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Peer review of the pesticide risk assessment for bees for the active substance thiamethoxam considering the uses as seed treatments and granules

European Food Safety Authority (EFSA)

Abstract

The EFSA was asked by the European Commission to perform an updated risk assessment of neonicotinoids, including thiamethoxam, as regards the risk to bees, as a follow-up of previous mandates received from the European Commission on neonicotinoids. The context of the evaluation was that required by the European Commission in accordance with Article 21 of Regulation (EC) No 1107/2009 to review the approval of active substances in light of new scientific and technical knowledge and monitoring data. In this context and in accordance with Article 31 of Regulation (EC) No 178/2002, EFSA has been previously asked by European Commission to organise an open call for data in order to collect new scientific information as regards the risk to bees from the neonicotinoid pesticide active substances clothianidin, thiamethoxam and imidacloprid applied as seed treatments and granules in the EU. The conclusions were reached on the basis of the evaluation of the supported uses as an insecticide of thiamethoxam applied as seed treatments and granules, on the new relevant data collected in the framework of the open call organised by EFSA and on the updated literature search performed by EFSA. The reliable endpoints, appropriate for use in regulatory risk assessment derived from the submitted studies and literature data as well as any other relevant data available at national level and made available to EFSA, are presented. Concerns are identified.

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Keywords: thiamethoxam, neonicotinoid, bee, seed, granule, peer review, risk assessment, pesticide.

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Summary

Thiamethoxam was included in Annex I to Directive 91/414/EEC on 1 February 2007 by Commission Directive 2007/6/EC and has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011. A specific conclusion has been issued by European Food Safety Authority (EFSA) on the risk assessment for bees as regards the authorised uses applied as seed treatments and granules.

The specific provisions of the approval were amended by Commission Implementing Regulation (EU) No 485/2013, to restrict the uses of clothianidin, thiamethoxam and imidacloprid, and to provide for specific risk mitigation measures for the protection of bees and to limit the use of the plant protection products containing these active substances to professional users. In particular, the uses as seed treatment and soil treatment of plant protection products containing clothianidin, thiamethoxam or imidacloprid have been prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing these active substances have been prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering. Furthermore, the European Commission requested EFSA to provide conclusions concerning an updated risk assessment for bees for clothianidin, thiamethoxam and imidacloprid, taking into account all uses other than seed treatments and granules, including foliar spray uses as mentioned in recital 7 of Commission Implementing Regulation (EU) No 485/2013. EFSA finalised its conclusion on the risk assessment for bees as regards all uses other than seed treatments and granules in July 2015.

It was a specific provision of the Commission Implementing Regulation (EU) No 485/2013 that the applicant was also required to submit to the European Commission further ecotoxicological studies by 31 December 2014. The outcome of the peer review of the confirmatory data assessment was reported in a Technical Report and a conclusion published in 2016.

Furthermore, according to recital 16 of Regulation (EU) No 485/2013, within 2 years from the date of entry into force of that Regulation, the European Commission foresees to initiate without undue delay a review of the new scientific information available.

For this purpose, with reference to Article 31 of Regulation (EC) No 178/2002 and in accordance with Article 21 of Regulation (EC) No 1107/2009, the European Commission requested EFSA to organise an open call for data in order to collect new scientific information as regards the risk to bees from the neonicotinoid pesticide active substances clothianidin, thiamethoxam and imidacloprid applied as seed treatments and granules in the European Union (EU).

The European Commission requested EFSA to provide conclusions concerning an updated risk assessment for bees for the three neonicotinoids (namely clothianidin, imidacloprid and thiamethoxam), taking into account:

- the new relevant data collected in the framework of the specific open call for data,
- any other new data from studies, research and monitoring activities that are relevant to the uses under consideration,
- the EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera, Bombus* spp. and solitary bees).

EFSA also considered the data available from a systematic literature review performed in June 2016, in order to collect all published scientific literature relevant for the current evaluation.

For exposure via residues in pollen and nectar, a low risk was concluded for some bee groups/use/scenario combinations, while a high risk was concluded in other cases. In the majority of cases where a higher tier (tier 3) risk assessment could be performed, the available data did not allow a low risk to be demonstrated, despite not indicating a clear high risk.

For the exposure via residues from dust drift, a low risk was concluded for those uses that foresee planting in permanent greenhouses. For all other uses, either a high risk was concluded or the assessment could not be finalised.

For exposure via water consumption, a low risk to honeybees was concluded for all uses via residues in puddles. A low risk to honeybees was concluded for residues in guttation fluid for the uses to sugar beet. A high risk was concluded for all other uses. A risk assessment for honeybees from exposure via surface water could not be performed.

Refer to Table 21 in the main text of the conclusion for crop-specific conclusion achieved at each assessment tier.

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Background

Thiamethoxam was included in Annex I to Directive 91/414/EEC[1] on 1 February 2007 by Commission Directive 2007/6/EC[2] and has been deemed to be approved under Regulation (EC) No 1107/2009[3], in accordance with Commission Implementing Regulation (EU) No 540/2011[4], as amended by Commission Implementing Regulation (EU) No 541/2011[5] and 487/2014[6]. A specific conclusion has been issued by European Food Safety Authority (EFSA) on the risk assessment for bees as regards the authorised uses applied as seed treatments and granules (EFSA, 2013a).

The specific provisions of the approval were amended by Commission Implementing Regulation (EU) No 485/2013[7], to restrict the uses of clothianidin, thiamethoxam and imidacloprid, to provide for specific risk mitigation measures for the protection of bees and to limit the use of the plant protection products containing these active substances to professional users. In particular, the uses as seed treatment and soil treatment of plant protection products containing clothianidin, thiamethoxam or imidacloprid have been prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing these active substances have been prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering. Furthermore, the European Commission requested EFSA to provide conclusions concerning an updated risk assessment for bees for clothianidin, thiamethoxam and imidacloprid, taking into account all uses other than seed treatments and granules, including foliar spray uses as mentioned in recital 7 of Commission Implementing Regulation (EU) No 485/2013. EFSA finalised its conclusion on the risk assessment for bees as regards all uses other than seed treatments and granules in July 2015 (EFSA, 2015a).

It was a specific provision of the Commission Implementing Regulation (EU) No 485/2013 that the applicant was also required to submit to the European Commission further ecotoxicological studies by 31 December 2014. The outcome of the peer review of the confirmatory data assessment was reported in a Technical Report and a conclusion published in 2016.

Furthermore, according to recital 16 of Regulation (EU) No 485/2013, within 2 years from the date of entry into force of that Regulation, the European Commission foresees to initiate without undue delay a review of the new scientific information available.

For this purpose, with reference to Article 31 of Regulation (EC) No 178/2002[8] and in accordance with Article 21 of Regulation (EC) No 1107/2009, in February 2015, the European Commission requested EFSA to organise an open call to collect new scientific information as regards the risk to bees from the neonicotinoid pesticide active substances clothianidin, thiamethoxam and imidacloprid applied as seed treatments and granules in the European Union (EU) (EFSA, 2015b) and then, following a second mandate received in November 2015, EFSA was requested to provide conclusions concerning an updated risk assessment for bees for the three neonicotinoids (namely clothianidin, imidacloprid and thiamethoxam).

The new relevant data collected in the framework of the open call for data and any other new data from studies, research and monitoring activities relevant for the uses under consideration were taken

[1] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32.

[2] Commission Directive 2007/6/EC of 14 February 2007 amending Council Directive 91/414/EEC to include metrafenone Bacillus subtilis, spinosad and thiamethoxam as active substances. OJ L 43, 15.2.2007, p. 13–18.

[3] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

[4] Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.

[5] Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11/6/2011, p.187–188.

[6] Commission Implementing Regulation (EU) No 487/2014 of 12 May 2014 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances Bacillus subtilis (Cohn 1872) Strain QST 713, identical with strain AQ 713, clodinafop, metrafenone, pirimicarb, rimsulfuron, spinosad, thiamethoxam, tolclofos-methyl and triticonazole. OJ L 138, 13.5.2014, p. 72–74.

[7] Commission Implementing Regulation (EU) No 485/2013 of 24 May 2013 amending Implementing Regulation (EU) No 540/2011, as regards the conditions of approval of the active substances clothianidin, thiamethoxam and imidacloprid, and prohibiting the use and sale of seeds treated with plant protection products containing those active substances. OJ L 139, 25.5.2013, p. 12–26.

[8] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1/2/2002, p. 1–24.

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into account. To address the mandate, EFSA also considered the data available from a previous systematic literature review, outsourced in 2013 (Fryday et al., 2015). Furthermore, an update of this systematic review was performed in June 2016, in order to collect all published scientific literature relevant for the current evaluation (EFSA, 2018a). The EFSA guidance document on the risk assessment of plant protection products on bees (EFSA, 2013c) was used for the current evaluation.

A consultation on the evaluation and preliminary conclusions of EFSA on the risk assessment for bees was conducted with Member States via a written procedure in September 2017. The draft conclusions drawn by EFSA, together with the points that required further consideration in the assessment, as well as the specific issues raised by Member States following the consultation were discussed at the Pesticides Peer Review Experts' Meeting 166 on ecotoxicology in October 2017. Details of the issues discussed together with the outcome of these discussions were recorded in the meeting report (EFSA, 2018b). After the expert meeting, EFSA finalised the conclusions and launched a second written procedure on the final draft in December 2017–January 2018 in order to provide their comments on those parts of the Conclusions and supporting documents that have been amended following the Peer Review Meeting. The compiled comments were considered by EFSA and are published as part of the background documents to the Conclusions (EFSA, 2018b).

In addition, key supporting documents to this are the Technical Report on the evaluation of data (2018a) and the Peer Review Report (EFSA, 2018b).

The Technical Report provides the methodology developed by EFSA relating to the evaluation of the available data for what concern their relevance for the current risk assessment and their scientific reliability. It is composed as follows:

- Technical Report on the evaluation of data (EFSA, 2018a)
- Study Evaluation Notes (Appendices D–O) to the Technical Report (EFSA, 2018a).

The Peer Review Report is a compilation of the documentation developed to evaluate and address all issues raised in the peer review; it comprises the following documents, in which all views expressed during the course of the peer review, including minority views where applicable, can be found:

- the comments received on the preliminary draft EFSA conclusion,
- the report of the scientific consultation with Member State experts.
- the comments received on the final draft conclusions.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the EU for which the applicant has not demonstrated that it has regulatory access to the information on which this conclusion report is based.

The active substance and its metabolites

Thiamethoxam is the ISO common name for (E,Z)-3-(2-chloro-1,3-thiazol-5-ylmethyl)-5-methyl-1,3,5-oxadiazinan-4-ylidene(nitro)amine (IUPAC).

Thiamethoxam belongs to the group of neonicotinoid compounds which are used as insecticides. They interact with the receptor protein of nicotinic acetyl choline receptors in the nerve fibre membrane of insects.

The available plant metabolism studies considered during other EFSA evaluations (see EFSA, 2014a,b) confirmed that, based on the total radioactive residue (TRR) values, clothianidin is the only relevant metabolite for thiamethoxam, when this is applied as seed treatment (See Appendix H). Therefore, in the present conclusion, the risk assessment will focus uniquely on the active substance thiamethoxam and its main metabolite clothianidin.

Assessment

1. Uses assessed

1.1. Uses

In accordance with the mandate received in February 2015, EFSA liaised with producers and Member States in order to collect feedback on the uses they would like to support for the EU market. In a second step, in December 2015, Member States were requested to validate the consolidated Good Agricultural Practices (GAPs) from applicants, providing feedback on the authorised uses in their respective countries. Full details of the GAPs are given in Appendix A; no granular products are

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included in the GAP for thiamethoxam. Table 1 provides a brief summary of the critical GAPs relevant to the risk assessment for bees. Only the highest and lowest of the maximum application and seed treatment rates are given in Table 1.

Table 1: Summary of the seed treatment uses considered in this conclusion

Crop	Lowest seed treatment rate (mg a.s./seed)	Highest seed treatment rate (mg a.s./seed)	Lowest application rate (g a.s./ha)	Highest application rate (g a.s./ha)	Notes
Broccoli	1.4	1.4	53	53	The seeds are sown in a greenhouse and transplanted to the field (or, for lettuce, to greenhouse) after 2 weeks. Crop is harvested before flowering.
Brussels sprout	1.4	1.4	49	49	
Cauliflower	1.4	1.4	36	36	
Head cabbage	1.4	1.4	88	88	
Kale	1.4	1.4	74	74	
Lettuce	0.805	0.805	80.5	80.5	
Carrot	0.061	0.061	120	120	Crop is harvested before flowering.
Maize	0.63	0.63	63	63	–
Winter oilseed rape	0.021	0.021	14.7	14.7	Single product also containing fludioxonil and metalaxyl-M
Sugar beet	0.45	0.6	58.5	78	Crop is harvested before flowering.

2. Summary of the data considered in this conclusion

For what concern the effect and exposure data, the present conclusion makes use of different sources.

The first source of data was the open call for data for new scientific information as regards the risk to bees from the use of the three neonicotinoid pesticide active substances clothianidin, imidacloprid and thiamethoxam applied as seed treatments and granules in the EU. EFSA launched this call from May 2015 to September 2015. More details on the open call for data are available in a dedicated technical report (EFSA, 2015b).

Other sources of data were the systematic literature search on the neonicotinoids and the risks to bees that EFSA outsourced in 2013 (Fryday et al., 2015) and the related update performed by EFSA in June 2016 (Appendix B to EFSA, 2018a).

The first systematic literature search comprised 546 (already screened) documents (Fryday et al., 2015), while the update of the literature search retrieved 874 documents. In addition, there were 376 contributions which were received during the open call for data.

Finally, in accordance with the European Commission mandate, Member States were also further requested to provide any monitoring data not yet available during the open call data. The data submitted were already included in the data set.

After duplicate removal, the overall initial list included 1599 documents. A title and abstract screening step identified 680 potentially relevant documents which were then subject to full text screening. During the full text screening, all experiments within the available documents were identified and totalled 968. Of these experiments, 588 were critically appraised and the data extracted.

Full details of the available data investigating the effects of thiamethoxam to bees, together with their assessment are given in the Technical Report on the evaluation of data and related appendices (EFSA, 2018a). Furthermore, for what concern the exposure data already used in previous assessments (EFSA, 2013a) were also considered, as a significant bulk of information on residue levels was already systematically collected and organised by EFSA during such previous assessments.

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3. Principles and assessment criteria

3.1. Aim of the assessment

The current EU agreed level of protection for bees is to ensure that effects on colonies/populations are negligible. This means that the exposure of the colonies/populations at the edge of the treated fields should not exceed a level leading to effect greater than negligible.

As requested by the European Commission mandate, to perform the risk assessment of the three active substances, the EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees), hereafter referred to as EFSA (2013c) was followed. The basis of the risk assessment according to EFSA (2013c) is to ensure that the specific protection goals (SPG) for honeybees, bumblebees and solitary bees are met.

Namely:

- For honeybees, to ensure that there is not a greater than 7% effect on colony strength, including after overwintering, and the level of forager mortality does not breach the tolerable level, for honeybee colonies located at the edge of treated fields which are exposed to the 90th percentile predicted exposure or less.
- For bumblebees, to ensure that there is not a greater than 7% impact on the colony for bumble bee colonies located at the edge of treated fields which are exposed to the 90th percentile predicted exposure or less.
- For solitary bees, to ensure that there is not a greater than 7% effect on the population of bees located at the edge of treated fields which are exposed to the 90th percentile predicted exposure or less.

These SPGs define the problem formulation for the present assessment.

3.2. Tier-1

According to EFSA (2013c), the exposure from seed treatments and granular formulations in the 'reated crop' and the 'successive crop' scenarios derives from residues in pollen and nectar following translocation from below ground (seeds or soil). The same route of exposure is considered relevant for the 'weeds' scenario in the case of granules application.

For what concern the surrounding area ('field margin' and 'adjacent crop' scenarios), the most relevant exposure is due to dust drift at the sowing (treated seeds)/application (granules).

Furthermore, a separate risk assessment for exposure via consumption of contaminated water should be carried out for honeybees.

Details about the entire Tier-1 risk assessment scheme can be found in EFSA (2013c).

The Tier-1 risk assessment was carried out using default exposure values in accordance with EFSA (2013c), while the selection of the toxicity endpoints is described below (Section 3.2.1). Whenever suitable toxicity data for bumblebees and solitary bees were lacking, a surrogate endpoint was extrapolated from the related honeybee data (assuming the endpoint is a factor of 10 lower). In this case, throughout the present conclusion, we refer to the Tier-1 as 'screening Tier-1'.

3.2.1. Selection of the endpoints

Several endpoints from laboratory studies were obtained from the data considered in this conclusion and had not been considered in previous EU assessments. These newer endpoints have been considered to amend the previously agreed EU endpoints (EFSA, 2015a) provided that the following criteria were fulfilled:

- The endpoint was considered as relevant for a risk assessment according to EFSA (2013c) and the GAPs under consideration (e.g. the endpoint type, the test species and the test item)
- The endpoint was assessed to be 'Fully reliable' or 'Reliable with minor restrictions' during the appraisal exercise (EFSA, 2018a);
- The endpoint, from a study with technical active substance, indicated higher toxicity than the previously agreed EU endpoint for the technical active substance.

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Moreover, for endpoints from formulation studies, the following criteria were considered:

- if the previously agreed EU endpoint was from a formulation study, this was replaced only if it was less relevant (e.g. study with a spray formulation) than the newer formulation endpoint
- the previously agreed EU endpoint is a surrogate extrapolated endpoint

Where no new endpoints were available, or the criteria above were not fulfilled, the previously agreed EU endpoints were selected for the risk assessment.

The data available and final selection of the endpoints used for the current risk assessment are given in Section 4.

3.3. Refinement of the exposure assessment

Within EFSA (2013c), no specific stepwise approach is offered for higher tier risk assessment. Nevertheless, among the options listed in the guidance, one possibility is to refine the exposure estimate, i.e. replace the default values with specific values. Within the scope of this conclusion, the risk assessment carried out with refined exposure estimates is referred to as 'Tier-2'. A further option given in EFSA (2013c) is to refine the assessment by use of higher tier effect studies performed in the field or under semifield conditions (see Section 3.4). Specific exposure assessment goals need to be determined in order to use such effect studies in a refined risk assessment, referred to as 'Tier-3'.

3.3.1. Residues in pollen and nectar

3.3.1.1. Data evaluation and selection

The newly available higher tier studies, reporting information on exposure, were evaluated in line with the validity criteria set in the literature evaluation protocol (EFSA, 2018a) and the protocol proposed in Appendix G of EFSA (2013c). The valid data on the residue levels occurring in nectar and pollen for the exposure scenarios for the treated field and the succeeding crops in line with these protocols were collated in a table. Residue determinations in available field studies were assessed for their reliability both in relation to their field and laboratory phases. For the field phase in order to refine the exposure, higher tier studies from at least five randomly selected locations in the area of use of the substance should be conducted. This minimum of five randomly selected locations in the area of use is prescribed by the guidance, to ensure that an estimate can be made of the distribution of residues that might really be encountered. This has the aim of accounting for the different temporal and spatial variability that occurs. In relation to the laboratory phase, the analytical methods were examined for their adequacy for determining residues at the low levels required. In some instances, the size of the samples collected in the field phase were lower than the sample size for which the method had been validated; in such cases, appropriate correction on the method validated limit of quantification (LOQ) (for the target sample size) was applied, i.e. the LOQ was increased to account for smaller than ideal sample availability of individual sampling events.

Due to the very similar toxicity profile expressed by the active substance thiamethoxam and its metabolite clothianidin, residue values of the two compounds were always summed within each sample before proceeding with further data elaborations.

Measured residue levels of pollen and nectar were reported for each type of sampling matrix (i.e. samples from the plant, from the bee, from the bee via pollen traps, from the comb and from soil). In general, the sampling scheme which aimed to determine residues in the same matrix (either in plant matrices or bee matrices) during the field studies was not exhaustive enough to guarantee that the time dependence of the residue over the period of interest could be captured. This prevents any analysis aimed to determine a mathematically rigorous percentile exposure value over time. Therefore, the maximum observed in the available samples was retained as representative of the exposure in each particular field experiment. This does not imply that the overall risk assessment has to be regarded as overly conservative since the sampling frequency pattern in the studies does not guarantee that the actual maximum occurrence was picked up by the maximum measured in the samples taken. Nevertheless, it is expected that the assessment based on these principles may still be considered to represent a realistic worst-case exposure for the different substances and uses assessed.

Treated Crop scenario

Regarding the field phases, the directly treated crop needed to be the crop being assessed. Appendix R of EFSA (2013c) indicates that extrapolation between the residue values from different

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crops is inappropriate when substances are systemic, which is interpreted to relate to seed treatment uses or when granules are placed with seed at the time of drilling. This is because the different physiology of different crops, including the time from emergence to flowering, leads to different translocation and levels of residues in different crops. When assessing the field phases of the available experiments, the most critical issues encountered were cross contamination from fields in the vicinity and/or due to historical uses in the same field, i.e. not resulting from the treated seeds of known application rates. Only data from studies for which there was a sufficient certainty that the residues observed were resulting from the application being investigated as prescribed in the study design, were retained for the exposure assessment. The presence or absence of residues measured in control plots was not part of the decision on retention.

For the exposure assessment, the measured residue values (mg analyte/kg pollen or nectar) were normalised for the seed loading (mg a.s./seed) to give Residue per Unit Dose (RUD) (where the unit dose is 1 mg a.s./seed) to make the residues independent from the application rate used in the studies. From one study, sometimes more than one RUD value was calculated and included in the collation table when more than one trial was conducted within the study. A standalone trial was defined when one or more of the following factors were different from other trials: type of formulation, plant species, application rate, test site, period of the trial, pre-treatment of the soil and test category (i.e. field and semifield trials, where semifield means bees used to obtain samples were restricted to foraging on treated plots).

According to EFSA (2013c), in order to refine the exposure, higher tier studies from at least five randomly selected locations in the area of use of the substance should be conducted. Therefore, a minimum of five RUD values for pollen and nectar were considered necessary to perform a refined exposure assessment for each exposure scenario for each use under consideration.

Where the residue detected in a trial was reported to be lower than the LOQ but greater than the limit of detection (LOD), as a worst-case assumption, the residue was considered to be equal to the LOQ for the RUD calculation. In the cases that no residues were detected, the residue was considered to be equal to the LOD for the RUD calculation.

According to EFSA (2013c), in order to perform an exposure assessment, it is preferable to use measured RUD values for pollen and nectar collected from bees (specific for honeybees, bumblebees and solitary bees), e.g. using pollen traps attached to honeybee hives or sampling nectar by extracting the honey stomach from forager bees. Taking the RUD values for pollen and nectar directly from the bees aims to give a better representation of the likely exposure to bees and bee colonies by accounting for dilution by non-contaminated pollen and nectar. Considering each bee taxon separately is needed to account for differences in their foraging behaviour that would be expected to mean that dilution was different between the categories. Alternatively, RUD values for pollen and nectar taken directly from the plant can be used in the exposure assessment. However, RUD values for plant pollen and nectar are considered to be an overestimation of the exposure to bees as dilution is not accounted for. Therefore, if there are a sufficient number of RUD values for bee nectar and/or pollen, from field trials, only these values were used for the exposure assessment. RUD values for pollen and nectar from bees taken from semifield studies were considered to be representative of situations where there was no dilution and therefore were considered together with the RUD values for plant pollen and nectar. In the cases where RUD values were available on both bee pollen/nectar and plant pollen/nectar from the same semifield study, the values for bees only were taken. Where less than five RUD values for bee pollen/nectar were available, these were combined with the RUD values for plant pollen/nectar and bee pollen/nectar from semifield, i.e. to obtain sufficient data to perform the exposure assessment. Figure 1 summarises the process for selecting the RUD values for the refined exposure assessment for the treated crop scenario.

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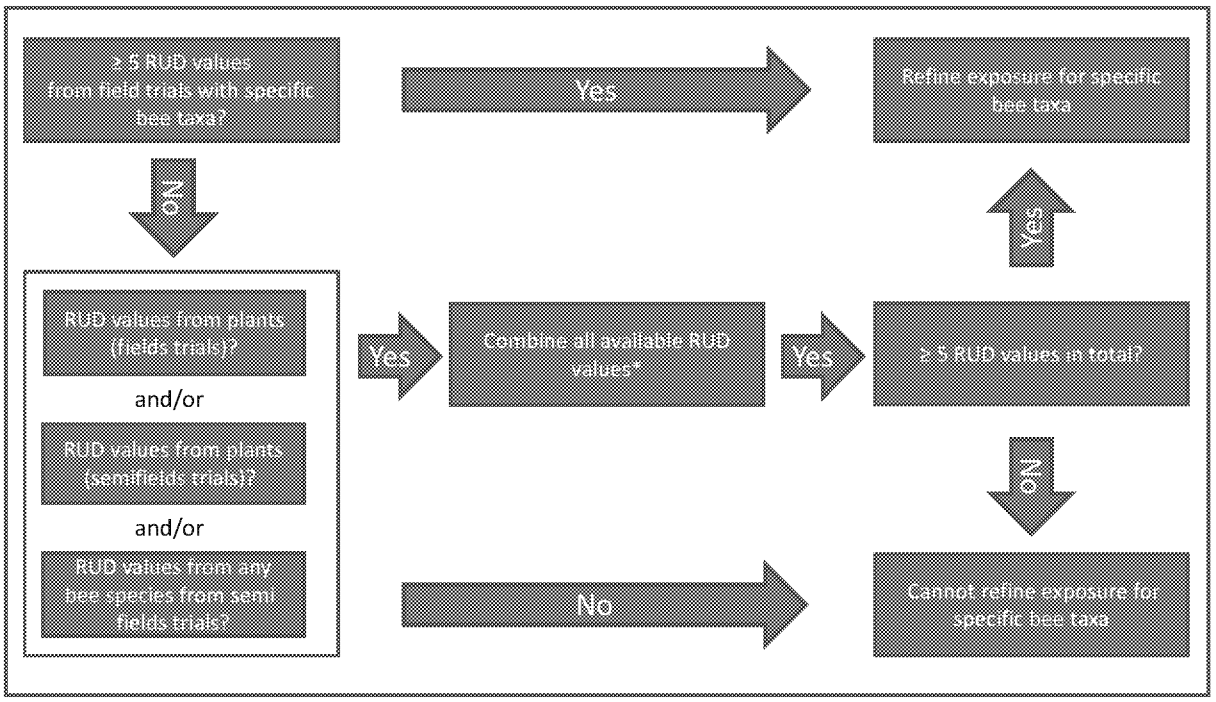

*If RUD values from both plants and bees are available from the same semifield trial, only retain RUDs from bees to avoid double counting

Figure 1: A summary of the selection process for RUD values for the refined exposure assessment

Succeeding crop scenario

A different approach from the treated crop scenario was used for the succeeding crop scenario. This is because the residues in the succeeding crop scenario are less dependent on the physiology of the treated crop, but are instead mainly driven by the active substance concentration in soil and by the physiology of the successive crop. For this reason, in the residue trials, residues in the topsoil/root zone had to have been measured before the planting of succeeding plant species. For trials to be retained in the assessment, these residues in soil needed to be roughly equivalent to or higher than that estimated to occur (Predicted Environmental Concentrations (PEC)) in soil from the uses being assessed.

Maximum residues in pollen and nectar from the retained trial sites were used to estimate exposure in the risk characterisation, whilst following the approach for the selection of residues directly from bees (either in open field or semifield trials) or via plant sampling as already discussed above for the treated crop scenario. As the residues trial site, selection was based just on measured soil residues, it was not necessary for the agricultural practice or product formulation type that had been used at any individual trial to match the uses being assessed. As measured residues in soil ensured that the trials covered the GAPs without necessarily being linked to a specific use, RUD values were not calculated.

Also in this case, in order to refine the exposure assessment, residues from at least five trials should are needed.

3.3.1.2. Calculation of refined shortcut values

Treated crop scenario

The residue values selected for the refined exposure assessment for the treated crop scenario (Appendix E) were used to calculate new shortcut values (SVs), which represents active substance intake per day (adults) or per developmental period (larvae). Such calculation was performed by means of the SHVAL tool (EFSA, 2013c, 2014b). This R-based tool fits theoretical distributions to the available data (e.g. for treated crops residues expressed as RUDs, consumption rates, sugar concentration in nectar), and then, it runs Monte Carlo simulations with 1000 iterations (see EFSA, 2014a,b for details). The result of such simulation is a distribution of intake values per day (or per developmental period for larvae). Finally, the 90th percentile of this distribution is selected as the relevant crop/substance specific SV. Separate simulations were carried out for each cast of each bee group (honeybee, bumblebee and solitary bees).

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No data were available to refine consumption rates or sugar concentration in nectar. Hence, for these variables, default values as presented in Appendix J of EFSA (2013c) were used in the simulations.

Succeeding crop scenario

The same procedure described for the treated crop scenario was also applied here. Nevertheless, actual residue values (not RUDs) were used as input for the SHVAL tool.

3.3.1.3. Estimation of the exposure assessment goal

Treated crop scenario

To consider the higher tier effect studies in the context of the risk assessment, the exposure within those effects studies were compared to the expected exposure for the GAPs under consideration. For the treated crop scenario, specific 'exposure assessment goals' were estimated by transforming the refined SVs used in the Tier-2 assessment. To transform the refined SVs to an exposure assessment goal, the SVs were multiplied by the seed loading rate (in terms of mg a.s./kg seed) for each use. For the succeeding crop scenario, the Tier-2 SVs are independent of the GAP, and therefore, they also represent the exposure assessment goal.

Figure 2 presents a general overview of the stepwise approach followed for the refinement of exposure assessment described under Section 3.3.1 for the treated crop scenario.

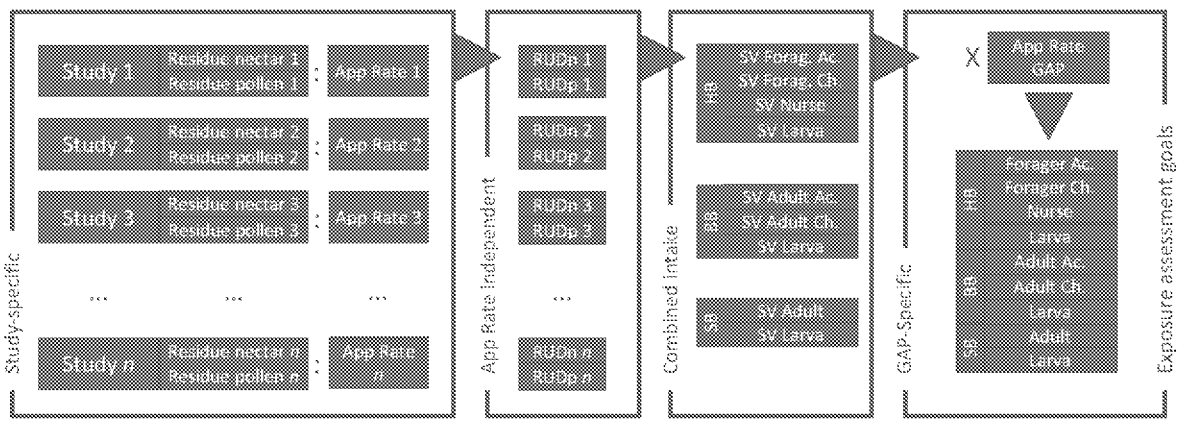

Figure 2: General overview of the refined of exposure assessment for the treated crop scenario

Succeeding crop scenario

For the succeeding crop scenario, refined SVs were calculated by using actual residue values, without any further normalisation for the application rate. As such, the refined SVs obtained as described in Section 3.3.1.2 represent as well the exposure assessment goals.

Figure 3 presents a general overview of the stepwise approach followed for the refinement of exposure assessment described under Section 3.3.1 for the succeeding crop scenario.

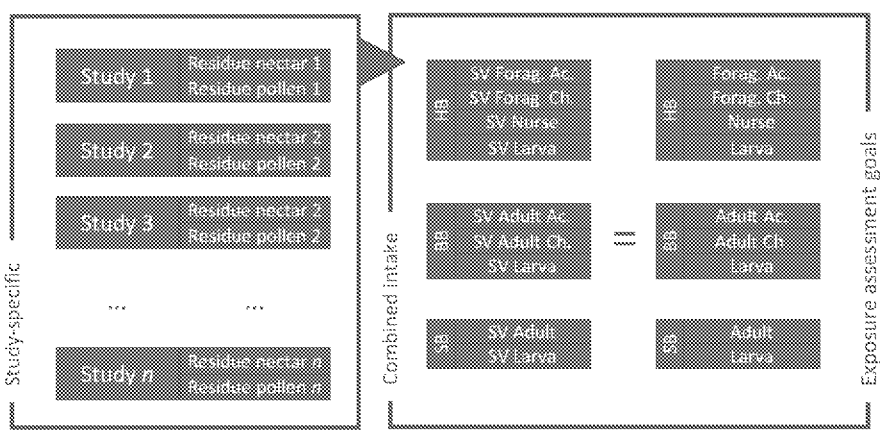

Figure 3: General overview of the refined of exposure assessment for the succeeding crop scenario

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3.3.2. Dust drift and deposition

According to the EFSA (2013c), exposure to dust drift in the field margin or in adjacent crops are considered relevant for seed treatment uses and granular formulations.

Field experiments measuring dust deposition to the horizontal ground outside the treated area at the time of drilling seed were considered reliable when: the quality of the treated seed (in terms of dust content and active substance in the dust) had been measured, the drilling machinery used was adequately described, the application rate in terms of mass of active substance per unit treated area was adequately measured, dust deposition at different distances downwind of the treated area was adequately determined and wind speed and direction measurements were available. In many of these experiments, dust drift outside the boundary of the treated field was also measured using vertical gauze netting. These vertical gauze results were not used further, as it was not clear how the results reported as g a.s./ha were derived and what they represent. Also, an agreed methodology is not available on how to use or interpret such values that may have utility in estimating exposure to field margin vegetation or adjacent crops when measured at the individual trial sites.

3.3.3. Residues in water sources

In accordance with the recommendation of the Guidance Document (EFSA, 2013c), measured residue in the guttation fluids exuded from the treated plant was considered for refining the assessment related to this route of exposure relevant for honeybees. EFSA (2013c) also specifies that the guttation concentration used in the risk assessment needs to cover the 90th percentile in guttation fluid for the crop of concern (considering location, growth stage and environmental conditions). For seed treatments and granules buried with seeds, it is proposed to refine the exposure estimate by conducting (at least) five field studies and to measure the concentrations in guttation water.

Therefore, in principle, a refinement of the exposure can be performed if at least five field studies are available for the same crop. For acute risk assessment, the relevant concentration within each experiment is the maximum measured residue value. For chronic risk assessment (both for adult and larva), if a decline of the a.s. concentrations in guttation fluids was observed, a time-weighted average (TWA) concentration was estimated (10d-TWA for adult, 5d-TWA for larva) and considered the relevant value.

No exposure refinement was necessary for assessing residues in puddles (see Section 5.1.3.2). A refined surface water exposure assessment could not be performed as agreed input parameters for FOCUS surface water modelling are not available.

3.4. Refinement with higher tier experiments

3.4.1. Building up the lines of evidence

Another approach offered by the Guidance Document (EFSA, 2013c) to refine the risk assessment is to carry out higher tier effect experiments. These experiments are normally carried out under field or semifields conditions, and aim at a higher environmental realism when compared to standard laboratory test.

These experiments present a wide variety of set-ups, designs and investigated endpoints. Therefore, a weight of evidence (WoE) scheme has been developed to integrate the relevant information from all available experiments. In order to perform a WoE risk assessment, it is first necessary to set the problem formulation and then identify the lines of evidence which address the problem. In the case of honeybee, bumble bee and solitary bee risk assessments performed in accordance with EFSA, 2013c, the problem formulation is already defined by the SPGs.

Within the WoE, it was considered that each 'lines of evidence' corresponds to the whole set of homogeneous endpoints measured in all available experiments. An endpoint in this context is defined as a parameter which could be informative of a potential effect caused by an exposure to an active substance (and its metabolites).

Within each experiment, the endpoint is identified by four dimensions:

- The **magnitude** of the observed deviation from the control. For endpoints measured as time series, the extremes of such deviation were recorded in both directions, together with a mean deviation. In case of such endpoints like forager mortality, this dimension should also account for the duration of a consistent deviation (e.g. increase of X% in forager mortality observed for Y consecutive days). Deviations in both directions were classified as: no deviation, negligible,

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small, medium and large deviation from the control. For this classification, the scales presented in Table 2 were used. These scales were adapted from Appendix B of EFSA, 2013c (Protection goals), except the scale for homing success, where the categories were arbitrarily chosen. An example for using these scales: if the average colony strength in a honeybee study at an observation time was 6% less in the treated group compared to the control, this was classified as a negative negligible deviation. If, at another observation day, the colony strengths in the treated group were 16% more than in the control, this was classified as a positive medium deviation. It has to be noted that pending on the availability of the data on the relevant endpoints (i.e. reported details), the deviation from the control was either calculated or only estimated (e.g. when only graphical presentation was available for the endpoint).

Table 2: Scale of deviation from the control used for the weight of evidence exercise

Departure class	All endpoints except mortality and homing success	Mortality (forager and in front of the hive)	Homing success
No deviation	0%	0%	0%
Negligible	> 0% to < 7%	See examples in Table B1 of Appendix B of EFSA (2013c)	> 0% to < 10%
Small	7% to < 15%	See examples in Table B1 of Appendix B of EFSA (2013c)	10% to < 20%
Medium	15% to < 35%	See examples in Table B1 of Appendix B of EFSA (2013c)	20% to < 50%
Large	≥ 35%	See examples in Table B1 of Appendix B of EFSA (2013c)	≥ 50%

- The **reliability** of the endpoint: this was established on the basis of the appraisal exercise (EFSA, 2018a) and gave a score to each endpoint from 0 (not reliable) to 3 (fully reliable). The reliability was used to weight the results obtained in different experiments, and to estimate, together with the level of consistency of the results, the level of certainty associated with the line of evidence.
- The level of **exposure**: this information is necessary to check where the level of exposure in the experiment stands compared to the exposure assessment goal(s). Furthermore, this information can be used to check whether a sort of exposure–response relationship can be identified. For oral exposure to residues in pollen and nectar, residue intake values were calculated for each caste of bee using the mean residue value on nectar and/or pollen obtained in the effects study. A sugar content of 15% was assumed for nectar for honeybees and bumblebees whereas for solitary bees, a sugar content of 10% was used (EFSA, 2013c). In case of colony-feeder studies, the sugar content of the sugar solution specified in the study was used. If this was not available, then a sugar content of 50% was assumed. The daily consumption values, for pollen and nectar, for each bee caste were taken from EFSA (2013c). Where a range of consumption values were available, a range of residue intake values were obtained. To be consistent with the approach followed during the refinement of the exposure, the exposure in the single effect studies was also considered to be determined by the sum of the exposure to the active substance thiamethoxam and its metabolite clothianidin.
- **The length of exposure:** this is defined as the time period in which there could have been exposure to residues of the active substance. It is noted that the 'length of exposure' referred to in this conclusion does not account for the subsequent consumption of food stores within colonies/nests. In field and semifield studies, this corresponds to the time period the bees could be exposed to the crop during flowering. For colony-feeder studies, the length of exposure is defined by the time period which the spiked sugar solution or pollen was given to the bees. This information is needed to check whether the length of exposure is realistic to that expected for the GAPs under consideration.

In order to visually illustrate these four dimensions of the endpoints and in order to help the interpretation of a 'line of evidence', graphical representations were prepared. A graphical representation of a 'dummy' example (invented example for illustrative purpose) is included in Figure 4 with an explanation of each element of the figure.

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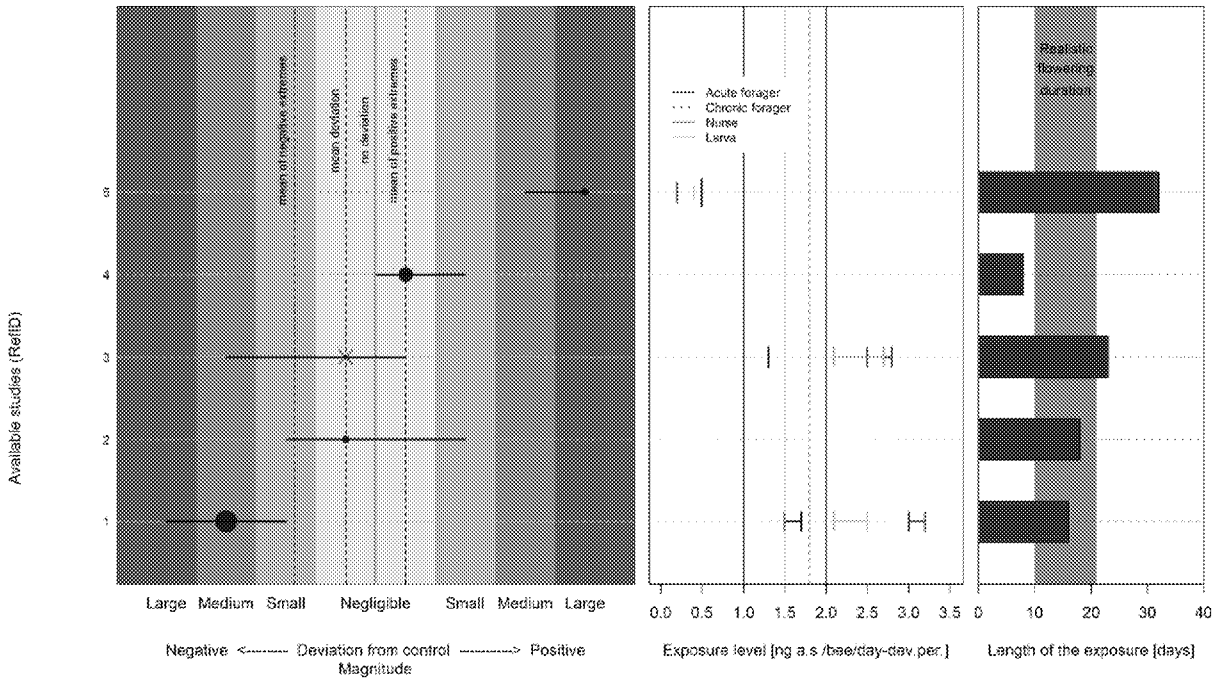

Figure 4: Lines of evidence for a 'dummy' example: colony strengths of honeybees for winter oilseed rape

The figures include the following information:

- Each row in the figure represents a higher tier effects study. The numbers given on the left hand side are the reference identification codes of the studies which can be traced back to the reliability assessment provided in the Technical report on evaluation of data and related Appendices from D to O (EFSA, 2018a; Appendix G). A summary of the reference identification codes according to the different assessment streams identified during the evaluation of the data is summarised below. Note that several studies investigated a number of exposure levels, and therefore, these studies maybe listed more than once (e.g. the highest exposure level that caused no or small deviation from the control and the lowest exposure level with apparent deviation from the control).

Assessment Stream	Reference identification code
All* (with interaction)	All*
All+ (no interaction)	All+
Clothianidin	C.
Imidacloprid	I.
Thiamethoxam	T.
Clothianidin * Imidacloprid (with interaction)	C * I.
Clothianidin + Imidacloprid (no interaction)	C + I.
Clothianidin * Thiamethoxam (with interaction)	C * T.
Clothianidin + Thiamethoxam (no interaction)	C + T.
Imidacloprid * Thiamethoxam (with interaction)	I * T.
Imidacloprid + Thiamethoxam (no interaction)	I + T.
Not substance specific	NS.

- The left hand panel relates to the biological observations whilst the centre and right hand panels relate to exposure.
- For each experiment, the black solid horizontal line represents the range of the observed deviations from the control (i.e. both negative and positive deviations). The magnitude of these deviations is categorised as negligible, small, medium or large. When this is not indicated, the endpoint was measured only once during the study or it was measured multiple

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times, but insufficient details were reported to evaluate the variability of the endpoint in time (e.g. only averages for the entire study duration were reported)

- The position of the blue circle gives an estimation of the overall deviation (mean) from the control for the entire duration of the study or during the year of use for those studies which extend over the winter.
- The size of the blue circle is an indication of the reliability score of the specific endpoint. A 'fully reliable' endpoint gives a large circle, an endpoint which was 'reliable with minor restrictions' gives a medium-sized circle and an endpoint which was 'reliable with major restrictions' gives a small circle.
- For transparency, the experiments giving endpoints which were assessed as 'not reliable' have also been included in the figure, but the overall deviation is represented by an X.
- To help interpret the figure, vertical dotted lines have been added to indicate the mean overall deviation, the mean negative deviation (if it could be calculated) and the mean positive deviation (if it could be calculated) across all of the reliable experiments (weighted for the reliability score of the endpoint).
- In the central panel of the figure, a representation of the estimated level of exposure achieved in the experiment is given for each bee caste (e.g. ng a.s./bee per day for adult bees and ng a.s./larvae per development period for larvae). When this is not indicated, reliable information on the exposure level achieved in the study was not available.
- The vertical lines in the centre panel of the figure represent the exposure assessment goal, for each bee caste, for the GAP under consideration (see Section 3.3.1.3).
- On the right hand side of the figure, the length of exposure (in days) in the experiment is represented by the red bars. The vertical purple column is the expected range of exposure length (e.g. the flowering period) for the crop under consideration.[9]

In order to conclude that the observed deviations are actual representations of a true effect caused by the exposure to the active substance (and its metabolites), several aspects were considered for each line of evidence.

- The presence/absence of a general trend, giving more weight to results with higher reliability.
- The level of consistency among experiments (similar results, exposure–response relationship, etc.)
- The level of precision offered by the available experiments (width of the effect size ranges)

In principle, each line of evidence should provide a piece of information characterised by a certain degree of strength (consistency), precision (degree of variability) and reliability.

Furthermore, in order to use the available information to conclude on the risk assessment, it is pivotal to check the level of the exposure in the effect experiments relative to the specific exposure assessment goals and to check whether the length of potential exposure in the effect study is within the realistic flowering period for the crop (or succeeding crop) under consideration.

3.4.2. Integrating the lines of evidence

In accordance to EFSA (2013c) and the newly available EFSA draft guidance document on the WoE (EFSA Scientific Committee, 2017), the overall process should account for the relevance of the single lines of evidence, before performing any integration.

In our scheme, there are endpoints (lines of evidence) that are directly linked to the protection goals, and have the potential to provide a straightforward response to the main issue reported in the problem formulation (see Section 3.1). For this reason, they are considered to be the higher class of endpoints in terms of relevance (Class 1). These are colony/population size (valid for all species); forager mortality (honeybees only) and all endpoints related to the reproductive output (bumblebees and solitary bees).

[9] A crop-specific time window for a reasonable flowering period was estimating by considering: (i) feedback from Member States; (ii) assumptions within the FOCUS scenarios; (iii) collating information reported in the present data set. For winter oilseed rape, a reasonable flowering period was estimated to last between 10 and 42 days. The selected maximum is longer than the assumptions contained in the FOCUS scenarios (maximum 28 days). During the expert meetings 166, some experts pointed out that 6 weeks of flowering may happen, but only in exceptional years. Nevertheless, within the present data set, flowering between 35 and 43 days was recorded in several experiments carried out in France, the United Kingdom, Germany and Hungary. For spring oilseed rape, a reasonable flowering period was estimated to last between 10 and 28 days. This was rather consistently reported by Member States, FOCUS and the available experiments in the data set. For maize, a reasonable flowering period was estimated to last between 10 and 21 days. Once again, this was rather consistently reported from all sources used for this estimation. The succeeding crop scenario is not represented by any specific crop. Therefore, on the basis of all of the available information on the flowering period of agricultural crops, it was decided that a reasonable flowering period would range from 5 to 42 days.

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Other endpoints have a rather clear conceptual link with one of the previous two (e.g. brood/cocoon production can clearly influence colony/population strength), even if this link cannot be explicitly quantified. These endpoints (lines of evidence) belong to Class 2 for relevance.

Other endpoints, on the contrary, may play a role in the colony/population health, but such link is not immediate in conceptual terms (e.g. average duration of foraging trips). These endpoints (lines of evidence) belong to Class 3.

Finally, there are endpoints that do not offer any explicit link with the protection goals (e.g. measurement of enzymatic levels at subindividual level). These endpoints are considered not relevant (Class 4) for addressing the protection goal according to EFSA, 2013c.

A full list of all endpoints considered in this assessment and a detailed description of their relationship with the SPGs is available in Appendix B. A less detailed summary is reported in the Table 3 below.

Table 3: A summary of the endpoint types and the related relevance class assigned within the scope of the present risk assessment

Bee group	Relevance class	Family of endpoint
Honeybees	1	Colony strength
		Forager mortality
		Overwintering assessment
	2	General mortality of individuals
		Brood production
		Homing success[(a)]
	3	Behavioural endpoints
		Comb building
		Weight of the hive
		Queen
		Disease
		Food storage
	4	Behaviour influencing exposure
		Subindividual mass
		Suborganism endpoints
		Thermoregulation capacity
Bumblebees	1	Reproductive output
		Colony strength
	2	Indirect reproduction
	3	Behaviour
		Weight of the nest (colony)
		Food storage
		General mortality
		Individual mass
		Homing success
	4	Behaviour influencing exposure
Solitary bees	1	Reproductive output[(b)]
	2	Indirect reproductive output
	3	Behaviour
		General mortality

(a): For the purposes of this conclusion, the endpoint 'homing success' is defined as the proportion of bees returning to the hive/colony after they were captured and subsequently released at a distance from the hive/colony.

(b): The number of solitary bee offspring emerging after winter was considered to represent the accumulation of several preceding endpoints related to reproductive success (e.g. number of completed nests, tubes with brood, cocoon production). Therefore, the WoE focussed primarily on the number of offspring emerging after the winter.

In order to account for this hierarchical structure within the current risk assessment scheme, a stepwise procedure was followed.

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As already mentioned, the first step is focussed on endpoints belonging to Class 1. If the available data are sufficient to provide a conclusive answer to the main risk assessment question, the assessment could stop. If, on the contrary, the available information is not sufficient and/or appropriate to provide a conclusive answer, the WoE is extended to other levels of relevance, in order to get a more comprehensive picture of the available data.

If the evidence in the first two levels of relevance (Classes 1 and 2) is not sufficient/appropriate to reach a conclusion, it is considered unlikely that less relevant endpoints will help achieving a conclusive assessment.

4. Outcome of the assessment: toxicity endpoints

4.1. Standard endpoints

Several laboratory toxicity endpoints were available within the data set analysed for this review. Some of these data have already been previously considered in previous EFSA output (e.g. EFSA, 2015a).

In the data set considered, there were several available laboratory studies, assessing the effects of thiamethoxam, or formulated products containing thiamethoxam, on several bee species. Some of these data have already been previously considered in previous EFSA output (e.g. EFSA, 2015a). Following the selection procedure given in Section 3.2.1, it was considered whether any of the newly available data should replace the previously EU agreed endpoints (EFSA, 2015a) and be used for the Tier-1 and Tier-2 risk assessments.

Five reliable acute contact endpoints were available for honeybees (four with the active substance and one with the A9807C formulation). One experiment with the active substance (ALL+.2025, Appendix M of EFSA, 2018a) provided an endpoint (lethal dose (LD_{50}) = 12.1 ng a.s./bee) which was a factor of 2 lower than the previously agreed endpoint (LD_{50} = 24 ng a.s./bee). In this experiment, the LD_{50} was only reported for an observation period of 120 hours, which is longer than the time window recommended in the OECD 214. Nevertheless, both validity criteria reported in OECD 214 were considered respected: the mortality in the control was still 4.6% after 120 h, and the toxicity of other tested substances (i.e. λ-cyalothrin, deltamethrin, esfenvalerate) was in the expected range, providing an indication that sensitivity of the system was appropriate, in lack of a formal positive control. Therefore, the LD_{50} (12.1 ng a.s./bee) was considered suitable for being used in the risk assessment. This issue was discussed and agreed during the expert meeting.

Three reliable acute oral endpoints were available for honeybees (two with the active substance and one with the A9807C formulation). None of these endpoints respected the criteria for substituting the previously agreed endpoint (LD_{50} = 5 ng a.s./bee).

No reliable data were available to derive a chronic lethal dietary dose (LDD_{50}) for honeybees.

No larval endpoint was available in the previous EFSA conclusions (EFSA, 2013a, 2015a). Within the data set considered for this review, two new experiments assessing toxicity of thiamethoxam on larvae were available. One of these two experiments (T.383, Appendix F of EFSA, 2018a) did not identify a suitable No Observed Effect Dose (NOED), as significant effects were seen at all tested concentrations. The authors of the other available experiment (T.382, Appendix F of EFSA, 2018a) identified the NOED at 840 ng a.i./larva/developmental period. However, this selection was questioned by EFSA, which instead established a NOED = 21.7 ng a.i./larva/developmental period (for detail, see Appendix F of EFSA, 2018a). This issue was discussed and agreed during the expert meeting.

For bumblebees, only one reliable acute oral (LD_{50} = 5 ng a.s./bee; T.1125, Appendix F of EFSA, 2018a) and one acute contact (LD_{50} = 27.5 ng a.s./bee; T.1125, Appendix F of EFSA, 2018a) experiments with a formulated product were available in the data set. These are the same that were already considered in the previous EFSA conclusions (EFSA, 2015a). No reliable chronic data were available for bumble bee adults and larvae.

No reliable toxicity data were available for solitary bees.

In accordance with EFSA, 2013c, where data are missing, surrogate endpoints can be calculated using toxicity data for honeybees divided by 10. This was done for solitary bees (adult acute and larvae) and for bumblebees (larvae).

Data were not available to derive a NOEL for the development of hypopharyngeal glands (HPG) in honeybees.

Due to lack of data, a Tier-1 and Tier-2 risk assessment could not be performed for chronic adult toxicity (any bee species) and development of HPG (honeybees).

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No data were available to assess whether thiamethoxam results in accumulative effects in honeybees.

A whole set of toxicity data was available for thiamethoxam metabolite clothianidin (EFSA, 2018c), but it is not reported here. The toxicity profile of clothianidin proved to be very similar to the one of thiamethoxam. Therefore, the entire risk assessment (with the exception of Tier-1) was carried out considering the sum of thiamethoxam and clothianidin.

On the basis of the above consideration, Table 4 summarises the toxicity endpoints selected for the Tier-1 and Tier-2 risk assessment.

Table 4: Toxicity endpoints selected for lower tier risk assessments

Risk assessment type	Endpoint	Honeybee	Bumble bee	Solitary bee
Acute contact	LD_{50} (µg a.s./bee)	0.0121	0.0275	0.00121[(a)]
Acute oral	LD_{50} (µg a.s./bee)	0.005	0.005	0.0005[(a)]
Chronic oral	10-day LDD_{50} (µg a.s./bee/day)	No endpoint available	No endpoint available	No endpoint available
Larval	NOEL (µg a.s./larva/ developmental period)	0.0217	0.00217[(a)]	0.00217[(a)]
HPG	NOEC (µg a.s./bee)	No endpoint available	Not applicable	Not applicable

NOEL: no observed effect level; NOEC: no observed effect concentration.
Note. From the previously EU agreed endpoints, only the acute contact endpoint and the larvae endpoint for honeybees bees were changed
(a): Extrapolated from the endpoint for honeybee by using a factor of 10.

4.2. Additional sublethal laboratory data

Several laboratory experiments testing sublethal effects of thiamethoxam on bees were available in the data set. Those effects were of various types, spanning from changes in behaviour to changes in enzymatic levels and modification of brain morphology.

A summary of the effects considered in the whole data set is reported in Table 5.

Table 5: Sublethal endpoint available for thiamethoxam

Organism	Effect
Apis cerana	Gene expression
Apis mellifera	Behaviour
	Brain morphological changes
	Cytotoxicity
	Enzymatic activity
	Food attractiveness
	Intoxication symptoms
	Larvae development
	Locomotion impairment
	Midgut death cell
	Nosema spores count
	Olfactory learning
	Sucrose responsiveness
	Water responsiveness
Bombus terrestris	Food attractiveness
	Olfactory learning

For most of the effects, only 1–2 experiments were available. On the contrary, almost half of the available experiments focussed on the so-called Proboscis Extension Reflex (PER), which is part of bees feeding behaviour. In general, when the antenna is stimulated by sugar water, the proboscis automatically sticks out to drink. This reflex was mainly used to investigate how exposure to thiamethoxam can impair the responsiveness to a stimulus (water, sugar solution) or to what extent it can affect memory performances.

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In the first kind of experiments, responsiveness was tested to water and sucrose. Both responses were tested on honeybees after oral and contact exposure, under acute and chronic regimes. These bioassays were run with doses from 0.1 to 1 ng/bee (acute) or 0.1 to 1 ng/bee/day (chronic). In none of the available experiments, significant effects on bee responsiveness were recorded. Sucrose responsiveness was unaltered in acute biassays, but presented different results under chronic exposure, with NOED ranging 0.1–1 ng/bee/day.

Data for both honeybees and bumblebees were available on the second kind of PER experiments (olfactory learning and memory performance). Experiments were available for assessing oral and contact exposure, under acute and chronic regimes. Single doses (up to 1 ng/bee) did not cause any significant impairment of honeybees in terms of learning and memory, irrespectively of the exposure route. Some effects were seen on both learning and memory after chronic exposure; but in general, these observations did not present a clear dose–response within the experiments. Furthermore, these significant effects were recorded at very different doses (from 0.007 ng/bee to 1 ng/bee) in different experiments, with slightly different designs. Effects of oral acute exposure were also tested on bumblebees in only one experiment, where the NOED was extremely low (0.000024 ng/bee). Effects were also seen under chronic exposure, but a NOED could not be established as bees were fed ad libitum.

Another sublethal effect that was studied in several experiments was impairment of locomotion. For acute tests, results were difficult to interpret due to opposite effects (activity inhibition/stimulation) observed after oral and contact tests. Either oral or contact chronic exposure to thiamethoxam caused a slight non-significant decrease of activity, not depending on the dose (max. tested 1 ng/bee/day).

In several studies, it was discussed that the investigated sublethal effects at individual or subindividual level may result in a colony/population level effect. It is acknowledged that an evident linkage (direct or indirect) between certain sublethal endpoints and colony/population level effects might exist. However, no appropriate information was available to establish or further describe these links. Therefore, these endpoints could not be linked to the protection goal and they were not considered further in the risk assessments.

5. Outcome of risk assessment

5.1. Risk assessments for seed dressing products

5.1.1. Risk via systemic translocation in plants – residues in nectar and pollen (treated crop scenario and succeeding crop scenario)

5.1.1.1. Tier-1 risk assessment

The Tier-1 risk assessment for the representative GAPs was performed by using the EFSA's BeeTool (v.3.) (Appendix Y of EFSA, 2013c) for honeybees and bumblebees, where suitable toxicity data were available. The outcome of these calculations is summarised in Table 6, and the detailed results are included in Appendix C. A screening Tier-1 assessment was carried out for solitary bees and for chronic larva bumblebees as only surrogate endpoints were available. Since no toxicity data were available for chronic adults and HPG development, no assessment was performed for these categories. High risk is indicated for all cases where one or more combinations (categories of acute and larva combined with the treated crop scenario and succeeding crop scenarios) identified a high risk. In the case of high risk based on screening Tier-1 with surrogate data, the outcome was indicated as 'low risk could not be demonstrated'. As mentioned in the following table, for vegetables and for sugar beet, the risk assessment was not performed for the treated crop scenario as this is not relevant for the respective GAPs (crops harvested before flowering). The detailed results are included in Appendix C.

No specific Tier-1 risk assessment was carried out for thiamethoxam metabolite clothianidin.

Indeed, it was concluded that the Tier-1 risk assessment for the parent substance (thiamethoxam) covers the risk due to the exposure of the metabolite clothianidin. Such decision was taken considering:

- the intrinsic conservativeness of the Tier-1 assessment;
- the very similar toxicity profiles expressed by the two compounds;
- the available information on plant metabolites, which suggest that the formation fraction of metabolite clothianidin is likely to be well below 100%.

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Table 6: Summary of the outcome of Tier-1 and screening Tier-1 risk assessment (acute and larvae only; no toxicity data for chronic and HPG)

Use	Honeybee		Bumble bee		Solitary bee	
	'Low' application rate	'High' application rate	'Low' application rate	'High' application rate	'Low' application rate	'High' application rate
Broccoli, Brussels sprout, cauliflower, head cabbage, kale, lettuce, carrot, sugar beet, maize, winter oilseed rape	High risk		High risk		Low risk not demonstrated	

As presented in the above table, the Tier-1 oral risk assessment for the treated crop and succeeding crop scenario for all seed treatment uses under consideration indicated a high risk to honeybees and bumblebees (for all crops except maize and winter oilseed rape, a high risk was only indicated for the succeeding crop scenario). The screening assessment for solitary bees indicated that a risk cannot be excluded (once again, for all crops except maize and winter oilseed rape, this was applicable for the succeeding crop scenario only). No risk assessment could be performed for chronic (all taxonomic groups) and honeybee HPG development. Lettuce could be sown and transplanted in greenhouses, without ever be placed in the field. When these operations happen in permanent structures, the exposure to any bee species is considered negligible, and a low risk is concluded.

5.1.1.2. Refined exposure assessment for the treated and succeeding crop scenario

Treated crop scenario

There were several reliable studies reporting measured residue values in nectar and pollen from thiamethoxam seed-treated crops grown. Of the seed treatment uses under consideration, relevant data were available only for maize and winter oilseed rape (i.e. the only two crops for which an high risk was identified at the Tier-1 for the treated crop scenario).

Most of the available data were not part of the data set assessed for this review, but were instead data already used in previous assessments (i.e. EFSA, 2013a) that have already been systematically collected and organised by EFSA during such previous assessments.

According to EFSA (2013c), in order to perform an exposure assessment, it is preferable to have measured residues in pollen and nectar collected from bees in open field conditions. Taking the pollen and nectar directly from the bees aims to give a better representation of the likely exposure to bees and bee colonies by accounting for dilution by non-contaminated pollen and nectar. As regards pollen, residues from pollen trap attached to the hive entrance are also considered suitable.

Residues measured in pollen collected from directly from honeybees (collection of forager or pollen traps) in open field conditions were available for both maize (n = 6) and winter oilseed rape (n = 6). For the latter crop, residues in nectar collected directly from honeybees were also available (n = 6). As residues from more than five independent trials were available for maize and winter oilseed rape, it was possible to carry out an exposure refinement for these two crops. The actual residue values used for establishing the exposure assessment goals are reported in Appendix D.

Residues from pollen and nectar collected directly from other bee species were not available. As an alternative, residues of pollen and nectar taken directly from the plant or collected by honeybees in confined conditions (e.g. tunnels) can be used in the exposure assessment. In this case, the exposure assessment is likely to represent an overestimation of the actual exposure to bees, as dilution is not accounted for. For maize, these kind of residue measurements in pollen were available for enough trials (n = 12 for pollen taken directly from plants and n = 6 for pollen taken from honeybee foragers in confined conditions). For winter oilseed rape also, residue measurements were available from pollen and nectar collected directly from plants (n = 1) and from honeybee foragers in confined conditions (n = 6). Therefore, a refined exposure could also be estimated for bumblebees and solitary bees for both crops.

In all the aforementioned cases, in accordance with the principles listed in Section 3.3.1.1, the retained value was the maximum measured residue level given by the sum of thiamethoxam and its metabolite clothianidin.

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The measured residue values were normalised for the seed loading [reference value = 1 mg a.s./seed] to give RUD values.

Such RUD values were log-transformed before being used as input for the EFSA SHVAL tool (EFSA 2013c, 2014a,b). A 90th percentile SV for exposure, in terms of residue intake, is given as output of this tool. Simulations were run for each bee species and each caste. Tier-1 data for pollen and nectar consumption and sugar content in nectar were assumed. To transform the refined SVs to an exposure assessment goal, the SVs are multiplied by the seed loading rate (in terms of mg a.s./kg seed) for each use listed in the GAPs. Presented in Tables 7 and 8 are the resulting refined SVs and exposure assessment goals for the GAPs for maize and winter oilseed rape.

Table 7: Revised shortcut value for honeybees, bumblebees and solitary bees for maize and winter oilseed rape applied as seed treatments

	Revised shortcut values	
	Maize	**Winter oilseed rape**
Honeybee		
Acute forager [µg/bee/day]	0[(a)]	0.0694
Chronic forager [µg/bee/day]	0[(a)]	0.0535
Nurse [µg/bee/day]	0.00005	0.0294
Larva [µg/larva/5 days]	0.000008	0.0398
Bumble bee		
Acute adult [µg/bee/day]	0.0003	0.2748
Chronic adult [µg/bee/day]	0.0003	0.2354
Larva [µg/larva/day]	0.0038	0.0567
Solitary Bee		
Adult [µg/bee/day]	0.0001	0.1494
Larva [µg/larva/30 days]	0.0038	0.2462

(a): Shortcut value for foragers for maize is 0 as forager bees do not consume pollen and maize does not produce nectar.

Table 8: Exposure assessment goals for honeybees, bumblebees and solitary bees for maize and winter oilseed rape applied as seed treatments

	Exposure assessment goals	
	Maize 0.63 mg a.s./seed	**Winter oilseed rape 0.021 mg a.s./seed**
Honeybee		
Acute forager [ng/bee/day]	0	1.459
Chronic forager [ng/bee/day]	0	1.124
Nurse [ng/bee/day]	0.033	0.619
Larva [ng/larva/5 days]	0.005	0.838
Bumble bee		
Acute adult [ng/bee/day]	0.189	5.771
Chronic adult [ng/bee/day]	0.189	4.945
Larva [ng/larva/10 days]	2.464[(a)]	11.907[(a)]
Solitary Bee		
Adult [ng/bee/day]	0.064	3.138
Larva [ng/larva/ 30 days]	2.414	5.170

(a): The exposure assessment goal for Bumble Bee larvae considers an additional factor of 10 to transform a SV expressed in terms of daily intake to an exposure assessment goal expressed in terms of intake for developmental period (10 days).

For the remaining uses of thiamethoxam listed in the GAP, no further exposure refinement was needed, as the treated crop scenario was not considered relevant (crop harvested before flowering).

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Succeeding crop scenario

Three semifields' experiments were available for residue measurements for succeeding crop (S08-01284, S08-01279, S08-01285). These were not part of the data set assessed for this review, but were instead data already available in previous assessments (i.e. EFSA, 2013a).

Within these experiments, maize-treated seeds (formulation A9700B) were planted. The crop was followed by barley seeds again treated with thiamethoxam (formulation A9638A). Finally, three bee attractive crops (*Phacelia*, oilseed rape and alfalfa) were grown on the same plots from non-treated seeds. Residues in soil, accounting for the sum of thiamethoxam and clothianidin, varied between 6 and 29 µg/kg. Pollen residues in the following crops, accounting for the sum of thiamethoxam and clothianidin, were generally higher in *Phacelia* (3–39 µg/kg) and lower in alfalfa (< 1–7.1 µg/kg) and oilseed rape (0.8–3 µg/kg). This ranking was not respected for nectar, where residues were higher in oilseed rape (2.2–7.7 µg/kg) and lower in Phacelia (1–2.1 µg/kg) and alfalfa (0.5–2.2 µg/kg).

In principle, these trials were considered useful for refining the exposure for the treated crop scenario. However, due to the low number of trials, the available information was not considered sufficient for refining the exposure. As a consequence, no exposure assessment goal could be established for the succeeding crop scenario.

5.1.1.3. Tier-2 risk assessment

Treated crop scenario

A Tier-2 risk assessment for the representative GAP for maize and winter oilseed rape was carried out. In these calculations, the Tier-1 SVs were replaced by the refined Tier-2 SVs. The outcomes of these calculations are summarised in Table 9.

On the basis of the Tier-2 risk assessment, a low acute risk to honeybees could be concluded for the use on maize. Furthermore, a low risk to honeybee larvae was identified for the uses on winter oilseed rape. For all other crop/species/caste combinations, the assessment outcome remained unchanged with respect to the Tier-1.

Table 9: Tier-2 risk assessment for honeybees for winter oilseed rape applied as seed treatments

Crop	Category	Honeybee		Bumble bee		Solitary bee	
		ETR	Trigger	ETR	Trigger	ETR	Trigger
Maize	Acute	0.006	0.2	**0.038**	0.036	**0.127**	0.04
	Larvae	Passed at Tier-1		**1.135**	0.2	**1.112**	0.2
Winter oilseed rape	Acute	**0.292**	0.2	**24.24**	0.036	**131.8**	0.04
	Larvae	0.039	0.02	**115.3**	0.02	**50.03**	0.02

ETR: exposure toxicity ratio.

On the basis of the Tier-2 risk assessment, a low acute risk to honeybees could be concluded for the use on maize. Furthermore, a low risk to honeybee larvae was identified for the uses on winter oilseed rape. For all other crop/species/caste combinations, the assessment outcome remained unchanged with respect to the Tier-1.

A risk assessment for chronic (all bee taxonomic groups) and honeybee HPG development could not be performed due to the lack of endpoints.

Succeeding crop scenario

As the exposure could not be refined for the succeeding crop scenario, no further assessment is performed.

5.1.1.4. Tier-3 risk assessment

As discussed in Section 3.4, a WoE approach was developed to utilise the information from the diverse range of higher tier effect experiments that were available.

The WoE risk assessment could only be performed for the GAPs for which an exposure assessment goal was calculated (Section 5.1.1.2). For the uses of thiamethoxam as a seed treatment, exposure assessment goals have been determined for all bee species, relative to the treated crop scenario of winter oilseed rape and maize. Therefore, a WoE approach was applied to these crop/species combinations of the treated crop scenario. As previously discussed, the WoE exercise has two fundamental steps: firstly, the identification/consideration of the lines-of-evidence and secondly, the integration of the lines-of-evidence.

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5.1.1.4.1. Weight of evidence higher tier risk assessment for honeybees

Lines of evidence

The Class 1 endpoints giving lines of evidence identified for the WoE assessment for honeybees were colony strength (during the season of application), overwintering assessment (which is based mainly on colony strength measurements after overwintering, but also considers information on overwintering colony survival) colony strength after overwintering and forager mortality. The Class 2 endpoints were mortality at the hive, brood production, drone production, homing success, queen mortality and worker longevity.

The lines of evidence for honeybees were considered against the exposure protection goal for the treated crop scenario for maize and winter oilseed rape. A visual representation of the identified lines of evidence was performed, as described in Section 3.4.1 and Figure 3. Owing the high volume of data, the results are presented in Appendix F (Section 1, Figures 5–15). For most endpoints, a figure is presented summarising the observations in the available higher tier effect studies. The general interpretation of the biological observations for each endpoint (e.g. number of reliable endpoints, general trend) is also presented in the Appendix F along with its final interpretation, which takes in to account the GAP/scenario specific exposure assessment goal and expected duration of exposure.

Integration of the lines of evidence

The second step of the WoE exercise is the integration of the lines of evidence. Tables 10 and 11 present the integration of the evidence for the treated crop scenario for maize and winter oilseed rape.

Table 10: Integration of the lines of evidence for honeybees for the treated crop scenario for maize

Honeybee	Treated crop scenario for maize
Class 1	
Colony strength	Refer to Appendix F, Section 1.1, Figure 5. A clear pattern of effects was not recorded. No information about the exposure was available for the large majority of the endpoints. Most of the experiments presented a potential exposure period longer than what expected from flowering in maize. The only reliable study with a proper exposure assessment indicated small negative departure from the control. However, the exposure in this study was around a factor of two higher than the exposure assessment goals and the exposure length was considerably longer than what could be expected from flowering in maize. Data in general presented high variability, low consistency and low reliability. **Line of evidence inconclusive.**
Overwintering assessment	Refer to Appendix F, Section 1.2, Figure 7. A clear pattern of effects was not recorded. No information about the exposure was available for the large majority of the endpoints. Most of the experiments presented a potential exposure period longer than what expected from flowering in maize. The only reliable study with a proper exposure assessment indicated medium negative departure from the control. However, the exposure in this study was around a factor of two higher than the exposure assessment goals and the exposure length was considerably longer than what could be expected from flowering in maize. Data in general presented low consistency and low reliability. **Line of evidence inconclusive.**
Forager mortality	This endpoint is not relevant for the treated crop scenario of maize, as honeybee foragers do not consume pollen and maize does not produce nectar.

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Honeybee	Treated crop scenario for maize
Class 2	
Brood abundance	Refer to Appendix F, Section 1.4, Figure 9. A clear pattern of effects was not recorded. No information about the exposure was available for the large majority of the endpoints. Most of the experiments presented a potential exposure period longer than what expected from flowering in maize. The only reliable study with a proper exposure assessment indicated a negligible deviation on average, but also indicated that negative deviations up to small are possible during the season. Nevertheless, both the exposure level and length were higher than what is expected from treated maize during flowering. Data in general presented high variability, low consistency and low reliability. **Line of evidence inconclusive.**
Mortality in front of the hive	Refer to Appendix F, Section 1.5, Figure 11. A pattern of lack of effects was available, which was nevertheless based on average mortality over time, and did not account for actual daily mortality, which should be the most relevant target for this kind of endpoint. No information about the exposure for any of the endpoints. Data in general presented good consistency (tendency for negligible positive deviation) but low reliability. **Line of evidence inconclusive.**
Homing success	This endpoint is not relevant for the treated crop scenario of maize, as honeybee foragers do not consume pollen and maize does not produce nectar.
Drone cells	Refer to Appendix F, Section 1.7, Figure 14. A clear pattern of effects was not recorded. No information about the exposure for any of the endpoints. Data in general presented extremely high variability, low consistency and low reliability. **Line of evidence inconclusive.**
Queen mortality	Refer to Appendix F, Section 1.8. Endpoint investigated in only one study assessed as reliable with major restrictions. Results suggest medium negative deviation. The current risk assessment scheme does not foresee an exposure assessment goal for honeybee queens. **Line of evidence inconclusive.**
Worker longevity	Refer to Appendix F, Section 1.9. Endpoint investigated in only one study assessed as reliable with minor restrictions. Results suggested negligible negative deviation from the control. No proper exposure assessment was available, but the exposure assessment goals for maize were likely achieved. **Weak evidence for negligible effects.**

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Honeybee	Treated crop scenario for maize	
Integration of lines of evidence	For maize, the only relevant Class 1 endpoints were colony strength and colony strength after winter. Forager mortality was not considered relevant as honeybee foragers do not consume pollen and maize does not produce nectar. Both Class 1 lines were inconclusive, as the lack of exposure estimation within the experiments made it impossible to relate the observed tendencies/variation to the exposure assessment goals for maize, which is pivotal to reach a conclusion. Class 2 endpoints also did not offer a better opportunity for linking the observed tendencies to a defined exposure, with only one minor exception, as there was weak evidence to show that worker longevity would only be negligibly shortened at exposure comparable with the exposure assessment goals for maize.	
Uncertainty analysis (− potential to make the true risk lower + potential to make the true risk higher)	**Quantification of the effects**	
	Most of the available endpoints were assessed to be reliable with major restrictions; therefore, the overall reliability of the WoE is limited.	−/+
	The reasons for the reliability assessment categorisation differed between the studies.	−/+
	The consistency of most lines of evidence was low.	−/+
	Some of the data were not presented in sufficient detail to derive accurate deviations from the control.	−/+
	Within some experiments, pre-exposure measurements revealed that some endpoints did not start at comparable level. This initial difference was accounted for in the derivation of the deviation from the control, but the accuracy of the quantification in this case is limited.	−/+
	Exposure in the experiments	
	A proper estimation of the exposure was missing in the large majority of the effect studies, which makes it impossible to check whether the exposure assessment goals were achieved.	−−/+++
	For the overwintering assessment, the lower food consumption of resting winter bees was not accounted for when estimating exposure in the experiments. This might have overestimating the exposure in the experiments.	+
	The level of the dilution of the residue concentrations of the consumed pollen and nectar in colony-feeder experiments with free flying bee could not be estimated from the available data.	+
	Confounding factors in the experiments	
	Of the multiple available field experiments on all bee species and all crops, measurements of some kinds of residues in the control were available for five. In three of these five studies, the control/reference was found to be contaminated by at least one neonicotinoid substance at levels compared to the treatment. This could potentially mask triggering of negative effects. The presence of external substances was also seen in the treatment, creating uncertainties about detecting effects not due to the treatment.	−−/++
	In some of the higher tier experiments where the bees were free flying, there were indications for the use of different pesticides, including insecticides. This may affect both control and treatment. There is also uncertainty that this practice could have been done also in experiments where this was not clearly reported.	−/+
	Exposure assessment goals	
	The exposure assessment goals were calculated using the maximum residue levels measured within each trial.	−
	The exposure assessment goals were calculated assuming residues equal to the LOQ every time measured concentration were < LOQ. In the cases that no residues were detected, the residue was considered to be equal to the LOD.	−
	The exposure assessment goals were calculated using residues in pollen considering empirical dilution (residues from foragers). No data are available to roughly quantify the possible dilution for maize.	+

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Honeybee	Treated crop scenario for maize
	For overwintering assessment, the exposure assessment goal was based on consumption from active bees, and could therefore be overestimating the actual exposure of bees during winter.
	In some residue studies (used for the exposure assessment goal), the sampling frequency and pattern did not guarantee that the actual maximum occurrence had been picked up.
	The limited number of valid residue studies available for the exposure assessment goal restricted the potential for the representativeness to cover 90th percentile exposure situations.
Conclusion	**A low risk** to honeybees from residues in pollen for the treated crop scenarios for maize **has not been demonstrated** with the weight of evidence exercise. The available data present low consistency, but overall do not offer a picture of clear effects. Most of the experiments were longer than the maize flowering period. However, a proper estimation of the exposure was missing in the large majority of the effect studies, which made it impossible to check whether the exposure assessment goals were met. The possibility of observing effects larger than negligible at the exposure assessment goal cannot be excluded. As such, a definitive crop-specific conclusion for maize cannot be achieved.

LOQ: limit of quantification; LOD: limit of detection; WoE: weight of evidence.

Table 11: Integration of the lines of evidence for honeybees for the treated crop scenario for winter oilseed rape

Honeybee	Treated crop scenario for winter oilseed rape
Class 1	
Colony strength	Refer to Appendix F, Section 1.1, Figure 6. A clear pattern of effects was not recorded. No information about the exposure for the large majority of the endpoints. Almost all experiments presented a potential exposure period which fitted with what expected from flowering in winter oilseed rape. The only two reliable endpoints for which there was some information about the exposure (one proper exposure assessment and one only considered as 'upper limit') indicated small to large negative deviation from the control at exposure levels lower or equal to the exposure assessment goal. The exposure period in one of these experiments was marginally longer than the estimated upper limit for the flowering duration of winter oilseed rape. The available data presented in general high variability, low consistency and low reliability. **Weak evidence for possible effects larger than negligible.**
Overwintering assessment	Refer to Appendix F, Section 1.2, Figure 8. A clear pattern of effects was not recorded. No information about the exposure was available for the large majority of the endpoints. Almost all experiments presented a potential exposure period which fitted with what expected from flowering in winter oilseed rape. Only one endpoint out of five indicated negative deviation. Nevertheless, this endpoint was the most reliable and the only one providing information about the actual level of exposure, which was lower than the exposure assessment goals. The available data presented in general low consistency and low reliability. **Weak evidence for possible effects larger than negligible.**

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Honeybee	Treated crop scenario for winter oilseed rape
Forager mortality	Refer to Appendix F, Section 1.3. Endpoint investigated in only one study assessed as reliable with major restrictions. Results suggested negligible negative deviation. Due to the design of the study (exposure gradient), a proper exposure assessment was not available. However, even when considering the maximum measured thiamethoxam concentration in nectar, the exposure assessment goal for forager was not achieved (concentration lower than all the ones used for derive the relevant exposure assessment goal). **Line of evidence inconclusive.**
Class 2	
Brood abundance	Refer to Appendix F, Section 1.4, Figure 10. A clear pattern of effects was not recorded. No information about the exposure was available for the large majority of the endpoints. Almost all experiments presented a potential exposure period which fitted with what expected from flowering in winter oilseed rape. The only two reliable endpoints for which there was some information about the exposure (one proper exposure assessment and one only considered as 'upper limit') indicated negative deviation from the control at exposure levels lower or equal to the exposure assessment goals. The exposure period in one of these experiments was marginally longer than the estimated upper limit for the flowering duration of winter oilseed rape. The available data presented in general high variability, low consistency and low reliability. **Weak evidence for effects larger than negligible.**
Mortality in front of the hive	Refer to Appendix F, Section 1.5, Figure 12. A pattern of lack of effects was available, which was nevertheless based on average mortality over time, and did not account for actual daily mortality, which should be the most relevant target for this kind of endpoint. No information about the exposure was available for any of the reliable endpoints. Data in general presented good consistency (tendency for negligible positive deviation) but low reliability. **Line of evidence inconclusive.**
Homing success	Refer to Appendix F, Section 1.6, Figure 13. A clear pattern of effect was recorded. Information on the exposure was available for all the reliable endpoints. Rather high consistency was recorded within and between the experiments, with some uncertainties regarding the effects by some environmental factors on the dose –response among studies. All tested doses were below the exposure assessment goal for acute foragers. The highest tested doses were just below the exposure assessment goal for acute foragers. **Strong evidence for effects larger than negligible.**
Drone cells	Refer to Appendix F, Section 1.7, Figure 15. A clear pattern of effects was not recorded. No information about the exposure was available for any of the endpoints. Data in general presented extremely high variability, low consistency and low reliability. **Line of evidence inconclusive.**

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Honeybee	Treated crop scenario for winter oilseed rape
Queen mortality	Refer to Appendix F, Section 1.8. Endpoint investigated in only one study assessed as reliable with major restrictions. Results suggest medium negative deviation. The current risk assessment scheme does not foresee an exposure assessment goal for honeybee queens. **Line of evidence inconclusive.**
Worker longevity	Refer to Appendix F, Section 1.9. Endpoint investigated in only one study assessed as reliable with minor restrictions. Results suggest negligible negative deviation. No proper exposure assessment is available, but likely the exposure in the experiment was lower than the exposure assessment goals. **Line of evidence inconclusive.**
Integration of lines of evidence	For oilseed rape, some weak indications are available that negative effects larger than negligible can occur on colony strength at the exposure assessment goal for winter oilseed rape (both during the season of application and after winter). However, such evidence is based on a very limited number of experiments, as the large majority of them lacked any exposure estimation, making it impossible to relate the observed tendencies to the exposure assessment goals for oilseed rape. The other Class 1 endpoint, forager mortality, was only properly measured in one study, which offers some indications for clear but negligible effects. Nevertheless, the exposure in this experiment (even if not fully quantifiable) was certainly lower than the exposure assessment goal, making the line of evidence inconclusive for the present risk assessment. The strongest available piece of evidence was for homing behaviour of forager honeybees. The available data confirmed that up to medium effects are seen when forager bees are exposed to doses lower than the relevant exposure assessment goal for winter oilseed rape. This evidence is somehow consistent with the available data for forager mortality, but effects may have been amplified by the design of the considered homing trials, where bees are released relatively far from their hive (1 km). The other relevant and usable Class 2 endpoint (brood abundance) provided again some weak indications for possibility of effects larger than negligible, but again such evidence is based on a very limited number of experiments, as the large majority of them lacked any exposure estimation. Other Class 2 lines of evidence did not provide significantly meaningful information for the risk assessment as the observed tendency could not be linked at all to defined exposure levels.
Uncertainty analysis (potential to make the true risk lower + potential to make the true risk higher)	**Quantification of the effects** Most of the available endpoints were assessed to be reliable with major restrictions; therefore, the overall reliability of the WoE is limited. −/+ The reasons for the reliability assessment categorisation differed between the studies. /+ The consistency of most lines of evidence was low. /+ Some of the data were not presented in sufficient detail to derive accurate deviations from the control. /+ Within some experiments, pre-exposure measurements revealed that some endpoints did not start at comparable level. This initial difference was accounted for in the derivation of the deviation from the control, but the accuracy of the quantification in this case is limited. /+ The magnitude of the effects seen in the homing trials is likely to be amplified (compared to the reality) by the distance of the release (1 km). −−

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Honeybee	Treated crop scenario for winter oilseed rape	
	Exposure in the experiments	
	A proper estimation of the exposure was missing in the large majority of the effect studies, which makes it impossible to check whether the exposure assessment goals were achieved.	−−−/+++
	For the overwintering assessment, the lower food consumption of resting winter bees was not accounted for when estimating exposure in the experiments. This might have overestimating the exposure in the experiments.	+
	The level of the dilution of the residue concentrations of the consumed pollen and nectar in colony-feeder experiments with free flying bee could not be estimated from the available data.	+
	Confounding factors in the experiments	
	Out of the multiple available field experiments on all bee species and all crops, measurements of some kinds of residues in the control were available for five. In three of these five studies, the control/reference was found to be contaminated by at least one neonicotinoid substance at levels comparable to the treatment. This could potentially mask triggering of negative effects. The presence of external substances was also seen in the treatment, creating uncertainties about detecting effects not due to the treatment.	/++
	In some of the higher tier experiments where the bees were free flying, there were indications for the use of different pesticides, including insecticides. This may affect both control and treatment. There is also uncertainty that this practice could have been done also in experiments where this was not clearly reported.	−/+
	Exposure assessment goals	
	The exposure assessment goals were calculated using the maximum residue levels measured within each trial.	−
	The exposure assessment goals were calculated assuming residues equal to the LOQ every time measured concentration were < LOQ. In the cases that no residues were detected, the residue was considered to be equal to the LOD.	−
	The exposure assessment goals were calculated using residues in pollen and nectar considering empirical dilution (residues from foragers). No data were available to roughly quantify the possible dilution for winter oilseed rape.	+
	For the determination of the exposure assessment goals, a 15% sugar content of the nectar was assumed, which is the low end value of the realistic range. This may have resulted in an overestimation of the exposure assessment goal.	+
	For overwintering assessment, the exposure assessment goal was based on consumption from active bees and could therefore be overestimating the actual exposure of bees during winter.	
	In some residue studies (used for the exposure assessment goal), the sampling frequency and pattern did not guarantee that the actual maximum occurrence had been picked up.	+
	The limited number of valid residue studies available for the exposure assessment goal restricted the potential for the representativeness to cover 90th percentile exposure situations.	+

ED_006569N_00037382-00030

Honeybee	Treated crop scenario for winter oilseed rape
Conclusion	**A low risk** to honeybees from residues in nectar and/or pollen for the treated crop scenarios for winter oilseed rape **has not been demonstrated** with the weight of evidence exercise. The available data related to colony strength presented low consistency, but overall did not offer a picture of clear effects. A proper estimation of the exposure was missing in the large majority of the effect studies, which made it impossible to check whether the exposure assessment goals were met or whether the deviations were driven by any exposure–effect relationship. The available information suggested that effects larger than negligible might occur on colony strength and brood at the exposure assessment goal for winter oilseed rape. However, this is based on rather weak evidence. The data related to forager mortality indicate negligible negative effects at exposure levels lower than the exposure assessment goal. The available information also suggested that exposure to thiamethoxam may impair homing behaviour of honeybees. This could in principle lead to an increase of forager mortality, but the quantification of such increase cannot be directly deduced from the available data, due to the artificial design of homing trials. Taking this into account, it cannot be excluded that the protection goal related to forager mortality could be breached at the exposure assessment goal. Overall, despite clear effects were not recorded for any of the endpoints directly related to the protection goals, the possibility of observing some effects larger than negligible cannot be excluded. As such, a crop-specific conclusion for winter oilseed rape cannot be achieved.

LOQ: limit of quantification; LOD: limit of detection; WoE: weight of evidence.

5.1.1.4.2. Weight of evidence higher tier risk assessment for bumblebees

Lines of evidence

The Class 1 endpoints giving lines of evidence identified for the WoE assessment for bumblebees were colony strength, queen production, drone production, worker production/abundance and brood production. Also, the reproductive output (males) in queenless microcolonies was considered as a separate Class 1 endpoint, due to its peculiarity. The Class 2 endpoints were day of the first oviposition, total caste biomass and emergence rates.

The lines of evidence for bumblebees were considered against the exposure protection goal for the treated crop scenario for maize and winter oilseed rape. A visual representation of the identified lines of evidence was performed, as described in Section 3.4.1 and Figure 3. Owing the high volume of data, the results are presented in Appendix F (Section 1, Figures 16–23). For most endpoints, a figure is presented summarising the observations in the available higher tier effect studies. The general interpretation of the biological observations for each endpoint (e.g. number of reliable endpoints, general trend) is also presented in the Appendix F along with its final interpretation, which takes into account the GAP/scenario specific exposure assessment goal and expected duration of exposure.

Integration of the lines of evidence

The second step of the WoE exercise is the integration of the lines of evidence. Tables 12 and 13 present the integration of the evidence for the treated crop scenario for maize and winter oilseed rape.

ED_006569N_00037382-00031

Table 12: Integration of the lines of evidence for bumblebees for the treated crop scenario for maize.

Honeybee	Treated crop scenario for maize
Class 1	
Queen production	Refer to Appendix F, Section 2.1, Figure 16. A clear pattern of effects was not recorded. No information about the exposure was available for the majority of the endpoints. Most of the experiments presented a potential exposure period longer than what expected from flowering in maize. Lack of negative deviations larger than negligible was suggested by the majority of the experiments, even at exposure higher (in terms of level) than the exposure assessment goals and longer than the maize flowering period. Negative deviations larger than negligible were only seen in two experiments: one of this presented an exposure higher than the exposure assessment goal and considerably longer than the maize flowering period. The other was derived from a field study on winter oilseed rape. In general, the data presented low consistency and low reliability. **Moderate evidence for negligible effects.**
Colony strength	Refer to Appendix F, Section 2.2, Figure 18. A rather clear pattern of lack of effects was available from the data, with deviations from the control ranging from negligible negative to small positive. Exposure information was available for three of four endpoints. For all of them, the exposure assessment goal for adult was exceeded. The exposure assessment goal for larvae was only exceeded for one endpoint, but the other two were not too far (less than a factor of 2). In general, the data presented fair consistency but low reliability. **Moderate evidence for negligible effects.**
Brood production	Refer to Appendix F, Section 2.3, Figure 20. A clear pattern of effects was not recorded. The exposure level was unknown in all the available experiments (all field experiments carried out on winter oilseed rape), and therefore, any comparison with the exposure assessment goals for maize was impossible. Rather low consistency and low reliability. **Line of evidence inconclusive.**
Drone production	Refer to Appendix F, Section 2.4, Figure 22. A clear pattern of effects was not recorded. Data to properly quantify the exposure to bumblebees were only available for three endpoints. Two of those were derived from the same experiment, where different doses were tested. Within this experiment, rather contradicting results were seen, with the highest dose producing a positive deviation and the lower dose resulting in a medium negative deviation. This lack of dose–response suggests that the observed deviations may be due to biological variation rather than the results of actual effects. Another endpoint suggested large negative deviation from the control. Nevertheless, it presented an exposure level higher than the exposure assessment goals and by an exposure duration considerably longer than the maize flowering period. As such, this was not really informative for the uses on maize. The remaining three endpoints were from field experiments on winter oilseed rape, and they indicated large negative, negligible and large positive deviation from the control. In general, the data presented low consistency and low reliability. **Weak evidence for negligible effects.**

ED_006569N_00037382-00032

Honeybee	Treated crop scenario for maize
Reproductive output of queenless microcolonies	Refer to Appendix F, Section 2.5, Figure 24. The data offer a rather clear pattern of effects, as all indicated large negative deviation from the control. Most of these endpoints were considered unreliable, with the exception of three. Among these, two presented an exposure considerably higher than the exposure assessment goals for maize and/or considerably longer than the maize-flowering period. Only one reliable endpoint was characterised by an exposure smaller than or equal to the exposure assessment goals for maize and only marginally longer than the flowering duration for maize. This was the only data point suggesting that negative effects may occur after exposure to thiamethoxam from contaminated maize pollen. In general, the data presented very high consistency and variable reliability. **Weak evidence for effects larger than negligible.**
Worker production	Refer to Appendix F, Section 2.6, Figure 27. A clear pattern of effects was not recorded. Data for three endpoints indicated that the exposure in the experiments was higher than the exposure assessment goals. For two of these endpoints, lack of negative deviations larger than negligible was observed. The third presented medium-negative deviation, but the exposure was considerably longer than the maize-flowering period. The remaining endpoints had no information about the exposure and were derived from field experiments on winter oilseed rape. In general, the data presented rather low consistency and low reliability. **Weak evidence for negligible effects.**
Class 2	
All	Refer to Appendix F, Section 2.7. Some endpoints measuring indirect reproduction of bumblebees (e.g. days of the first oviposition, emergence rate, total caste biomass) were measured in single experiments. Nevertheless, these endpoints were either not properly quantified or very much correlated with endpoints considered within class 1. Considering this, Class 2 endpoints will not be considered for the risk assessment to bumblebees.
Integration of lines of evidence	All Class 1 endpoints offer weak to moderate evidence, due to the lack of exposure characterisation for many the endpoints, the general low consistency within the single lines of evidence and the low reliability of the endpoints. Nevertheless, the general outcome that can be appreciated is a lack of negative effects larger than negligible when the exposure is comparable to the exposure assessment goals for maize. The only exception to this trend is represented by the results of the reproduction in queenless microcolonies. Most of the endpoints within such line of evidence could not be used for the risk assessment on maize. Nevertheless, one endpoint was somehow indicating that large negative effects may be seen also at exposure (level and length) comparable to the one expected from maize. It should, however, be considered that this line of evidence, despite being somehow indicative of potential reproductive inhibition, is derived from a biological process (workers producing aploid brood) that is not the standard reproduction strategy for bumblebees. If effects on the reproduction would be triggered under normal colony development conditions, this would have been reflected by the other lines of evidence (queen production, drone production, worker production and brood production), which, in this case, tended to indicate lack of effects larger than negligible or were inconclusive. Class 2 endpoints were not considered in the present integration.

ED_006569N_00037382-00033

Honeybee	Treated crop scenario for maize	
Uncertainty analysis (– potential to make the true risk lower + potential to make the true risk higher)	**Quantification of the effects**	
	Most of the available endpoints were assessed to be reliable with major restrictions; therefore, the overall reliability of the WoE is limited.	–/+
	The reasons for the reliability assessment categorisation differed between the studies.	–/+
	The consistency of most lines of evidence was rather low.	–/+
	Some of the data were not presented in sufficient detail to derive accurate deviations from the control.	–/+
	Exposure in the experiments	
	A proper estimation of the exposure was missing in the large majority of the effect studies, which makes it impossible to check whether the exposure assessment goals were achieved.	––/+++
	The level of the dilution of the residue concentrations of the consumed pollen and nectar in colony-feeder experiments with free flying bee could not be estimated from the available data.	+
	For some colony-feeder experiments where bees were fed with sugar solution, the actual percentage of sugar was unknown and therefore assumed to be 50%. This would have an impact on the assumed consumption and in turn on the active substance intake. Some studies followed a colony-feeder type test design with an exposure period longer than a flowering period of the crop of interest.	–/+
	Confounding factors in the experiments	
	Out of the multiple available field experiments on all bee species and all crops, measurements of some kinds of residues in the control were available for five. In three of these five studies, the control/reference was found to be contaminated by at least one neonicotinoid substance at levels comparable to the treatment. This could potentially mask triggering of negative effects.	––/++
	The presence of external substances was also seen in the treatment, creating uncertainties about detecting effects not due to the treatment.	
	In some of the higher tier experiments where the bees were free flying, there were indications for the use of different pesticides, including insecticides. This may affect both control and treatment.	–/+
	There is also uncertainty that this practice could have been done also in experiments where this was not clearly reported.	
	Exposure assessment goals	
	The exposure assessment goals were calculated using the maximum residue levels measured within each trial.	–
	The exposure assessment goals were calculated assuming residues equal to the LOQ every time measured concentration were < LOQ. In the cases that no residues were detected, the residue was considered to be equal to the LOD.	–
	The exposure assessment goals were calculated using residues in pollen without dilution (from plants or from honeybees in confined conditions). No data are available to roughly quantify the possible dilution for maize.	–
	In some residue studies (used for the exposure assessment goal), the sampling frequency and pattern did not guarantee that the actual maximum occurrence had been picked up.	+
	The limited number of valid residue studies available for the exposure assessment goal, restricted the potential for the representativeness to cover 90th percentile exposure situations.	+

ED_006569N_00037382-00034

Honeybee	Treated crop scenario for maize
	Specific issues
	Several effects due to exposure to clothianidin were identified in the clothianidin conclusion (EFSA, 2018c). It should be noted that these effects are expected at an exposure that is comparable to those relevant for thiamethoxam. Indeed, in the clothianidin conclusion (EFSA, 2018c), a low risk could not be demonstrated based on exposure assessment goals comparable to those used for the present risk assessment. Such effects were not identified with the available data on thiamethoxam. In principle, as some of the available data are related to field studies, bees were probably exposed to clothianidin as well, clothianidin being the main thiamethoxam metabolite. However, the mismatch of the available data set between the two substances creates significant uncertainty about the present conclusion.
Conclusion	Despite all investigated lines offer only weak evidence, all but one available lines of evidence seem to indicate that a **low risk** to bumblebees should be expected from residues in pollen for the treated crop scenarios related to the use of thiamethoxam as maize seed treatment. In principle, this conclusion should also cover for the exposure to the metabolite clothianidin which may form from the use of thiamethoxam on maize. However, specific information on the exposure to clothianidin was not considered in a separate manner for the present assessment. As relevant effects were identified in the clothianidin conclusion (EFSA, 2013c) for bumblebee, this constitutes a significant uncertainty for the present assessment.

LOQ: limit of quantification; LOD: limit of detection; WoE: weight of evidence.

Table 13: Integration of the lines of evidence for bumblebees for the treated crop scenario for winter oilseed rape

Honeybee	Treated crop scenario for winter oilseed rape
Class 1	
Queen production	Refer to Appendix F, Section 2.1, Figure 17. A clear pattern of effects was not recorded. No information about the exposure was available for the majority of the endpoints. When exposure was known (three endpoints), it was always lower than the exposure assessment goals. Two of such endpoints (from the same experiment) indicated lack of negative deviation, while the other indicated large negative deviation. Nevertheless, this last one presented an exposure which was considerably longer than the winter oilseed rape flowering period. The other endpoints were all derived from field experiments with winter oilseed rape. Three of them presented positive or negligible negative deviations from the control. One presented a small negative deviation. In general, the data presented low consistency and low reliability. **Line of evidence inconclusive.**

ED_006569N_00037382-00035

Honeybee	Treated crop scenario for winter oilseed rape
Colony strength	Refer to Appendix F, Section 2.2, Figure 19. A rather clear pattern of lack of effects was available from the data, with deviations from the control ranging from negligible negative to small positive. All available exposure levels tested in the available experiments were below the respective exposure assessment goal for winter oilseed rape. The smaller difference was around a factor 1.5–2. Overall, the available data did not indicate adverse effects on bumblebee colony strength after exposure to thiamethoxam. Nevertheless, the tested exposure levels did not meet the exposure assessment goal for winter oilseed rape. Fair consistency but low reliability. **Line of evidence inconclusive.**
Brood production	Refer to Appendix F, Section 2.3, Figure 21. A clear pattern of effects was not recorded. The exposure level was unknown in all the available experiments (all field experiments carried out on winter oilseed rape), and therefore, any comparison with the exposure assessment goals for winter oilseed rape was impossible. Rather low consistency and low reliability. **Line of evidence inconclusive.**
Drone production	Refer to Appendix F, Section 2.4, Figure 23. A clear pattern of effects was not recorded. Data to properly quantify the exposure to bumblebees were only available for three endpoints. Two of those were derived from the same experiment, where different doses were tested. Within this experiment, rather contradicting results were seen, with the highest dose producing a positive deviation and the lower dose resulting in a medium negative deviation. This lack of dose–response suggests that the observed deviations may be due to biological variation rather than the results of actual effects. Another endpoint suggested large negative deviation from the control at an exposure level lower than the exposure assessment goals. Nevertheless, the exposure duration was considerably longer than the winter oilseed rape flowering period. The remaining three endpoints were from field experiments on winter oilseed rape, and they indicated large negative, negligible and large positive deviation from the control. In general, the data presented low consistency and low reliability. **Line of evidence inconclusive.**
Reproductive output of queenless microcolonies	Refer to Appendix F, Section 2.5, Figure 25–26. The data offer a rather clear pattern of effects, as all indicated large negative deviation from the control. Most of these endpoints were considered unreliable, with the exception of three. Among these, one presented an exposure considerably higher than the exposure assessment goals for maize or considerably longer than the maize flowering period. Two reliable endpoints were characterised by an exposure smaller than the exposure assessment goals for winter oilseed rape, and appropriate length when compared to winter oilseed rape flowering period. In general, the data presented very high consistency and variable reliability. **Moderate evidence for effects larger than negligible.**

ED_006569N_00037382-00036

Honeybee	Treated crop scenario for winter oilseed rape
Workers	Refer to Appendix F, Section 2.6, Figure 28. A clear pattern of effects was not recorded. Data for three endpoints indicated that the exposure in the experiments was lower than the exposure assessment goals. For two of these endpoints, lack of negative deviations larger than negligible was observed. The third presented medium-negative deviation, but the exposure was longer than the winter oilseed rape flowering period. The remaining endpoints had no information about the exposure and were derived from field experiments on winter oilseed rape. Deviations ranged from medium negative to large positive. In general, the data presented low consistency and low reliability. **Weak evidence for possible negative effects larger than negligible.**
Class 2	
All	Refer to Appendix F, Section 2.7. Some endpoints measuring indirect reproduction of bumblebees (e.g. days of the first oviposition, emergence rate, total caste biomass) were measured in single experiments. Nevertheless, these endpoints were either not properly quantified or very much correlated with endpoints considered within class 1. Considering this, Class 2 endpoints will not be considered for the risk assessment to bumblebees.
Integration of lines of evidence	Most of the available lines of evidence were inconclusive for the present risk assessment on the use on winter oilseed rape. Only weak evidence suggests that negative effects larger than negligible may occur on worker production. The results of the reproduction in queenless microcolonies, on the contrary, presented moderate evidence that negative effect larger than negligible (up to large) may occur at exposure comparable to the exposure assessment goals for winter oilseed rape. It should, however, be considered that this line of evidence, despite being somehow indicative of potential reproductive inhibition, is derived from a biological process (workers producing aploid brood) that is not the standard reproduction strategy for bumblebees. Class 2 endpoints were not considered in the present integration.
Uncertainty analysis	**Quantification of the effects**
(– potential to make the true risk lower + potential to make the true risk higher)	Most of the available endpoints were assessed to be reliable with major restrictions; therefore, the overall reliability of the WoE is limited. –/+ The reasons for the reliability assessment categorisation differed between the studies. –/+ The consistency of most lines of evidence was rather low. /+ Some of the data were not presented in sufficient detail to derive accurate deviations from the control. –/+
	Exposure in the experiments
	A proper estimation of the exposure was missing in the large majority of the effect studies, which makes it impossible to check whether the exposure assessment goals were achieved. ––––/++++ The level of the dilution of the residue concentrations of the consumed pollen and nectar in colony-feeder experiments with free flying bee could not be estimated from the available data. + For some colony-feeder experiments where bees were fed with sugar solution, the actual percentage of sugar was unknown and therefore assumed to be 50%. This would have an impact on the assumed consumption and in turn on the active substance intake. –/+

ED_006569N_00037382-00037

Honeybee	Treated crop scenario for winter oilseed rape	
	Confounding factors in the experiments	
	Out of the multiple available field experiments on all bee species and all crops, measurements of some kinds of residues in the control were available for five. In three of these five studies, the control/reference was found to be contaminated by at least one neonicotinoid substance at levels comparable to the treatment. This could potentially mask triggering of negative effects. The presence of external substances was also seen in the treatment, creating uncertainties about detecting effects not due to the treatment.	−/+
	In some of the higher tier experiments where the bees were free flying, there were indications for the use of different pesticides, including insecticides. This may affect both control and treatment. There is also uncertainty that this practice could have been done also in experiments where this was not clearly reported.	−/+
	Exposure assessment goals	
	The exposure assessment goals were calculated using the maximum residue levels measured within each trial.	−
	The exposure assessment goals were calculated assuming residues equal to the LOQ every time measured concentration were < LOQ. In the cases that no residues were detected, the residue was considered to be equal to the LOD.	−
	The exposure assessment goals were calculated using residues in pollen without dilution (from plants or from honeybees in confined conditions). No data are available to roughly quantify the possible dilution for winter oilseed rape.	−
	For the determination of the exposure assessment goals, a 15% sugar content of the nectar was assumed, which is the low end value of the realistic range. This may have resulted in an overestimation of the exposure assessment goal	+
	In some residue studies (used for the exposure assessment goal), the sampling frequency and pattern did not guarantee that the actual maximum occurrence had been picked up.	+
	The limited number of valid residue studies available for the exposure assessment goal, restricted the potential for the representativeness to cover 90th percentile exposure situations.	+
	Specific issues	
	Several effects due to exposure to clothianidin were identified in the clothianidin conclusion (EFSA, 2018c). It should be noted that these effects are expected at an exposure that is comparable to those relevant for thiamethoxam. Indeed, in the clothianidin conclusion (EFSA, 2018c), a high risk was identified based on exposure assessment goals comparable to those used for the present risk assessment. Such effects were not identified with the available data on thiamethoxam. In principle, as some of the available data are related to field studies, bees were probably exposed to clothianidin as well, clothianidin being the main thiamethoxam metabolite. However, the mismatch of the available data set between the two substances creates significant uncertainty about the present conclusion.	+++
Conclusion	**A low risk** to bumblebees from residues in pollen and nectar **has not been demonstrated** with the weight-of-evidence exercise for the treated crop scenario related to the use of thiamethoxam as seed treatment of winter oilseed rape. The available data present low consistency. The possibility of observing negative effects larger than negligible cannot be excluded. However, a proper estimation of the exposure was missing in the majority of the effect studies, which makes it impossible to check whether the exposure assessment goals were achieved. As such, a definitive crop-specific conclusion for winter oilseed rape cannot be achieved.	

LOQ: limit of quantification; LOD: limit of detection; WoE: weight of evidence.

ED_006569N_00037382-00038

5.1.1.4.3. Weight of evidence higher tier risk assessment for solitary bees

Lines of evidence

Several reproductive endpoints were measured for solitary bees (e.g. completed nests, tubes with brood, cocoon production). It was however decided that the endpoint for the number of offspring emerging after winter (i.e. the reproductive output) represents the accumulation of all of these endpoints.

For this reason, it was decided to base the solitary bee WoE risk assessment on this endpoint only.

Nevertheless, in some experiments, despite an equal number of cocoons is released before the exposure starts, the number of emerging females can be extremely different. As this difference is not related to the exposure, the reproductive output has been, when needed, normalised for the number of initially hatching females.

In open-field conditions, hatched females may also nest outside of the artificial nests prepared for the experiment. For this reason, the reproductive output is also presented after normalisation for the mean number of nesting females. However, this endpoint should be considered with care, as the mismatch between the number of initially hatched and the number of nesting females counted in the experiment may or may not be related to effects caused by the treatment.

The lines of evidence for solitary bees were considered against the exposure protection goal for the treated crop scenario for maize and winter oilseed rape. A visual representation of the identified lines of evidence was performed, as described in Section 3.4.1 and Figure 3. Owing the high volume of data, the results are presented in Appendix F (Section 3, Figures 24–40). For most endpoints, a figure is presented summarising the observations in the available higher tier effect studies. The general interpretation of the biological observations for each endpoint (e.g. number of reliable endpoints, general trend) is also presented in the Appendix F along with its final interpretation, which takes into account the GAP/scenario-specific exposure assessment goal and expected duration of exposure.

Integration of the lines of evidence

The second step of the WoE exercise is the integration of the lines of evidence. Tables 14 and 15, present the integration of the evidence for the treated crop scenario for maize and winter oilseed rape.

Table 14: Integration of the lines of evidence for solitary bees for the treated crop scenario for maize

Honeybee	Treated crop scenario for maize
Class 1	
Reproductive output per hatched female	Refer to Appendix F, Section 3.1.1, Figure 29. A rather clear pattern of effect was recorded. Tendency for small to large negative deviation. The only endpoint showing an opposite direction is the less reliable one. Information about the exposure was not available for 3/4 of the endpoints. The only endpoint with an estimation of the exposure show large-negative effects. Within this experiment, the exposure to adult bees was from two to eight times higher than the maize exposure assessment goal, but the exposure to larvae was almost seven times lower than the exposure assessment goal. The length of the exposure was only reported in two experiments and was always longer than the expected flowering duration for maize. In general, the data showed some consistency and good reliability. Even if a rather clear pattern of effects could be detected, none of the available experiments seems appropriate to investigate the effects due to exposure during maize flowering. **Line of evidence inconclusive.**
Reproductive output per nesting female	Refer to Appendix F, Section 3.1.2, Figure 31. See interpretation for reproductive output per hatched female (maize). **Line of evidence inconclusive.**

ED_006569N_00037382-00039

Honeybee	Treated crop scenario for maize
Class 2	
Weight of the cocoons (females)	Refer to Appendix F, Section 3.2, Figure 33. The data showed a tendency for negligible to small-negative deviation. No information about the exposure was available for any of the endpoints. The length of the exposure was only reported in one experiment and was longer than the expected flowering duration for maize. In general, the data showed good consistency and fair reliability. Despite the rather consistent biological observations, in lack of any information about the exposure, the line of evidence was considered **inconclusive.**
Weight of the cocoons (males)	Refer to Appendix F, Section 3.3, Figure 35. A clear picture of effects was not available. No information about the exposure was available for any of the endpoints. The length of the exposure was only reported in one experiment and was longer than the expected flowering duration for maize. In general, the data presented some inconsistency and fair reliability. **Line of evidence inconclusive.**
Weight of the offspring (females)	Refer to Appendix F, Section 3.4, Figure 37. The available experiments offered a picture of lack of effects (larger than negligible). The only available exposure estimation to adult bees was from two to eight times higher than the maize exposure assessment goal, but the exposure to larvae was almost seven times lower than the exposure assessment goal. The length of the exposure was only reported in two experiments and was always longer than the expected flowering duration for maize. The data presented good consistency and reliability. Even if no effects (larger than negligible) were seen in the available data set, it is not possible to verify whether bigger effects would be seen at the exposure assessment goals (particularly the one for larvae). **Line of evidence inconclusive.**
Weight of the offspring (males)	Refer to Appendix F, Section 3.5, Figure 39. The available experiments offered a picture of lack of effects (larger than negligible). The only available exposure estimation to adult bees was from two to eight times higher than the maize exposure assessment goal, but the exposure to larvae was almost seven times lower than the exposure assessment goal. The length of the exposure was only reported in two experiments and was always longer than the expected flowering duration for maize. The data presented good consistency and reliability. Even if no effects (larger than negligible) were seen in the available data set, it is not possible to verify whether bigger effects would be seen at the exposure assessment goals (particularly for larvae). **Line of evidence inconclusive.**

ED_006569N_00037382-00040

Honeybee	Treated crop scenario for maize	
Integration of lines of evidence	The two available Class 1 lines of evidence are quite comparable, as the only difference is the normalisation factor. The only difference is reported for the endpoints in one experiment which passes from small-negative deviation when normalised for initially hatched female to large-negative deviation when normalised for mean nesting females. Nevertheless, the normalisation per average number of nesting females should be considered with care. Firstly, a reduced number of nesting female could be due to treatment effects. Secondly, in the field experiments (T.721, T.722, T.723), the total number of nesting females over the entire experiment period was not reported; therefore, the number of nesting females used as normalisation factor was an average over time. Overall, the two Class 1 lines of evidence offered a rather clear pattern of effects due to the exposure to thiamethoxam. On the contrary, Class 2 lines of evidence (cocoon and offspring weight, considered separately for male and female) did not show any particular evidence for negative effects larger than negligible (small to negligible in the case of female cocoon weight). Nevertheless, in all cases, a proper comparison with the expected exposure from maize could not be performed. The actual exposure was only available for one experiment: here, the exposure to adult bees was from two to eight times higher than the maize exposure assessment goal, but the exposure to larvae was almost seven times lower than the exposure assessment goal. The exposure length in this and in another experiment (the only two for which this information was available) was longer than the expected flowering duration for maize. As such, none of the available experiments seemed appropriate to investigate the effects due to exposure during maize flowering.	
Uncertainty analysis (− potential to make the true risk lower + potential to make the true risk higher)	**Quantification of the effects**	
	The normalisation per average number of nesting females should be considered with care as a reduced number of nesting female could be due to treatment effects. In the field experiments, the average over time was used as normalisation factor.	−/+
	Exposure in the experiments	
	A proper estimation of the exposure was missing in ¾ of the effect studies, which makes it impossible to check whether the exposure assessment goals were achieved.	−−−/+++
	Confounding factors in the experiments	
	Out of the multiple available field experiments on all bee species and all crops, measurements of some kinds of residues in the control were available for five. In three of these five studies, the control/reference was found to be contaminated by at least one neonicotinoid substance at levels comparable to the treatment. This could potentially mask triggering of negative effects. The presence of external substances was also seen in the treatment, creating uncertainties about detecting effects not due to the treatment.	−−/++
	In some of the higher tier experiments where the bees were free flying, there were indications for the use of different pesticides, including insecticides. This may affect both control and treatment. There is also uncertainty that this practice could have been done also in experiments where this was not clearly reported.	−/+
	Exposure assessment goals	
	The exposure assessment goals were calculated using the maximum residue levels measured within each trial.	−
	The exposure assessment goals were calculated assuming residues equal to the LOQ every time measured concentration were < LOQ. In the cases that no residues were detected, the residue was considered to be equal to the LOD.	−

ED_006569N_00037382-00041

Honeybee	Treated crop scenario for maize	
	The exposure assessment goals were calculated using residues in pollen without dilution (from plants or from honeybees in confined conditions). No data are available to roughly quantify the possible dilution for maize.	–
	In some residue studies (used for the exposure assessment goal) the sampling frequency and pattern did not guarantee that the actual maximum occurrence had been picked up.	–
	The limited number of valid residue studies available for the exposure assessment goal, restricted the potential for the representativeness to cover 90th percentile exposure situations.	–
	Specific issues	
	Data are only available on one solitary bee species (*Osmia bicornis*) out of the hundreds present in Europe.	–/++
Conclusion	**A low risk** to solitary bees from residues in pollen **has not been demonstrated** with the weight of evidence exercise for the treated crop scenario related to the use of thiamethoxam as seed treatment of maize. The available data indicate that the reproductive output of solitary bees may be impaired from small to large extent by exposure to thiamethoxam, while Class 2 endpoints did not show any evidence for negative effects larger than negligible. Nevertheless, in all cases, a proper comparison with the expected exposure from maize could not be performed. The actual exposure was only available for one experiment: here, the exposure to adult bees was from two to eight times higher than the maize exposure assessment goal, but the exposure to larvae was almost seven times lower than the exposure assessment goal. The exposure length in this and in another experiment (the only two for which this information was available) was longer than the expected flowering duration for maize. Overall, the available information does not allow to refine the risk assessment for the treated crop scenario related to the use of thiamethoxam as seed treatment of maize.	

LOQ: limit of quantification; LOD: limit of detection; WoE: weight of evidence.

Table 15: Integration of the lines of evidence for solitary bees for the treated crop scenario for winter oilseed rape

Honeybee	Treated crop scenario for winter oilseed rape
Class 1	
Reproductive output per hatched female	Refer to Appendix F, Section 3.1.1, Figure 30. A rather clear pattern of effect was recorded. Tendency for small to large negative deviation. The only endpoint showing an opposite direction is the less reliable one. No information about the exposure for 3/4 of the endpoints. The only endpoint with an estimation of the exposure show large-negative effects. Within this experiment, the exposure to adult bees was at least six times lower than the winter oilseed rape exposure assessment goal, and the exposure to larvae was almost 14 times lower than the exposure assessment goal. For the other three experiments, no exposure estimation was available. Nevertheless, as these were all field studies carried out with winter oilseed rape, it is likely that the exposure was lower or equal to the exposure assessment goals for the same crop (as these were estimated to cover the 90th percentile of possible exposure and were based on no-dilution conditions). In general, the data showed some consistency and good reliability. **Moderate evidence for effects larger than negligible.**
Reproductive output per nesting female	Refer to Appendix F, Section 3.1.2, Figure 32. See interpretation for reproductive output per hatched female (winter oilseed rape). Good consistency (better than what observed for reproductive output per hatched female) and good reliability. **Moderate evidence effects larger than negligible.**

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Honeybee	Treated crop scenario for winter oilseed rape
Class 2	
Weight of the cocoons (females)	Refer to Appendix F, Section 3.2, Figure 34. The data showed a tendency for negligible to small-negative deviation. No information was available about the exposure for any of the endpoints. Nevertheless, as these were all field studies carried out with winter oilseed rape, it is unlikely that the exposure in the available experiments was higher than the exposure assessment goals for the same crop. The length of the exposure was only reported in one experiment and was within the expected flowering duration for winter oilseed rape. The other studies were anyway field experiments on winter oilseed rape. The data presented good consistency and fair reliability. **Weak evidence of effects between small and negligible.**
Weight of the cocoons (males)	Refer to Appendix F, Section 3.3, Figure 36. A clear picture of effects was not available. The average tendency was for a negative negligible deviation. No information about the exposure was available for any of the endpoints. Nevertheless, as these were all field studies carried out with winter oilseed rape, it is unlikely that the exposure in the available experiments was higher than the exposure assessment goals for the same crop. The length of the exposure was only reported in one experiment and was within the expected flowering duration for winter oilseed rape. The other studies were anyway field experiments on winter oilseed rape. The data presented some inconsistency and fair reliability. **Line of evidence inconclusive.**
Weight of the offspring (females)	Refer to Appendix F, Section 3.4, Figure 38. The available experiments offered a picture of lack of effects (larger than negligible). The only available exposure estimation to adult bees was at least six times lower than the winter oilseed rape exposure assessment goal, and the exposure to larvae was almost 14 times lower than the exposure assessment goal. The length of the exposure was only reported in two experiments and was always within the expected flowering duration for winter oilseed rape. The data presented good consistency and reliability. Even if no effects (larger than negligible) were seen in the available data set, it is not possible to verify whether bigger effects would be seen at the exposure assessment goals (particularly the one for larvae). **Line of evidence inconclusive.**
Weight of the offspring (males)	Refer to Appendix F, Section 3.5, Figure 40. The available experiments offered a picture of lack of effects (larger than negligible). The only available exposure estimation to adult bees was at least six times lower than the winter oilseed rape exposure assessment goal, and the exposure to larvae was almost 14 times lower than the exposure assessment goal. The length of the exposure was only reported in two experiments and was always within the expected flowering duration for winter oilseed rape. The data presented good consistency and reliability. Even if no effects (larger than negligible) were seen in the available data set, it is not possible to verify whether bigger effects would be seen at the exposure assessment goals (particularly for larvae). **Line of evidence inconclusive.**

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Honeybee	Treated crop scenario for winter oilseed rape	
Integration of lines of evidence	For the general considerations about the integration of the two class-1 lines of evidence, please refer to the evaluation for maize. Overall, the two Class 1 lines of evidence offered a rather clear pattern of effects due to the exposure to thiamethoxam. A proper comparison with the exposure assessment goals from winter oilseed rape could only be performed for one experiment, where the exposure to adult bees was at least six times lower than the winter oilseed rape exposure assessment goal, and the exposure to larvae was almost 14 times lower than the exposure assessment goal. For the other three experiments, no exposure estimation was available. Nevertheless, as these were all field studies carried out with winter oilseed rape, it is likely that the exposure was lower or equal to the exposure assessment goals for the same crop. On the contrary, Class 2 lines of evidence (cocoon and offspring weight, considered separately for male and female) did not show any particular evidence for negative effects larger than negligible (small to negligible in the case of female cocoon weight) at exposure levels certainly lower and/or unlikely higher than the exposure assessment goals for winter oilseed rape.	
Uncertainty analysis (– potential to make the true risk lower + potential to make the true risk higher)	**Quantification of the effects**	
	The normalisation per average number of nesting females should be considered with care as a reduced number of nesting female could be due to treatment effects. In the field experiments, the average over time was used as normalisation factor.	/+
	Exposure in the experiments	
	A proper estimation of the exposure was missing in ¾ of the effect studies, which makes it impossible to check whether the exposure assessment goals were achieved.	––/++
	Confounding factors in the experiments	
	Out of the multiple available field experiments on all bee species and all crops, measurements of some kinds of residues in the control were available for 5. In three of these five studies, the control/reference was found to be contaminated by at least one neonicotinoid substance at levels comparable to the treatment. This could potentially mask triggering of negative effects. The presence of external substances was also seen in the treatment, creating uncertainties about detecting effects not due to the treatment.	––/++
	In some of the higher tier experiments where the bees were free flying, there were indications for the use of different pesticides, including insecticides. This may affect both control and treatment. There is also uncertainty that this practice could have been done also in experiments where this was not clearly reported.	/+
	Exposure assessment goals	
	The exposure assessment goals were calculated using the maximum residue levels measured within each trial.	––
	The exposure assessment goals were calculated assuming residues equal to the LOQ every time measured concentration were < LOQ. In the cases that no residues were detected, the residue was considered to be equal to the LOD.	–
	The exposure assessment goals were calculated using residues in pollen and nectar without dilution (from plants or from honeybees in confined conditions). In the available field experiments, the proportion of oilseed rape pollen collected by *Osmia* never exceeded 28%.	
	For the determination of the exposure assessment goals, a 10% sugar content of the nectar was assumed, which is the low end value of the realistic range. This may have resulted in an overestimation of the exposure assessment goal.	–

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Honeybee	Treated crop scenario for winter oilseed rape	
	In some residue studies (used for the exposure assessment goal), the sampling frequency and pattern did not guarantee that the actual maximum occurrence had been picked up.	+
	The limited number of valid residue studies available for the exposure assessment goal, restricted the potential for the representativeness to cover 90th percentile exposure situations.	+
	Specific issues	
	Data are only available on one solitary bee species (*Osmia bicornis*) out of the hundreds present in Europe.	–/++
Conclusion	A **high risk** to solitary bees from residues in nectar and/or pollen for the treated crop scenarios for winter oilseed rape is indicated by the weight-of-evidence exercise, chiefly by Class 1 lines of evidence. The available data indicate that the reproductive output of solitary bees (either normalised by the number of initially hatched female or the average number of nesting females) may be impaired from small to large extent by exposure to thiamethoxam. Within the experiment for which an exposure assessment was available, the exposure to adult bees was at least six times lower than the winter oilseed rape exposure assessment goal, and the exposure to larvae was almost 14 times lower than the exposure assessment goal. For the remaining experiments, no exposure estimation was available. Nevertheless, as these were all field studies carried out with winter oilseed rape, it is likely that the exposure was lower or equal to the exposure assessment goals for the same crop.	

LOQ: limit of quantification; LOD: limit of detection; WoE: weight of evidence.

5.1.2. Risk from contamination of adjacent vegetation via dust drift (field margin and adjacent crop scenario)

5.1.2.1. Tier-1 risk assessment

The Tier-1 risk assessment for the representative GAPs were performed by using the EFSA's BeeTool (v.3.) (Appendix Y of EFSA, 2013c) for honeybees and bumblebees, where suitable toxicity data were available. A screening Tier-1 assessment was carried out for solitary bees and for chronic larva bumblebees as only surrogate endpoints were available. Since no suitable toxicity data were available for chronic adults and HPG development, no assessment was performed for these scenarios.

It was assumed that a deflector was used during the seed drilling. With the exception of carrots, the vegetables are sown in greenhouse. When these are permanent structures, no dust deposition to neighbouring areas was considered for these uses, and a low risk is thus concluded without further assessments.

The outcome of these calculations is summarised in Tables 16 and 17. A low risk is indicated only if both categories (acute and larva) for both the field margin and adjacent crop scenarios resulted in low risk. When one or more combinations indicated a high risk or that a low risk cannot be demonstrated (screening Tier-1 with surrogate data), then this is indicated in the Tables below. The detailed results are included in Appendix D.

Table 16: Summary of the outcome of Tier-1 and screening risk assessment for the contact route of exposure

Use	Honeybee		Bumble bee		Solitary bee	
	'Low' application rate	'High' application rate	'Low' application rate	'High' application rate	'Low' application rate	'High' application rate
Broccoli, Brussels sprout, cauliflower, head cabbage, kale, lettuce	High risk		High risk		Low risk not demonstrated	
Carrot, maize	High risk		High risk		Low risk not demonstrated	

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Use	Honeybee		Bumble bee		Solitary bee	
	'Low' application rate	'High' application rate	'Low' application rate	'High' application rate	'Low' application rate	'High' application rate
Winter rape	Low risk only with a deflector		High risk		Low risk not demonstrated	
Sugar beet	Low risk		Low risk		Low risk	

Table 17: Summary of the outcome of Tier-1 and screening risk assessment for the dietary route of exposure (acute and larvae only; no toxicity data for chronic and HPG)

Use	Honeybee		Bumble bee		Solitary bee	
	'Low' application rate	'High' application rate	'Low' application rate	'High' application rate	'Low' application rate	'High' application rate
Broccoli, Brussels sprout, cauliflower, Head cabbage, kale, lettuce	High risk		High risk		Low risk not demonstrated	
Carrot, maize	High risk		High risk		Low risk not demonstrated	
Winter rape	Low risk only with a deflector		Low risk not demonstrated		Low risk not demonstrated	
Sugar beet	Low risk		Low risk only with a deflector		Low risk only with a deflector	

5.1.2.2. Exposure assessment for the field margin and adjacent crop scenario

Available experiments measuring dust deposition to the horizontal ground outside the treated area at the time of drilling seeds treated with thiamethoxam formulations were assessed. Whereas the studies were considered relevant to confirm that dust from seeds formed at the time of planting will containing active substance and may be a significant route of exposure for non-target organisms, the quantitative results reported were considered not applicable for current assessment either due reporting, methodological or representativeness issues. Therefore, assessment following Tier-1 in the guidance was used to address dust drift and deposition.

In the open call for data information was provided on the measurement of the dust content of oilseed rape and maize seeds (Heubach values); and in most cases for oilseed rape, also information on active ingredient content in the dust (Heubach a.i. values) was provided from seed samples from seed merchants. Dust was quantifiable/present in all seed batches tested. In maize seed, measured dust was just reported to be significantly below the industry standard of below 3 g dust/100 kg seed. Oilseed rape, seeds treated in 2013 from 326 seed treatment sites, had a 90th percentile total dust Heubach value of 0.192 g/700,000 seeds. These values for Heubach a.i. were 6 mg/700,000 seeds for clothianidin (156 sites), 1.4 mg/700,000 seeds for imidacloprid (52 sites) and 7.8 mg/700,000 seeds for thiamethoxam (104 sites).

Heubach a.i. values in seed samples from an additional 10 different seed treatment facilities also where seed was treated in 2013 were 0.21, 0.27, 0.33, 0.46, 0.6, 0.96, 1.29, 1.3, 8.9 and 16.6 mg/700,000 seeds for clothianidin.

As all these results are from the same year, so they do not provided any information on dustiness of the seed being supplied to farmers in different years and whether dust levels have reduced in recent years. It is clear that the Heubach a.i. values can be variable. It is clear that reducing the dust content of seed to be treated as well as any dust produced during the treatment process as well as any that might be generated during storage and transport of seed is a good target for improved risk management. However with the information available in this review, it was not possible to account for this in any refined exposure and/or risk characterisation.

5.1.2.3. Tier-2 risk assessment

As no refined exposure assessment for dust drift was available, no Tier-2 risk assessment could be performed.

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5.1.2.4. Tier-3 risk assessment

Only one field study (T.1424) in the available data set investigated effects on honeybees exposed via dust drift. Specifically, this study monitored bees after drilling of thiamethoxam-treated maize seeds. The only class 1–2 endpoints measured was mortality in front of the hive. A significant increase in the number of dead bees was found on the sowing day (dead bees increased by around 50% compared to the control), followed by a decrease during the following days. However, the endpoint was considered not reliable (see Appendix F of EFSA, 2018a for details). Therefore, no further considerations on this route of exposure can be done.

5.1.3. Risk via water consumption

5.1.3.1. Guttation water

Tier-1

The Tier-1 risk assessments for exposure to honeybees via residues in guttation fluid are presented in Appendix D. The resulting acute and larvae exposure toxicity ratio (ETR) values all exceeded the respective trigger values indicating that further consideration is needed.

It should be highlighted that the EFSA evaluation of the confirmatory data for imidacloprid and clothianidin (EFSA, 2016b,c) concluded that the exposure of honeybees from contaminated guttation fluids in the crops considered therein (winter cereals, sugar beet, and potatoes) was of low relevance. Such conclusion was confirmed during the expert meeting related to this assessment (Pesticide Peer Review Meeting 166), despite the experts acknowledged that such an assessment was based on studies presenting major limitations. On the basis of this, no risk assessment from exposure to contaminated guttation fluids was carried out, and a low risk was concluded.

Lettuce could be sown and transplanted in greenhouses, without ever be placed in the field. When these operations happen in permanent structures, the exposure to any bee species is considered negligible, and a low risk is concluded.

Tier-2

Eight different experiments measuring thiamethoxam concentration in guttation fluids from treated maize plants were available. Therefore, an exposure refinement in agreement with EFSA (2013c) could be carried out.

Two of these experiments only reported maximum measured values or ranges of concentrations. On the contrary, for six of these experiments, a clear time-dependent decline of active substance (a.s.) concentrations could be observed and evaluated. Therefore, TWA concentrations could be calculated for those experiments. As no adult chronic endpoint is available for honeybees, only 5 days' TWA concentrations were calculated, which is the appropriate time window for the larva risk assessment.

In order to be consistent with what done for pollen and nectar, concentrations thiamethoxam and its metabolite clothianidin were summed for each sample. The two experiments reporting only maximum values did not report concentration of the metabolite clothianidin and were therefore excluded from further analysis.

The available data were fitted to Single First Order (SFO) kinetics and, where appropriate (in terms of visual fit and χ^2 test), to First Order Multi Compartment (FOMC) kinetics. The R-based package 'mkin' was used for this analysis.

Both the maximum and the TWA concentrations were log-transformed and fitted to a normal distribution, in order to estimate a 90th percentile. This operation was done for consistency with the data elaboration performed for pollen and nectar using the EFSA SHVAL tool.

The results of this process are reported in Table 18.

Table 18: Available maximum and 5d-TWA concentration of thiamethoxam+metabolite clothianidin measured in guttation fluids of maize

Trial ID	5d-TWA [µg/L]	Max [µg/L]
S09-01639 (0.7 mg a.s./seed)	6,981	29,595
S09-02828 (0.27 mg a.s./seed)	521	5,756
S09-02828 (0.64 mg a.s./seed)	1,135	11,145
S10-01857 (0.68 mg a.s./seed)	12,239	31,318

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Trial ID	5d-TWA [µg/L]	Max [µg/L]
S10-01860 (0.69 mg a.s./seed)	16,546	52,576
S10-01859 (0.68 mg a.s./seed)	21,885	45,990
ALL+.1383 (1.0 mg a.s./seed)	–	227,000[(a)]
ALL+.2001 (1.0 mg a.s./seed)	–	11,900[(a)]
Estimated 90th percentile (random sample n = 1,000)	**29,225**	**61,061**

(a): Values excluded from the analysis as they did not include measurements of the metabolite clothianidin.

On the basis of the estimated 90th percentile concentrations in guttation fluids, a refined risk assessment was carried out by assuming default water consumption (11.4 µL/day for forager, 111 µL/5 days for larva). On the basis of this Tier-2 assessment illustrated in Table 19, a low risk could not be concluded for either acute exposure to honeybee forager or chronic exposure to honeybee larva. In both cases, the estimated ETR largely exceed the relevant triggers.

Table 19: Tier-2 risk assessment to honeybees exposed via consumption of contaminated guttation fluids

Crop	Category	Conc [µg a.s./L]	Intake [ng/bee/time]	Endpoint [µg a.s./bee]	ETR	Trigger
Maize	Acute forager	61,061.2	696.1	5	**139**	0.2
Maize	Larva	29,224.83	3,244.0	21.7	**149**	0.2

Tier-3

The available data set included three-field studies (T.486, T.1146 and T.1147), investigating the effects on honeybees hives potentially exposed via guttation fluids from winter oilseed rape, grown from thiamethoxam treated seeds.

These three experiments had a very similar design and measured some parameters that are relevant for the risk assessment. In particular, colony strength (Class 1 endpoint) and brood (Class 2 endpoint) were measured pre-exposure, once around 55 days after the exposure period (autumn) and then twice after the winter. Mortality in front of the hive (Class 2 endpoint) was also frequently measured (from daily to every three days).

The EFSA GD (EFSA, 2013c) indeed offers an approach to refine the risk due to exposure via guttation fluids by using field experiments. In order to properly address the risk, the GD recommends that:

- the field studies should be conducted in areas where the distance to the nearest permanent water source is equal to or larger than the 90th percentile case in the area of use of the substance.

AND

- the concentrations in the guttation fluids are above the median case for the area of use of the substance.

For the three available field experiments, none of the two conditions was demonstrated to be met. The presence (and abundance) of alternative water sources was not documented and no bees were seen taking up guttation fluids. Samples of guttation fluids were collected for analysis, but the results of the analytical part were not yet available when the experiments were assessed (see Appendix F of EFSA, 2018a).

Due to the considerations reported above, the available field studies cannot be used to satisfactorily inform the risk assessment due to exposure via guttation fluids. Nevertheless, for sake of transparency, a brief summary of the results for the main measured endpoints is reported below. Results for experiment T.1147 are not reported, as all endpoints were considered unreliable due to major issues with the control performances. All endpoints from the remaining two studies were classified as reliable with major restrictions (Table 20).

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Table 20: Summary of the results of the reliable biological observations relative to the field studies performed to address the risk to honeybees via winter oilseed rape guttation fluids

Endpoint	T.486	T.1146
Occurrence of guttation	Autumn: 23 of 35 days Spring: 10 of 13 days Average fraction of plants exhibiting guttation: 58.5%	Autumn: 30 of 33 days Spring: 6 of 10 days Average fraction of plants exhibiting guttation: 44.6%
Frequency of bees seen taking up guttation fluids	No bees were seen taking up guttation fluids	No bees were seen taking up guttation fluids
Colony strength	**Positive** negligible deviations with respect to the control	Small- to medium-**negative** deviations with respect to the control
Brood	Medium- to large-**positive** deviation with respect to the control	From large-negative to small-positive deviation with respect to the control. The mean tendency was a large-**negative** deviation
Mortality in front of the hive	Negligible difference between control and treatment	Negligible difference between control and treatment

5.1.3.2. Puddle water

It was not necessary to perform exposure modelling to predict residues of thiamethoxam in puddles as the concentrations in surface runoff calculated by PRZMsw (a surrogate approach for estimating puddle concentrations following EFSA, 2013c) are always negligible when seeds are drilled below the soil surface. Consequentially, a low risk to honeybees from residues in puddles for the seed treatment uses under consideration is concluded. Experts from Member States noted that the EFSA (2013c) approach might represent a best case as cultivation following harvesting of the treated crop redistributes soil residues, such that concentrations at the soil surface will be present to desorb into puddles. PRZM calculations as prescribed by FOCUS surface water do not account for this as the FOCUS PRZM tool and FOCUS surface water runoff scenarios do not account for soil cultivation.

5.1.3.3. Surface water

In the absence of agreed input parameters for FOCUS surface water modelling, no exposure assessment for the representative uses could be performed. Therefore, the risk to honeybees consuming residues in surface water could not be assessed. Lettuce could be sown and transplanted in greenhouses, without ever be placed in the field. When these operations happen in permanent structures, the emission to surface water is considered negligible, and a low risk is concluded.

6. Overall conclusion

The conclusion of the risk assessment to bees for the uses of thiamethoxam as seed treatment is summarised below, considering the different scenarios. It should be highlighted that as only seed treatment uses were listed in the GAP, the weed scenario was never considered relevant, in agreement with EFSA (2013c).

For the crop-specific conclusion achieved at each assessment tier, please refer to Table 21.

Risk via systemic translocation in plants – residues in nectar and pollen

Treated crop scenario

A risk assessment for the treated crop scenario was not considered relevant for uses of thiamethoxam on **broccoli**, **Brussel sprout**, **cauliflower**, **head cabbage**, **kale**, **lettuce**, **carrot** and **sugar beet**, as these crops are harvested before flowering. As such, a **low risk** to **all bee species** was concluded for the treated crop scenario.

A risk assessment was carried out for the uses on winter oilseed rape and maize. A high risk at the Tier-1 was concluded for both crops and all bee groups. It should be noted that, in lack of specific toxicity data, the high risks for solitary bees were identified using uniquely surrogate toxicity estimation based on honeybee data (low risk not demonstrated).

The availability of residue data for maize and winter oilseed rape allowed carrying out a Tier-2 risk assessment for the uses on these crops.

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- The Tier-2 risk assessment for uses on winter oilseed rape resulted in a high risk for all bee species.
- The Tier-2 risk assessment for maize highlighted a high risk for bumblebees and solitary bees. The risk assessment for honeybees could not be finalised, in lack of data about chronic toxicity to adults and HPG development (a low risk was nevertheless indicated for acute toxicity to adults and prolonged toxicity to larvae).

A Tier-3 risk assessment was also carried out for the uses on maize and winter oilseed rape, using data from colony-feeder and field experiments.

- The Tier-3 risk assessment for uses on **winter oilseed rape** resulted in a clear **high risk** for **solitary bees**, while the conclusion for **honeybees** and **bumblebees** was less straightforward. Despite clear and consistent effects were not recorded for honeybees and bumblebees, the analysis of the data through a WoE exercise **did not allow excluding the possibility of observing effects larger than negligible** on the parameters linked, directly and indirectly, to the respective protection goals.
- The Tier-3 risk assessment for **maize** highlighted a **low risk for bumblebees**. Once again, a definitive conclusion could not be drawn for honeybees and solitary bees based on the available data. This was mainly because the available experiments were not suitable to address the risk due to exposure to contaminated maize pollen, among other reasons. The data **did not allow excluding the possibility of observing effects larger than negligible** on the parameters linked, directly and indirectly, to the respective protection goals.

Succeeding crop scenario

A high risk at the Tier-1 was concluded for all crops and all bee groups. It should be noted once again that, in lack of specific toxicity data, the high risk for solitary bees was identified using uniquely surrogate toxicity estimation based on honeybee data. In lack of sufficient information to perform a refined exposure assessment, the risk assessment was not further refined. It should also be noted that lettuce could be sown and transplanted in greenhouses, without ever be placed in the field. When these operations happen in permanent structures, the exposure to any bee species is considered negligible, and a low risk is concluded.

Risk from contamination of adjacent vegetation via dust drift

Field margin and adjacent crop scenarios

On the basis of the Tier-1 risk assessment, a **high risk** to **all bee groups** was indicated for the uses on **broccoli**, **Brussel sprout**, **cauliflower**, **head cabbage**, **kale**, **lettuce, carrots** and **maize**. Nevertheless, all the previous crops with the exception of carrots and maize are sown in greenhouses. When these structures are permanent, exposure to bees is considered negligible and a low risk is concluded.

For the uses on winter oilseed rape, a **high risk** (based on surrogate data) was concluded for **bumblebees** and **solitary bees**. The risk assessment for **honeybees could not be finalised**, in lack of data about chronic toxicity to adults and HPG development (a low risk was nevertheless indicated for acute toxicity to adults and prolonged toxicity to larvae, when a deflector is used).

For the uses on **sugar beet** (both seeding rates), **the risk assessment could not be finalised in lack of data about chronic toxicity to adults and HPG development** (whereas a low risk was indicated for acute toxicity to adults and prolonged toxicity to larvae for all bee groups – for bumblebees and solitary bees only when a deflector is used).

The available data did not allow performing any refined risk assessment for exposure via dust drift.

Risk via consumption of contaminated water

Guttation fluids

A **low risk** to **honeybees** was concluded for the uses on **sugar beet**, in agreement with the evaluation of the confirmatory data for imidacloprid and clothianidin (EFSA, 2016b,c) and confirmed during the expert meeting related to this assessment.

For all other crops, a low risk to honeybees could not be demonstrated using the screening assessment based on the solubility of thiamethoxam. Nevertheless, lettuce could be sown and transplanted in greenhouses, without ever be placed in the field. When these operations happen in permanent structures, the exposure to any bee species is considered negligible, and a low risk is concluded.

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A refined exposure could be performed for **maize**. The refined risk assessment indicated **high risk** to **honeybees**.

Several field experiments were available to refine the risk from consumption of contaminated guttation fluids from **winter oilseed rape**. Nevertheless, those experiments were not considered suitable to satisfactorily inform the risk assessment due to exposure via guttation fluids.

Puddle water

A **low risk** is concluded to **honeybees** from residues in puddles for the seed treatment uses under consideration.

Surface water

In the absence of agreed input parameters for FOCUS surface water modelling, no exposure assessment for the representative uses could be performed. Therefore, the **risk** to **honeybees** consuming residues in surface water **could not be finalised**. Lettuce could be sown and transplanted in greenhouses, without ever be placed in the field. When these operations happen in permanent structures, the emission to surface water is considered negligible, and a low risk is concluded.

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Table 21: Summary of the overall risk assessment broken up by use, taxonomic group and tier

Use (all seed treatments)	Tier	Honeybee								Bumble bee					Solitary bee				
		Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop	Guttation fluid	Surface water	Puddle water	Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop	Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop
Broccoli Harvested before flowering (1.4 mg a.s./seed) Sown in permanent greenhouse	Tier-1	L	N/R	L	L	R1	R2	X	L	L	N/R	L	L	R1	L	N/R	L	L	R2
	Tier-2																		
	Tier-3																		
Broccoli Harvested before flowering (1.4 mg a.s./seed) Sown in non-permanent greenhouse	Tier-1	L	N/R	R1	R1	R1	R2	X	L	L	N/R	R1	R1	R1	L	N/R	R2	R2	R2
	Tier-2																		
	Tier-3																		
Brussel sprout Harvested before flowering (1.4 mg a.s./seed) Sown in permanent greenhouse	Tier-1	L	N/R	L	L	R1	R2	X	L	L	N/R	L	L	R1	L	N/R	L	L	R2
	Tier-2																		
	Tier-3																		
Brussel sprout Harvested before flowering (1.4 mg a.s./seed) Sown in non-permanent greenhouse	Tier-1	L	N/R	R1	R1	R1	R2	X	L	L	N/R	R1	R1	R1	L	N/R	R2	R2	R2
	Tier-2																		
	Tier-3																		
Cauliflower Harvested before flowering (1.4 mg a.s./seed) Sown in permanent greenhouse	Tier-1	L	N/R	L	L	R1	R2	X	L	L	N/R	L	L	R1	L	N/R	L	L	R2
	Tier-2																		
	Tier-3																		
Cauliflower Harvested before flowering (1.4 mg a.s./seed) Sown in non-permanent greenhouse	Tier-1	L	N/R	R1	R1	R1	R2	X	L	L	N/R	R1	R1	R1	L	N/R	R2	R2	R2
	Tier-2																		
	Tier-3																		
Head cabbage Harvested before flowering (1.4 mg a.s./seed) Sown in permanent greenhouse	Tier-1	L	N/R	L	L	R1	R2	X	L	L	N/R	L	L	R1	L	N/R	L	L	R2
	Tier-2																		
	Tier-3																		

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Use (all seed treatments)	Tier	Honeybee								Bumble bee					Solitary bee				
		Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop	Guttation fluid	Surface water	Puddle water	Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop	Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop
Head cabbage Harvested before flowering (1.4 mg a.s./seed) Sown in non-permanent greenhouse	Tier-1	L	N/R	R1	R1	R1	R2	X	L	L	N/R	R1	R1	R1	L	N/R	R2	R2	R2
	Tier-2																		
	Tier-3																		
Kale Harvested before flowering (1.4 mg a.s./seed) Sown in permanent greenhouse	Tier-1	L	N/R	L	L	R1	R2	X	L	L	N/R	L	L	R1	L	N/R	L	L	R2
	Tier-2																		
	Tier-3																		
Kale Harvested before flowering (1.4 mg a.s./seed) Sown in non-permanent greenhouse	Tier-1	L	N/R	R1	R1	R1	R2	X	L	L	N/R	R1	R1	R1	L	N/R	R2	R2	R2
	Tier-2																		
	Tier-3																		
Lettuce Harvested before flowering (0.805 mg a.s./seed) Sown in permanent greenhouse Transplanted to permanent greenhouse	Tier-1	L	N/R	L	L	L	L	L	L	L	N/R	L	L	L	L	N/R	L	L	L
	Tier-2																		
	Tier-3																		
Lettuce Harvested before flowering (0.805 mg a.s./seed) Sown in permanent greenhouse Transplanted to field or non-permanent greenhouse	Tier-1	L	N/R	L	L	R1	R2	X	L	L	N/R	L	L	R1	L	N/R	L	L	R2
	Tier-2																		
	Tier-3																		
Lettuce Harvested before flowering (0.805 mg a.s./seed) Sown in non-permanent greenhouse	Tier-1	L	N/R	R1	R1	R1	R2	X	L	L	N/R	R1	R1	R1	L	N/R	R2	R2	R2
	Tier-2																		
	Tier-3																		
Carrot Harvested before flowering (0.061 mg a.s./seed)	Tier-1	L	N/R	R1	R1	R1	R2	X	L	L	N/R	R1	R1	R1	L	N/R	R2	R2	R2
	Tier-2																		
	Tier-3																		

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Use (all seed treatments)	Tier	Honeybee								Bumble bee					Solitary bee				
		Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop	Guttation fluid	Surface water	Puddle water	Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop	Treated crop scenario	Weed scenario	Field margin	Adjacent crop	Succeeding crop
Maize (0.63 mg a.s./seed)	Tier-1	R1	N/R	R1	R1	R1	R2	X	L	R1	N/R	R1	R1	R1	R2	N/R	R2	R2	R2
	Tier-2	X					R1			R1					R2				
	Tier-3	R2								L					R2				
Winter oilseed rape (0.021 mg a.s./seed)	Tier-1	R1	N/R	X	X	R1	R2	X	L	R1	N/R	R1	R1	R1	R2	N/R	R2	R2	R2
	Tier-2	R1								R1					R2				
	Tier-3	R2					R2			R2					R1				
Sugar beet (0.45 mg a.s./seed)	Tier-1	L	N/R	X	X	R1	L	X	L	L	N/R	X	X	R1	L	N/R	X	X	R2
	Tier-2																		
	Tier-3																		
Sugar beet (0.6 mg a.s./seed)	Tier-1	L	N/R	X	X	R1	L	X	L	L	N/R	X	X	R1	L	N/R	X	X	R2
	Tier-2																		
	Tier-3																		

L: A low risk is concluded for the risk assessment.
R1: A high risk is concluded on the basis of the assessment.
R2: A low risk cannot be demonstrated as a result of the assessment (screening-type risk assessment or incomplete conclusion at Tier 3).
X: Assessment not finalised (lack of exposure or endpoint for effects).
Empty grey box: no assessment.
N/R: Scenario not relevant.

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Overall appraisal of the uncertainty related to the risk assessment

In order to reach the aforementioned conclusions on the risk assessment of imidacloprid, clothianidin, and thiamethoxam, EFSA has considered a large number of documents, reporting very diverse experiments, where many heterogeneous endpoints were measured under different conditions and using different methodologies.

One of the most relevant outputs of this complex exercise is to account for the uncertainty related to the overall assessment. At the lower tier (e.g. Tier-1 and screening), this is accounted for by the use of conservative estimates which is particularly important when standard Tier-1 parameters have been extrapolated from more worse-case situations (e.g. in cases where data were lacking for a particular crop). On the contrary, as acknowledged in EFSA, 2013c, there are several routes of exposures which are not covered by the risk assessment scheme. (e.g. insect honeydew, exposure via soil)

At higher tiers (Tier-2 and Tier-3), the uncertainty starts to act in two opposing ways, and it is worth breaking it up in different factors, whose relative importance can be investigated more in detail.

Several factors were identified as source of uncertainty when establishing the revised SVs and exposure assessment goals. Some of them indicated that the estimated exposure assessment goals might be overestimated with respect to the actual exposure to bees (e.g. calculation of the exposure assessment goals using the maximum value from each trial, assuming residues equal to the LOQ every time they were > LOQ,) consequently have the potential to decrease the actual risk in comparison with the present assessment. On the contrary, other factors may act in the opposite way (e.g. the sampling frequency was insufficient ensure that the peak residue was captured, limited number of residue trials resulting in a lower capacity to ensure that the 90th percentile determination was captured).

Similar factors were identified as source of uncertainty for the estimates of exposure within the effect experiments. An even greater level of uncertainty is identified for experiments for which there were insufficient information to be able to quantify the exposure to bees within the study. For some sources of uncertainty which were applicable to both the calculation of the exposure assessment goals and the estimated exposure within the experiments, it was ensured that the same assumption was equally applied to both. In this way, the uncertainty is balanced, e.g. the same percentage of sugar content in nectar was assumed for both the exposure assessment goal and the estimated exposure in the experiments.

Other sources of uncertainty are related to the quantification of the effects. In this case, the direction of the uncertainty is rarely identifiable, as the uncertainty itself is linked to low reliability of the experimental design/methodology, to the lack of reference (pre-exposure) measurements and to the lack of precision in reporting the results.

Finally, one of the most important sources of uncertainty is related to the presence of 'confounding factors' in most of the higher tier experiments, particularly those performed under field conditions.

As an example, other chemicals (i.e. herbicides, fungicides, acaricides or other classes of insecticides) were often applied to both the treatments and the control plots in line with standard field practises. Nevertheless, the relative influence that exposure to these substances might have on the bees in the control and in the treatment is unknown.

Furthermore, putting together the information from all field experiments considered for the present risk assessment review (encompassing imidacloprid, clothianidin and thiamethoxam), EFSA noted that in more than 40% of the cases (15 experiments out of 35), some matrices collected from the controls (e.g. from hives, plants or soils) were contaminated with at least one neonicotinoid substance. Contamination of controls was sometimes even indicated in experiments where bee colonies were exposed via contaminated sugar solutions.

It is worth noting that, in the large majority of the cases, the residue analysis only focused on the substance used in the treatment and on its metabolites. There were only six studies where residues for a wider range of neonicotinoid substances were investigated. Five of these studies reported residues of substances not included in the study design at quantifiable concentrations. Cross-contamination from substances other than the test item resulted, in some cases, in residue levels comparable to those due to the applied treatment.

Similar issues had been already pointed out by EFSA in relation to other studies not included in the present review (EFSA, 2013a,b).

This finding can be explained considering that neonicotinoids substances have been largely used in Europe for several years and on a wide range of crops. Furthermore, neonicotinoids insecticides are persistent in the environment, particularly in soil. EFSA (2008) reported field DT_{50} value ranging from 104 to 228 days for imidacloprid. For the other two substances, some DT_{50} values are reported in the

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respective EU review reports (European Commission 2006a,b). The mean/median DT_{50} values reported therein are 156 days for clothianidin and 174 days for thiamethoxam. It might be worth noting that the main soil metabolite of thiamethoxam is clothianidin, so that the DT_{50} of the active substance alone is not fully representative of the whole exposure time-variable profile.

It is important to note that this finding has r implications on different aspects of the present Tier-3 risk assessment for the treated crop and succeeding crops scenarios. Firstly, it impaired the reliability of some experiments where contamination of controls was recorded. Furthermore, it creates great uncertainty around the reliability of the results for those studies where either residue measurements were not available or, as in the vast majority of the studies, where substances other than the test item were not properly investigated. In general, this finding highlights a general disadvantage about the use of field studies for addressing the risk assessment. It exposed a source of uncertainty related to the biological observations from field studies, particularly for their interpretation and their reliability when used in the risk assessment.

It is very likely that one cause of the control contamination/cross contamination recorded in the available studies was due to applications performed during previous years on the control plots. Other sources may be from other treated crops or contaminated plants in the landscape. It is acknowledged that the same mechanism had the potential to artificially increase the exposure in the 'treated' groups of the experiments, thus potentially amplifying effects expected from the treatment alone. Nevertheless, widespread use of these substances makes this situation likely to occur in the environment, and the data should not necessarily be disregarded as uninformative for the present risk assessment.

7. Overview of the concerns identified for each representative use considered

Table 22: Summary of concerns for each scenario according to the risk assessment scheme in EFSA (2013c), accounting for particular conditions proposed to be taken into account to manage the risks identified

Use (all seed treatments)	Honeybee	Bumble bee	Solitary bee
Broccoli Harvested before flowering (1.4 mg a.s./seed) Sown in permanent or not permanent greenhouse	X	X	X
Brussel sprout Harvested before flowering (1.4 mg a.s./seed) Sown in permanent or not permanent greenhouse	X	X	X
Cauliflower Harvested before flowering (1.4 mg a.s./seed) Sown in permanent or not permanent greenhouse	X	X	X
Head cabbage Harvested before flowering (1.4 mg a.s./seed) Sown in permanent or not permanent greenhouse	X	X	X
Kale Harvested before flowering (1.4 mg a.s./seed) Sown in permanent or not permanent greenhouse	X	X	X
Lettuce Harvested before flowering (0.805 mg a.s./seed) Transplanted to field or to non-permanent greenhouse	X	X	X
Lettuce Harvested before flowering (0.805 mg a.s./seed) Sown in and transplanted to permanent greenhouse			

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Use (all seed treatments)	Honeybee	Bumble bee	Solitary bee
Carrot Harvested before flowering (0.061 mg a.s./seed)	X	X	X
Maize (0.63 mg a.s./seed)	X	X	X
Winter oilseed rape (0.021 mg a.s./seed)	X	X	X
Sugar beet (0.45 mg a.s./seed)	X	X	X
Sugar beet (0.6 mg a.s./seed)	X	X	X

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Abbreviations

$1/n$	slope of Freundlich isotherm
λ	wavelength
a.s.	active substance
DT_{50}	period required for 50% dissipation (define method of estimation)
ETR	exposure toxicity ratio
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FOMC	First Order Multi Compartment (FOMC)
GAP	Good Agricultural Practice
HPG	hypopharygeal glands
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
K_{Foc}	Freundlich organic carbon adsorption coefficient
LD_{50}	lethal dose, median; dosis letalis media
LDD_{50}	lethal dietary dose; median
LOD	limit of detection
LOQ	limit of quantification
mm	millimetre (also used for mean measured concentrations)
MRL	maximum residue level
NOEC	no observed effect concentration
NOED	No Observed Effect Dose
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
PER	Proboscis Extension Reflex
RUD	residue per unit dose
SFO	single first order
SPG	specific protection goal
SVs	shortcut values
TRR	total radioactive residue
TWA	time-weighted average
WoE	Weight of Evidence

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Appendix A – List of Uses

Appendix A, full details of the GAPs can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2018.5179

Appendices from B to H

Appendices from B to H are provided as a separate document which can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2018.5179

Appendix B – Overview of endpoint types and related relevance class assigned within the scope of the present risk assessment

Appendix C – Tier 1 risk assessment based on EFSA (2013c)

Appendix D – Measured residue values and RUD values used for calculation of exposure assessment goals

Appendix D can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2018.5179

Appendix E – Residue intake in the effect studies

Appendix F – Tier-3 lines of evidence

Appendix G – List of study references

Appendix H – Used compound codes

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