricides and/or plant protection products in 197 beeswax samples collected between 2003 and 2008. Chlorfenvinphos, τ-fluvalinate, and bromopropylate were the three most commonly found residues, with detection frequencies of 95.9, 93.6, and 87.9%, respectively. Yáñez et al.[20] looked for the presence of residues of 7 neonicotinoids in 30 beeswax samples collected in autumn 2011 in Murcia (southeastern Spain). Thiamethoxam, acetamiprid, and imidacloprid were found with detection frequencies of 26.7, 13.3, and 3.3%, respectively.

In Italy, Boi et al.[21] performed a 10 year survey of acaricide residues in beeswax. They took into account analysis results of 5 acaricide residues in 1319 beeswax samples analyzed between 2005 and 2014. Coumaphos, τ-fluvalinate, and chlorfenvinphos were the three most commonly found residues, with detection frequencies of 49, 38, and 25%, respectively.

In Switzerland, Bogdanov and colleagues[8,22,23] performed a long-term (between 1991 and 2002) monitoring of the residue levels of four acaricides in Swiss commercial beeswax through the analysis of representative samples of all wax produced in Switzerland. Coumaphos, bromopropylate, and τ-fluvalinate were detected each year, except in 1991 (τ-fluvalinate was not detected that year). Flumethrin was not detected. Between 1994 and 2000, these wax samples were also searched for 36 chlorinated and 32 organophosphorus pesticides residues. Trace amounts of hexachlorobenzene (HCB), chlorpyrifos, and iodofenphos were detected.

In North America, Mullin et al.[24] looked for the presence of residues of 200 miticides, insecticides, fungicides, and herbicides in 259 beeswax samples collected between 2007 and 2008. In these samples, 87 pesticides and metabolites were found. Coumaphos, τ-fluvalinate, and chlorpyriphos were the three most commonly found residues, with detection frequencies of 98.1, 98.1, and 63.2%, respectively. Although this study represents an important source of data on contamination levels of beeswax, we decided to focus on the situation in Europe. This study is therefore not taken into account in our scenario analysis. However, it should be noted that the five most commonly found residues according to this study (coumaphos, τ-fluvalinate, chlorpyriphos, chlorothalonil, and amitraz) are well included in our scenario analysis according to the other references/sources above-mentioned.

Hazard Characterization. The ADIs of the 68 substances that have already been detected in beeswax in Europe, according to different references/sources, are shown in Table 2.

On the basis of Table 2, the most toxic substances for humans (if several ADI values are mentioned for the same residue in Table 2, only the lowest ADI value is taken into consideration), considering chronic oral exposure (i.e., compounds for which the ADI is ≤ 0.001 mg/kg bw/day), are carbofuran, iodofenphos, coumaphos, chlorfenvinphos, τ-fluvalinate, hexachlorobenzene (HCB), parathion, mevinphos, chlorpyriphos, cymiazole, and dimethoate (in decreasing order of toxicity). Substances for which no toxicity data are available were excluded.

On the basis of the selected physicochemical characteristics (see Table 2) and/or authorized use of the chemical substances, this list was expanded by selecting, among the substances already detected in beeswax and above-mentioned, the following substances. First, we added the five most hydrophilic substances (on the basis of data of water solubility in Table 2), which consequently most likely concentrate in honey, namely, mevinphos and dimethoate, already above-mentioned on the basis of their toxicity, thiamethoxam, pirimicarb, and acetamiprid. Second, we added the five most lipophilic substances (on the basis of octanol/water partition coefficients in Table 2), which consequently most likely concentrate in beeswax, namely, τ-fluvalinate, already above-mentioned because of its toxicity, dichlorodiphenyltrichloroethane (DDT, sum of isomers), acrinathrin, flumethrin, and permethrin (sum of isomers). Third, we added residues of

DOI: 10.1021/acs.jafc.6b02813
J. Agric. Food Chem. XXXX, XXX, XXX−XXX

Table 1. Residues (Alphabetically Ordered) of Plant Protection Products and Veterinary Substances Detected in Beeswax in Europe According to Various References/Sources

residue	pesticide/veterinary substance type according to PPDB/VSDB[a]	ref./source:	Nguyen et al.[15]	Simon-Delso et al.[16]	Ravoet et al.[5]	Chauzat and colleagues[17,18]	Wallner[2]	Serra-Bonvehi and Orantes-Bermejo[19]	Yáñez et al.[20]	Boi et al.[21]	Bogdanov and colleagues[8,22,23]	ILVO results
		origin of beeswax:	Belgium	Belgium	Belgium	France	Germany or other countries	Spain or other countries	Spain	Italy or third countries	Switzerland	Belgium or third countries
4,4′-dibromo benzophenone (4,4′-DBBP)	major degradation product of bromopropylate: acaricide				×							
acetamiprid[b]	insecticide								×			
acrinathrin[b]	insecticide, acaricide							×				
amitraz[b]	insecticide, acaricide, antiparasitic				×			×		×		
atrazine	herbicide		×									×
azinphos-methyl	insecticide, acaricide, molluscicide					×						
bitertanol	fungicide		×									
boscalid	fungicide			×	×							×
bromophos	insecticide				×							
bromopropylate	acaricide		×		×		×	×			×	×
captan	fungicide, bactericide			×								
carbendazim	fungicide, metabolite											×
carbofuran[b]	insecticide, nematicide, acaricide, metabolite											×
chloramphenicol[c]	antibiotic, antimicrobial, antibacterial, medicinal drug											×[c]
chlordimeform	acaricide, insecticide, ovicide							×				
chlorfenvinphos[b]	insecticide, acaricide, sheep dip				×			×		×		×
chlorothalonil	fungicide			×								
chlorpropham	herbicide, plant growth regulator											×
chlorpyriphos[b]	insecticide		×	×		×		×			×	×
coumaphos[b]	antiparasitic, insecticide, acaricide, anthelmintic, ectoparasiticide		×	×	×	×	×	×		×	×	×
cyfluthrin	insecticide					×						
cymiazole[b]	acaricide, ecoparasiticide									×		
cypermethrin[b]	insecticide, sheep dip					×						×
cyprodinil	fungicide			×								
DDT (sum of isomers)[b]	insecticide				×							×
deltamethrin[b]	insecticide, metabolite					×						
diethofencarb	fungicide											×
diethyltoluamide (DEET)	insecticide, repellent				×							×
dimethoate[b]	insecticide, acaricide, metabolite											×
endosulfan	insecticide, acaricide					×		×				×
fenitrothion	insecticide					×						
flufenacet	herbicide											×
flumethrin[b]	acaricide, insecticide, sheep dip, ectoparasiticide							×				×
flusilazole	fungicide		×									×
τ-fluvalinate[b]	insecticide, acaricide		×	×	×	×	×	×		×	×	×
hexachlorobenzene (HCB)[b]	fungicide, biocide, metabolite, wood preservative										×	

Table 1. continued

residue	pesticide/veterinary substance type according to PPDB/VSDB[a]	ref./source:	Nguyen et al.[15]	Simon-Delso et al.[16]	Ravoet et al.[5]	Chauzat and colleagues[17,18]	Wallner[2]	Serra-Bonvehi and Orantes-Bermejo[19]	Yáñez et al.[20]	Boi et al.[21]	Bogdanov and colleagues[8,22,23]	ILVO results
		origin of beeswax:	Belgium	Belgium	Belgium	France	Germany or other countries	Spain or other countries	Spain	Italy or third countries	Switzerland	Belgium or third countries
hexachlorocyclohexane (HCH, sum of the isomers α and δ)	insecticide, other substance				×							
imidacloprid	insecticide, antiparastic								×			×
indoxacarb	insecticide			×								
iodofenphos[b]	insecticide, acaricide										×	
iprodione	fungicide			×								×
lindane (= γ-HCH)	insecticide, acaricide		×		×	×						
linuron	herbicide											×
malathion	insecticide, acaricide, antiparasitic					×		×				
metazachlor	herbicide											×
mevinphos[b]	insecticide, acaricide					×						
parathion[b]	insecticide, acaricide					×						
parathion-methyl	insecticide				×							×
pentachloroanisole	major degradation product of pentachlorophenol (PCP): insecticide, herbicide, fungicide, molluscicide, plant growth regulator, wood preservative; degradation product of quintozene: fungicide											×
permethrin (sum of isomers)[b]	insecticide, antiparasitic											×
phenylphenol (*ortho*-) (= 2-phenylphenol)[c]	fungicide, other substance											×[c]
piperonyl butoxide	product performance enhancer			×	×							×
pirimicarb[b]	insecticide		×									
procymidone	fungicide					×						
propargite	acaricide				×							×
pyrazophos	fungicide											×
pyrimethanil	fungicide			×								
rotenone	insecticide, antiparasitic		×									
sulfonamides[d]	antibacterial, anti-infective, antibiotic, antimicrobial, medicinal drug											×
tebuconazole	fungicide, plant growth regulator			×								
tebufenozide	insecticide			×								
terbuthylazine	herbicide, microbiocide, algicide			×								×
terbuthylazine-2-hydroxy	metabolite of terbuthylazine: herbicide, microbiocide, algicide											×
tetradifon	acaricide, insecticide											×
thiamethoxam[b]	insecticide								×			×
thymol[b]	antimicrobial, antibacterial, antiseptic, miticide, repellent											×
trifloxystrobin	fungicide		×	×								
vinclozolin	fungicide					×						×

[a]PPDB, Pesticide Properties DataBase (http://sitem.herts.ac.uk/aeru/ppdb/en/atoz.htm); VSDB, Veterinary Substances DataBase (http://sitem.herts.ac.uk/aeru/vsdb/atoz.htm). [b]Substances selected in the "hazard characterization" point. [c]Only detected in beeswax imported in Belgium. [d]Only sulfadiazine was detected.

DOI: 10.1021/acs.jafc.6b02813
J. Agric. Food Chem. XXXX, XXX, XXX−XXX

Table 2. Acceptable Daily Intakes (ADIs) (mg/kg Body Weight/Day) of Chemical Substances (Alphabetically Ordered) Detected in Beeswax in Europe According to Different References/Sources (Table 1) and Their Respective Solubility in Water at 20 °C (mg/L) and Octanol/Water Partition Coefficient at pH 7 and 20 °C (log P)

	ADI according to					
chemical substance	PPDB/VSDB[a]	EMA[b]	EUPD[c]	another source	water-solubility according to PPDB/VSDB[a]	log P according to PPDB/VSDB[a]
4,4′-dibromo-benzophenone (4,4′-DBBP)	not listed		not listed		–[d]	4.93[d]
acetamiprid[e]	0.025		0.07		2950	0.8
acrinathrin[e]	0.01		0.01		0.0022	6.3
amitraz[e]	0.003	0.003	0.003		0.1	5.5
atrazine	0.02		0.02		35	2.7
azinphos-methyl	0.005		0.005		28	2.96
bitertanol	0.003		0.003		3.8	4.1
boscalid	0.04		0.04		4.6	2.96
bromophos	0.04		0.04		40	5.21
bromopropylate	0.03		0.03		0.1	5.4
captan	0.1		0.1		5.2	2.5
carbendazim	0.02		0.02		8	1.48
carbofuran[e]	0.00015		0.00015		322	1.8
chloramphenicol	–	no value can be estimated	not listed		2500	1.14
chlordimeform	–		not listed	0.003[f]	270	2.89
chlorfenvinphos[e]	0.0005		0.0005		145	3.8
chlorothalonil	0.015		0.015		0.81	2.94
chlorpropham	0.05		0.05		110	3.76
chlorpyriphos[e]	0.001		0.001		1.05	4.7
coumaphos[e]	no assigned value	0.00025	no toxicological information		1.5	3.86
cyfluthrin	0.003	0.003	0.003		0.0066	6
cymiazole[e]	–	0.001	not listed		150	0.6
cypermethrin[e]	0.05	0.015	0.05		0.009	5.3
cyprodinil	0.03		0.03		13	4
DDT (sum of isomers)[e]	0.01		0.01		0.006	6.91
deltamethrin[e]	0.01	0.01	0.01		0.0002	4.6
diethofencarb	0.43		0.43		27.64	2.89
diethyltoluamide (DEET)	–		not listed		912	2.18
dimethoate[e]	0.001		0.001		39800	0.704
endosulfan	0.006		0.006		0.32	4.75
fenitrothion	0.005		0.005		19	3.32
flufenacet	0.005		0.005		56	3.2
flumethrin[e]	0.004	0.0018	not listed		200	6.2
flusilazole	0.002		0.002		41.9	3.87
τ-fluvalinate[e]	0.005	0.0005	0.005		0.00103	7.02
hexachlorobenzene (HCB)[e]	–		no toxicological information	0.0005[g]	0.0047	3.93
hexachlorocyclohexane (HCH, sum of the isomers α and δ)	–		no toxicological information	0.005[h]	10[d,i]	4.14[d,i]
imidacloprid	0.06		0.06		610	0.57
indoxacarb	0.006		0.006		0.2	4.65
iodofenphos[e]	–		no toxicological information	0.0002[f]	0.1	5.51
iprodione	0.06		0.06		12.2	3.1
lindane (= γ-HCH)	0.003		no toxicological information		8.52	3.5
linuron	0.003		0.003		63.8	3
malathion	0.03		0.03		148	2.75
metazachlor	0.08		0.08		450	2.49
mevinphos[e]	0.0008		no toxicological information		600000	0.127
parathion[e]	0.0006		0.0006		12.4	3.83
parathion-methyl	0.003		no toxicological information		55	3
pentachloroanisole	–[j]		no toxicological information[j]	0.003[g,j]	0.354[d]	5.45[d]

DOI: 10.1021/acs.jafc.6b02813
J. Agric. Food Chem. XXXX, XXX, XXX−XXX

Table 2. continued

chemical substance	ADI according to PPDB/VSDB[a]	EMA[b]	EUPD[c]	another source	water-solubility according to PPDB/VSDB[a]	log P according to PPDB/VSDB[a]
permethrin (sum of isomers)[e]	0.05	0.01	no toxicological information		0.2	6.1
phenylphenol (*ortho*-) (= 2-phenylphenol)	0.4		0.4		700[d]	3.09[d]
piperonyl butoxide	0.2	0.2	no toxicological information		14.3	4.75
pirimicarb[e]	0.035		0.035		3100	1.7
procymidone	0.0028		0.0028		2.46	3.3
propargite	0.007		no assigned value due to missing data		0.215	5.7
pyrazophos	0.004		0.004		4.2	3.8
pyrimethanil	0.17		0.17		121	2.84
rotenone	–		no toxicological information		15	4.16
sulfonamides	–	no assigned value	not listed	0.05[k,l]	1500[k]	0.89[k]
tebuconazole	0.03		0.03		36	3.7
tebufenozide	0.02		0.02		0.83	4.25
terbuthylazine	0.004		0.004		6.6	3.4
terbuthylazine-2-hydroxy	–		not listed		not listed	not listed
tetradifon	–		no toxicological information	0.02[f]	0.078	4.61
thiamethoxam[e]	0.026		0.026		4100	−0.13
thymol[e]	0.03	no assigned value	0.03		596	3.96
trifloxystrobin	0.1		0.1		0.61	4.5
vinclozolin	0.01		0.005		3.4	3.02

[a]PPDB, Pesticide Properties DataBase (http://sitem.herts.ac.uk/aeru/ppdb/en/atoz.htm); VSDB, Veterinary Substances DataBase (http://sitem.herts.ac.uk/aeru/vsdb/atoz.htm). [b]EMA, European Medicines Agency (cf. maximum residue limit assessment reports: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/vet_mrl_search.jsp&mid=WC0b01ac058008d7ad). [c]EUPD, EU Pesticides Database (http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN). [d]ChemIDplus, a TOXNET database (http://chem.sis.nlm.nih.gov/chemidplus/). [e]Substances selected in the "hazard characterization" point. [f]According to Australian government.[32] [g]According to INERIS.[33] [h]According to Japan Analytical Chemistry Consultants.[34] [i]Value for δ-HCH. [j]Value for pentachlorophenol (PCP). [k]Value for sulfamethazine. [l]According to JECFA (http://apps.who.int/food-additives-contaminants-jecfa-database/chemical.aspx?chemID=3194).

substances authorized in beekeeping in at least one European Union Member State as veterinary substances or that may theoretically be used on the basis of the "cascade[10] system" and that are not selected according to the above-mentioned criteria (amitraz and thymol for the substances authorized in beekeeping, cypermethrin and deltamethrin for the substances concerned with the cascade[10] system).

Taking into account that three substances are mentioned twice above, the list of selected substances contains therefore the 22 residues mentioned in Table 3.

Exposure Assessment. As explained in the Introduction, given that residues in beeswax can be transferred to honey, the above residue selections, made on the basis of European beeswax contamination data, were considered for honey, too, as a worst-case scenario.

Table 3 shows the assessment of the consumers' (= adult of 60 kg bw) potential chronic exposure via food to the above selected residues, as well as the MRLs or proposed action limits taken into consideration for honey and beeswax.

The contribution of the honey and beeswax to the daily consumers' (= adult of 60 kg bw) exposure varies from 0.51 μg (i.e., 0.5 μg from the daily consumption of honey + 0.013 μg from the daily consumption of beeswax) for chlorfenvinphos, cymiazole, dimethoate, hexachlorobenzene (HCB), iodofenphos, mevinphos, parathion, and permethrin (sum of isomers) to 10.26 μg (i.e., 10 μg from the daily consumption of honey + 0.258 μg from the daily consumption of beeswax) for amitraz, on the basis of the consumption scenario of 50 g of honey and 1.29 g of beeswax per day (representing the 95th percentile of the chronic daily intakes of an adult of 60 kg bw).

With regard to flumethrin, τ-fluvalinate, and thymol, no MRL due to the veterinary use of these substances is required in honey according to European Commission Regulation (EU) 37/2010.[25] The consumers' exposure to these substances through the consumption of honey and beeswax could not have been calculated. The risk for the consumer associated with these substances is, however, discussed below.

Risk Characterization. In a general way, and on the basis of the data mentioned in Table 3 and related to the various above selected residues, the food consumption of contaminated honey and beeswax does not compromise the consumer's health, assuming no exposure via other foodstuffs (e.g., meat, milk, eggs). As a matter of fact, the contribution of the consumption (95th percentile) of honey and beeswax to consumers' (= adult of 60 kg bw) exposure amounts to a maximum of 34% of the ADI for coumaphos: 33.33% via the consumption of 50 g of honey plus 0.86% via the consumption of 1.29 g of beeswax.

On the other hand, if the whole range of foodstuffs is considered, the highest TMDI is that of flumethrin, which corresponds to 100% of the ADI.[26] It is true only on the basis of foodstuffs other than honey and beeswax. In that case, an

DOI: 10.1021/acs.jafc.6b02813
J. Agric. Food Chem. XXXX, XXX, XXX−XXX

Table 3. Estimation of Consumers' Potential Chronic Exposure to the Various Residues (Alphabetically Ordered) Selected in the Hazard Characterization Step and Maximum Residue Limits (MRL) or Proposed Action Limits Selected for Honey and Beeswax[a]

	substance authorized in the EU		MRL in honey					daily contribution of	
residue	in beekeeping[b]	as a plant protection product[c]	due to veterinary use[d] (μg/kg)	due to plant protection product use[c] (μg/kg)	ADI (μg/60 kg bw person)	TMDI[d] (μg/person, (% ADI))	MRL or proposed action limit for honey and beeswax (μg/kg)	50 g of honey (μg, (% ADI))	1.29 g of beeswax (μg, (% ADI))
acetamiprid	no	yes		50 (= LLAD)	1500		50	2.5 (0.17)	0.065 (0.004)
acrinathrin	no	yes		50 (= LLAD)	600		50	2.5 (0.42)	0.065 (0.011)
amitraz	yes	no	200	10 (= default MRL)	180	174.6[e,f] (97)	200	10[g] (5.56)	0.258 (0.143)
carbofuran	no	no		50 (= LLAD)	9		50	2.5 (27.78)	0.065 (0.722)
chlorfenvinphos	no	no		10 (= LLAD)	30		10	0.5 (1.67)	0.013 (0.043)
chlorpyrifos	no	yes		50 (= LLAD)	60		50	2.5 (4.17)	0.065 (0.108)
coumaphos	yes	no	100	10 (= default MRL)	15	1.95[f] (13)	100	5[h] (33.33)	0.129 (0.860)
cymiazole	no	no, because not listed[i]			60		lowest possible LOQ		
cypermethrin	no	yes		50 (= LLAD)	900	543[j] (61)	50	2.5 (0.28)	0.065 (0.007)
DDT (sum of isomers)	no	no		50	600		50	2.5 (0.42)	0.065 (0.011)
deltamethrin	no	yes		30 (= LLAD)	600	480[k] (80)	30	1.5 (0.25)	0.039 (0.007)
dimethoate	no	yes		10 (= default MRL)	60		10	0.5 (0.83)	0.013 (0.022)
flumethrin	yes	no, because not listed[i]	no MRL required[l]		108	108 (100)	lowest possible LOQ[l]	na[l]	na[l]
τ-fluvalinate	yes	yes	no MRL required	50 (= LLAD)	30	13[m] (43)	50	2.5 (8.33)	0.065 (0.217)
hexachlorobenzene (HCB)	no	no		10 (= default MRL)	30		10	0.5 (1.67)	0.013 (0.043)
iodofenphos	no	no		10 (= default MRL)	12		10	0.5 (4.17)	0.013 (0.108)
mevinphos	no	no		10 (= default MRL)	48		10	0.5 (1.04)	0.013 (0.027)
parathion	no	no		10 (= default MRL)	36		10	0.5 (1.39)	0.013 (0.036)
permethrin (sum of isomers)	no	no		10 (= default MRL)	600	383 (64)	10	0.5 (0.08)	0.013 (0.002)
pirimicarb	no	yes		50 (= LLAD)	2100		50	2.5 (0.12)	0.065 (0.003)
thiamethoxam	no	yes		50 (= LLAD)	1560		50	2.5 (0.16)	0.065 (0.004)
thymol	yes	yes	no MRL required	no MRL required	1800	na[n]	na[n]	na[n]	na[n]

[a]EU, European Union; ADI, acceptable daily intake; bw, body weight; LLAD, lower limit of analytical determination; LOQ, limit of quantification; MRL, maximum residue limit; na, nonapplicable; TMDI, theoretical maximum daily intake. [b]According to EMA.[3] [c]According to EUPD: EU Pesticides Database (http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN) and European Regulation (EC) 396/2005.[11] [d]According to European Commission Regulation (EU) 37/2010.[25] [e]Included the contribution of the use as plant protection product. [f]The contribution of 20 g of honey is already included in the TMDI. [g]The additional contribution to the TMDI is 6 μg, as 4 μg is already included in the TMDI. [h]The additional contribution to the TMDI is 3 μg, as 2 μg is already included in the TMDI. [i]"No, because not listed" means that the substance is not mentioned in the list and therefore it cannot be used as a plant protection product in the EU, whereas "no" means that the substance is mentioned in the list as a "not approved" substance. [j]Included the contribution of the use as a plant protection product (280 μg/person). [k]Included the contribution of the use as a plant protection product (346 μg/person). [l]According to EMA,[26] the establishment of a MRL for honey was not necessary because the residue levels in honey were generally lower than the limit of detection of the analytical method (1−2 μg/kg), and this while at the same time the concentration of flumethrin in the beeswax from the same treated hives amounted to 130 μg/kg. However, because the TMDI represents 100% of the ADI without taking into account the contribution of the consumption of honey and beeswax and because this substance is quite toxic for humans (ADI = 0.0018 mg/kg bw/day), it is recommended that "zero tolerance" is applied for honey and for beeswax. [m]Estimated value of the intake from treated agricultural products.[27] [n]Because no MRL is required for the veterinary use for any animal species,[28] the TMDI has not been determined and no action limit is necessary for honey and beeswax.

DOI: 10.1021/acs.jafc.6b02813
J. Agric. Food Chem. XXXX, XXX, XXX−XXX

additional contribution to the TMDI through the consumption of honey and beeswax should be excluded. Therefore, it is recommended that "zero tolerance" is applied to residues of flumethrin in honey and in beeswax, particularly because this substance is quite toxic to humans: ADI = 0.0018 mg/kg bw/day and despite the fact that the establishment of a MRL for honey was not necessary according to EMA,[26] given its lipophilic character. EMA[26] indicates that the residue levels in honey were generally lower than the limit of detection of the analytical method (1−2 μg/kg), while at the same time the concentration of flumethrin in the beeswax from the same treated hives amounted to 130 μg/kg.

The TMDI of amitraz exceeds slightly the ADI if the consumption of 50 g of honey and 1.29 g of beeswax (= representing the 95th percentile of the chronic daily intakes of an adult of 60 kg bw) is added. The TMDI amounts then to 100.5% of the ADI.

The third highest TMDI (in percentage of the ADI) is that of deltamethrin. The TMDI amounts to 80.3% of the ADI when the consumption of 50 g of honey and 1.29 g of beeswax (= representing the 95th percentile of the chronic daily intakes of an adult of 60 kg bw) is added.

With regard to τ-fluvalinate, given that this substance is toxic to humans, ADI = 0.0005 mg/kg bw/day and that a MRL of 50 μg/kg for honey, due to the plant protection product use of this substance, is set out by European Regulation (EC) 396/2005,[11] we considered that this value should be applied as the action limit for honey and beeswax, despite the fact that the establishment of a MRL for honey due to the veterinary use of this substance was not necessary according to EMA,[27] given its lipophilic character. EMA[27] indicates that transfer of τ-fluvalinate residues from beeswax to honey was shown to be negligible.

With regard to thymol, no MRL is required for veterinary use in any animal species, given that this substance is possibly naturally present in foods, can be used as a food flavoring, and is quickly metabolized and eliminated.[28] The TMDI was therefore not determined, and no action limit is necessary.

In conclusion, taking into account the scenarios considered in Table 3, the food consumption of honey and beeswax contaminated by the 22 residues selected and considered separately does not compromise consumers' health (for an adult of 60 kg body weight). Specifically, "zero tolerance" should be applied as the action limit to residues of flumethrin in honey and in beeswax. It is recommended that operators in the beekeeping sector meet limits set out in Table 3 and, if necessary, they should take measures to reduce beeswax contamination by residues. For instance, they should renew more frequently or purify[29,30] the beeswax they use, or they could use food synthetic waxes. The proposed action limits should be applied uniformly within the European Union given that values mentioned in Table 3 are relevant for the European level. At the same time, due to the limited number of available references on the topic, efforts are needed to better monitor beeswax contamination by residues and to explore potential adverse synergic effects between chemical residues present in honey and/or in beeswax to refine this scenario analysis.

UNCERTAINTIES

Uncertainties in this paper concern the facts that

- the ADI or solubility of substances found in beeswax is not always known, which might influence the selection carried out in the hazard characterization step;
- the TMDI is not always known for the substances selected in the hazard characterization step;
- there are few data concerning the presence of residues in beeswax and the presence of a residue not listed in the hazard identification step can therefore not be excluded;
- the performance of the analytical methods, especially the LODs, used in the different references/sources cited in this paper could have influenced the hazard identification step; and
- consumers could be exposed to different residues at the same time through the consumption of contaminated honey and beeswax and that adverse synergistic effects could eventually occur. These potential "cocktail effects" were not taken into account in this paper.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We acknowledge the members of the working group (Advice 12-2015,[31] dossier SciCom 2014/13) for their collaboration and of the Scientific Committee of the FASFC for their supervision and validation of this study.

ABBREVIATIONS USED

ADI, acceptable daily intake; bw, body weight; CVMP, Committee for Medicinal Products for Veterinary Use; EMA, European Medicines Agency; FASFC, Federal Agency for the Safety of the Food Chain; ILVO, Institute for Agricultural and Fisheries Research; JECFA, Joint FAO/WHO Expert Committee on Food Additives; LOD, limit of detection; MRL, maximum residue limit; TMDI, theoretical maximum daily intake.

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