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RESEARCH ARTICLE

Title and authorship (single page)

Residues in beeswax: a health risk for the consumer of honey and beeswax?

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Abstract and keywords (single page)

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 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, the "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 which 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 non-volatile[2]. Veterinary substances can also be applied to honeybee colonies to control other bee 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, like antibiotics, not allowed in the 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 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 i.e. through consumption of “comb honey”, “chunk honey or cut comb in honey” or as food additive E901[7]. The latter is used as glazing agent in the preparation of pastries, for the treatment of some fruits, as food supplement (capsules and tablets) and as flavor carrier. There is currently no legal requirement concerning the possible presence of plant protection product and veterinary substance residues in beeswax, neither at European level, nor at Belgian level.

In order to prevent and/or control those potential risks in the food chain it is proposed to implement action limits to 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 the honey to which residues levels are generally low[9]. We identified therefore residues which 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 b.w. 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 (including Safety information)

Based on 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 intake (ADI), water solubility and octanol/water partition coefficient were summarized in table 2.

From that list, plant protection products or veterinary substances were selected (see the hazard characterization step and table 3) based on 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 out for honey, based on veterinary use of the substance, this value was also selected as 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 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 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), the "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 per person, i.e. 0.022 g per kg body weight for a 60 kg weighing 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 the 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 of beeswax were calculated on 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, the consumers' exposure through the consumption of honey and beeswax is compared to the ADI.

Results/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.

In Belgium, Nguyen et al.[15] looked for the presence of 55 pesticides residues in 48 beeswax samples, collected between March 2004 and March 2005 and originating from 16 randomly selected apiaries in the Walloon Region (southern part of Belgium); in each apiary 3 randomly selected beehives were sampled. The three most commonly found residues were flusilazole, bromopropylate and coumaphos, with a detection frequency 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 north of the Walloon Region (southern part of Belgium) and in the Brussels-Capital Region (central part of Belgium). τ-Fluvalinate, coumaphos and boscalid were the

three most commonly found residues, with a detection frequency 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 part of 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 a detection frequency of 100%, 90%, 70% and 70%, respectively. In addition, other data coming from analyses carried out between 2004 and 2014 are available at the Institute for Agricultural and Fisheries Research (ILVO). When considered separately, the analyses only pertain 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 the North to the South of France were selected and in each of these departments 5 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 a detection frequency 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 a detection frequency 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 a detection frequency 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 a detection frequency 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 (south east of Spain). Thiamethoxam, acetamiprid and imidacloprid were found with a detection frequency 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 a detection frequency 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 4 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 organo-phosphorous 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 a detection frequency 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. But it should be noted that the five most commonly found residues according to this study (coumaphos, τ-fluvalinate, chlorpyriphos, chlorothalonil, amitraz) are well included in our scenario analysis according to the other references/sources above mentioned.

Hazard characterization

The ADI of the 68 substances which have already been detected in beeswax in Europe, according to different references/sources, is shown in table 2.

Based on table 2, the most toxic[a] substances for humans, considering chronic oral exposure (i.e. compounds for which the ADI is below or equal to 0.001 mg/kg b.w./day), are carbofuran, iodofenphos, coumaphos, chlorfenvinphos, τ-fluvalinate,

[a] If several ADI values are mentioned for a same residue in table 2, only the lowest ADI value is taken into consideration.

hexachlorobenzene (HCB), parathion, mevinphos, chlorpyriphos, cymiazole and dimethoate (in decreasing order of toxicity). Substances for which no toxicity data are available were excluded.

Based on 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. Firstly, we added the 5 most hydrophilic substances (based on data of water-solubility in table 2), which consequently most likely concentrate in honey, namely mevinphos and dimethoate, already above mentioned based on their toxicity, thiamethoxam, pirimicarb and acetamiprid. Secondly, we added the 5 most lipophilic substances (based on octanol/water partition coefficients in table 2), which consequently most likely concentrate in beeswax, namely τ-fluvalinate, already above mentioned based on its toxicity, dichlorodiphenyltrichloroethane (DDT, sum of isomers), acrinathrin, flumethrin and permethrin (sum of isomers). Thirdly, we added residues of substances authorized in beekeeping in at least one European Union Member State as veterinary substances or which 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 by the "cascade[10] system").

Taking into account that three substances are mentioned twice above, the list of the 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 residues selection, made based on European beeswax contamination data, was considered for honey too, as a worst-case scenario.

Table 3 shows the assessment of the consumers' (= adult of 60 kg b.w.) potential chronic exposure via the food to the above selected residues, as well as the MRL's 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 b.w.) exposure varies from 0.51 µg (i.e. 0.5 µg from the daily consumption of 50 g honey + 0.013 µg from the daily consumption of 1.29 g beeswax) for chlorfenvinphos, cymiazole, dimethoate, hexachlorobenzene (HCB), iodofenphos, mevinphos, parathion and permethrin (sum of isomers), and to 10.26 µg (i.e. 10 µg from the daily consumption of 50 g honey + 0.258 µg from the daily consumption of 1.29 g beeswax) for amitraz, on the basis of the consumption scenario of 50 g honey and 1.29 g beeswax per day (= representing both the 95th percentile of the chronic daily intakes of an adult of 60 kg b.w.).

Concerning 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 based on 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 the consumers' (= adult of 60 kg b.w.) exposure amounts to maximum 34% of the ADI for coumaphos: 33,33% via the consumption of 50 g honey plus 0,86% via the consumption of 1,29 g 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 other foodstuffs than honey and beeswax. In that case, an additional contribution to the TMDI through the consumption of honey and beeswax should be excluded. Therefore, it is recommended that the “zero tolerance” is applied to residues of flumethrin in honey and in beeswax. This, particularly since this substance is quite toxic to humans: ADI = 0.0018 mg/kg b.w./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 to 2 µg/kg), and this while at the same time the concentration of flumethrin in the beeswax coming from the same treated hives amounted up to 130 µg/kg.

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

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

Concerning τ-Fluvalinate, given that this substance is toxic to humans: ADI = 0.0005 mg/kg b.w./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 action limit for honey and beeswax. This, 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.

Concerning 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 flavouring 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 the consumer's health (for an adult of 60 kg body weight). Specifically, the "zero tolerance" should be applied as 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 the 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. In the same time, due to the limited number of available references on the topic, efforts are needed to better monitor the 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 fact that the ADI and/or solubility of substances found in beeswax is not always known, which might influence the selection carried out in the hazard characterization step;
- the fact that the TMDI is not always known for the substances selected in the hazard characterization step;
- the fact that there are not many data concerning the presence of residues in beeswax, and that the presence of a residue not listed in the hazard identification step can therefore not be excluded;
- the fact that 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;
- the fact that 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.

Abbreviations Used

ADI: Acceptable Daily Intake

b.w.: 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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501

502 **Figure captions**

503 None

Tables

Table 1. Residues (alphabetically ordered) of plant protection products and veterinary substances detected in beeswax in Europe according to various references/ sources.

			Reference/source									
			Nguyen *et al.*[15]	Simon-Delso *et al.*[16]	Ravoet *et al.*[5]	Chauzat and colleagues [17,18]	Wallner[2]	Serra-Bonvehí 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
Residue	**Pesticide/Veterinary substance type according to PPDB/VSDB[a]**											
4,4'-dibromo benzophenone (4,4'-DBBP)	Major degradation product of bromopropylate: acaricide				X							
Acetamiprid[b]	Insecticide								X			
Acrinathrin[b]	Insecticide, Acaricide							X				

Amitraz[b]	Insecticide, Acaricide, Antiparasitic				X			X		X		
Atrazine	Herbicide		X									X
Azinphos-methyl	Insecticide, Acaricide, Molluscicide					X						
Bitertanol	Fungicide		X									
Boscalid	Fungicide			X	X							X
Bromophos	Insecticide				X							
Bromopropylate	Acaricide		X		X		X	X			X	X
Captan	Fungicide, Bactericide			X								
Carbendazim	Fungicide, Metabolite											X
Carbofuran[b]	Insecticide, Nematicide, Acaricide, Metabolite											X
Chloramphenicol[c]	Antibiotic,											X[c]

	Antimicrobial, Antibacterial, Medicinal drug											
Chlordimeform	Acaricide, Insecticide, Ovicide							X				
Chlorfenvinphos[b]	Insecticide, Acaricide, Sheep dip				X			X		X		X
Chlorothalonil	Fungicide			X								
Chlorpropham	Herbicide, Plant growth regulator											X
Chlorpyriphos[b]	Insecticide		X	X		X		X			X	X
Coumaphos[b]	Antiparasitic, Insecticide, Acaricide, Anthelmintic, Ectoparasiticide		X	X	X	X	X	X		X	X	X
Cyfluthrin	Insecticide					X						

Cymiazole[b]	Acaricide, Ecoparasiticide									X		
Cypermethrin[b]	Insecticide, Sheep dip					X						X
Cyprodinil	Fungicide			X								
DDT (sum of isomers)[b]	Insecticide				X							X
Deltamethrin[b]	Insecticide, Metabolite					X						
Diethofencarb	Fungicide											X
Diethyltoluamide (DEET)	Insecticide, Repellent				X							X
Dimethoate[b]	Insecticide, Acaricide, Metabolite											X
Endosulfan	Insecticide, Acaricide					X		X				X
Fenitrothion	Insecticide					X						
Flufenacet	Herbicide											X

Flumethrin[b]	Acaricide, Insecticide, Sheep dip, Ectoparasiticide							X				X
Flusilazole	Fungicide		X									X
τ-Fluvalinate[b]	Insecticide, Acaricide		X	X	X	X	X	X		X	X	X
Hexachlorobenzene (HCB)[b]	Fungicide, Biocide, Metabolite, Wood preservative										X	
Hexachlorocyclohexane (HCH, sum of the isomers α and δ)	Insecticide, Other substance				X							
Imidacloprid	Insecticide, Antiparastic								X			X
Indoxacarb	Insecticide			X								
Iodofenphos[b]	Insecticide, Acaricide										X	
Iprodione	Fungicide			X								X

Lindane (= γ-HCH)	Insecticide, Acaricide		X		X	X						
Linuron	Herbicide											X
Malathion	Insecticide, Acaricide, Antiparasitic					X		X				
Metazachlor	Herbicide											X
Mevinphos[b]	Insecticide, Acaricide					X						
Parathion[b]	Insecticide, Acaricide					X						
Parathion-methyl	Insecticide				X							X
Pentachloroanisole	Major degradation product of pentachlorophenol (PCP): Insecticide, Herbicide, Fungicide, Molluscicide, Plant growth regulator, Wood preservative;											X

	Degradation product of quintozene: fungicide											
Permethrin (sum of isomers)[b]	Insecticide, Antiparasitic											X
Phenylphenol (*ortho*-) (= 2-phenylphenol)[c]	Fungicide, Other substance											X[c]
Piperonyl butoxyde	Product performance enhancer			X	X							X
Pirimicarb[b]	Insecticide		X									
Procymidone	Fungicide					X						
Propargite	Acaricide				X							X
Pyrazophos	Fungicide											X
Pyrimethanil	Fungicide			X								
Rotenone	Insecticide, Antiparasitic		X									

Sulfonamides[d]	Antibacterial, Anti-infective, Antibiotic, Antimicrobial, Medicinal drug											X
Tebuconazole	Fungicide, Plant growth regulator			X								
Tebufenozide	Insecticide			X								
Terbuthylazine	Herbicide, Microbiocide, Algicide			X								X
Terbuthylazine-2-hydroxy	Metabolite of terbuthylazine: Herbicide, Microbiocide, Algicide											X
Tetradifon	Acaricide, Insecticide											X
Thiamethoxam[b]	Insecticide								X			
Thymol[b]	Antimicrobial,											X

	Antibacterial, Antiseptic, Miticide, Repellent											
Trifloxystrobin	Fungicide		X	X								
Vinclozolin	Fungicide					X						X

Legend:

[a] *PPDB: Pesticide Properties DataBase* (http://sitem.herts.ac.uk/aeru/ppdb/en/atoz.htm) or *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.

Table 2. Acceptable daily intakes (ADI's), in mg/kg b.w./day, of chemical substances (alphabetically ordered) detected in beeswax in Europe according to different references/sources (table 1) and their respective solubility in water (mg/l) and octanol/water partition coefficient (log P).

Chemical substance	ADI in mg/kg b.w./day according to PPDB/VSDB[a]	ADI in mg/kg b.w./day according to EMA[b]	ADI in mg/kg b.w./day according to EUPD[c]	ADI in mg/kg b.w./day according to another source	Water-solubility at 20°C (mg/l) according to PPDB/VSDB[a]	Octanol/water partition coefficient at pH 7 and at 20°C (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		2,950	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	-	Not any value can be estimated	Not listed		2,500	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		39,800	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		600,000	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]
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 butoxyde	0.2	0.2	No toxicological information		14.3	4.75
Pirimicarb[e]	0.035		0.035		3,100	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]	1,500[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		4,100	-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

Legend:

ADI = acceptable daily intake; b.w. = body weight.

[a] *PPDB: Pesticide Properties DataBase* (http://sitem.herts.ac.uk/aeru/ppdb/en/atoz.htm) or *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).

Table 3. Estimation of the 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.

Residue	Substance authorized in beekeeping in the EU[a]	Substance authorized as a plant protection product in the EU[b]	MRL in honey due to veterinary use (µg/kg)[c]	MRL in honey due to plant protection product use (µg/kg)[b]	ADI (µg/person (of 60 kg b.w.))	TMDI (µg/person, (% ADI))[c]	MRL or proposed action limit for honey and beeswax (µg/kg)	Daily contribution of 50 g honey (µg, (% ADI))	Daily contribution of 1.29 g beeswax (µg, (% ADI))
Acetamiprid	No	Yes		50 (= LLAD)	1,500		**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[d,e] (97)	**200**	10[f] (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[e] (13)	**100**	5[g] (33.33)	0.129 (0.860)
Cymiazole	No	No, because not listed[h]			60		**Lowest possible LOQ**		

Cypermethrin	No	Yes		50 (= LLAD)	900	543[l] (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[l] (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[h]	No MRL required[k]		108	108 (100)	**Lowest possible LOQ[k]**	na[k]	na[k]
τ-Fluvalinate	Yes	Yes	No MRL required	50 (= LLAD)	30	13[l] (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)	2,100		**50**	2.5 (0.12)	0.065 (0.003)
Thiamethoxam	No	Yes		50 (= LLAD)	1,560		**50**	2.5 (0.16)	0.065 (0.004)
Thymol	Yes	Yes	No MRL required	No MRL required	1,800	na[m]	**na[m]**	na[m]	na[m]

Legend:

ADI = acceptable daily intake; b.w. = body weight; LLAD = lower limit of analytical determination; LOQ = limit of quantification; MRL = maximum residue limit; MRPL = minimum required performance limit; na = non applicable; TMDI = theoretical maximum daily intake.

[a] According to EMA[3].

[b] 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].

[c] According to European Commission Regulation (EU) 37/2010[25].

[d] Included the contribution of the use as plant protection product.

[e] The contribution of 20 g honey is already included in the TMDI.

[f] The additional contribution to the TMDI is 6 µg, as 4 µg are already included in the TMDI.

[g] The additional contribution to the TMDI is 3 µg, as 2 µg are already included in the TMDI.

[h] 'No, because not listed' means that the substance is not mentioned in the list and therefore it can not be used as a plant protection product in the European Union (EU), while 'No' means that the substance is mentioned in the list as a *not approved* substance.

[i] Included the contribution of the use as plant protection product (280 µg/person).

[j] Included the contribution of the use as plant protection product (346 µg/person).

[k] According to EMA[26], the establishment of a MRL for honey was not necessary since the residue levels in honey were generally lower than the limit of detection of the analytical method (1 to 2 µg/kg), and this while at the same time the concentration of flumethrin in the beeswax coming from the same treated hives amounted up to 130 µg/kg. However, since the TMDI represents 100 % of the ADI without taking into account the contribution of the consumption of honey and beeswax and since this substance is quite toxic for humans (ADI = 0.0018 mg/kg b.w./day), it is recommended that the "zero tolerance" is applied for honey and for beeswax.

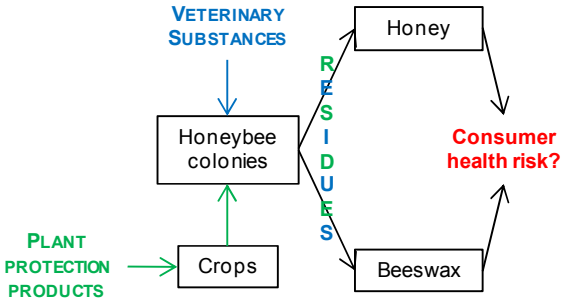
[l] Estimated value of the intake from treated agricultural products[27].

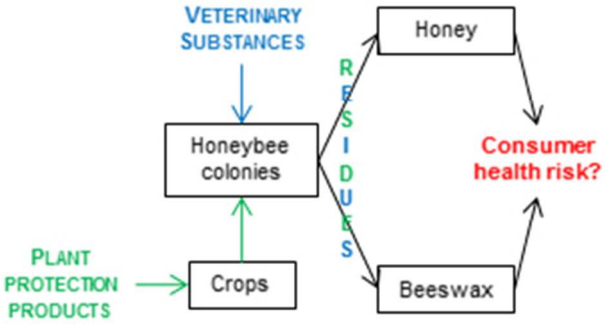
[m] Since no MRL is required for the veterinary use for any animal species[28], the TMDI has not been determined and no action limit is necessary for honey and beeswax.

Figure graphics

None

Graphic for table of contents





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