Evaluation of honey bee larvae data: sensitivity to PPPs and impact analysis of EFSA Bee GD

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1. Introduction

In July 2013, the European Food Safety Authority (EFSA) published a guidance document on the risk assessment of plant protection products on bees (EFSA Bee GD, [1]) which intended to provide guidance for notifiers and authorities in the context of the review of plant protection products (PPPs) and their active substances under Regulation (EC) 1107/2009 (EC 2009). Initial ECPA impact analysis [2] assessed whether the GD brings the desired improvement to the bee larval risk assessment. It indicates that overall less than half of the uses passed the screening tier risk assessment.

Since the guidance was first published, a number of honey bee larvae toxicity studies have been conducted according to newly developed test methods.

The objective of this poster is to summarize available industry data and to assess the pass rates according to the EFSA Bee GD. It thus updates preliminary results, which have been presented in 2018 [3]. Moreover, the poster compares the obtained data with the outcome of an alternative approach proposed by ECPA [4], compares the day 8 and day 22 endpoint (NOED) derived from OECD GD 239 and relates the findings with available pass rates from adult chronic tests [5].

2. Methods and data sources

Experimental data from 138 active substances or formulated products were available, covering 44 fungicides, 62 herbicides plus 4 plant growth regulators (PGRs) and 28 insecticides comprising insect growth regulators (IGRs), acaricides, and nematicides. Mixtures of fungicides & insecticides were attributed to insecticides as they drive the toxicity. Overall, 215 uses were covered: 72 fungicide spray and solid uses, 91 herbicide spray uses, incl. 8 PGR uses and in total 52 insecticide spray and solid uses, incl. 2 nematicide and 3 IGR uses.

As study methods have developed in recent years, the data had been generated according to different methods: single exposure studies until day 7 (OECD TG 237) and repeated exposure studies until day 8 or until day 22 (OECD GD 239).

For the honey bee (HB) Tier 1 risk assessment (RA), 'exposure-toxicity-ratios' (ETRs) were calculated according to the EFSA Bee GD for different exposure scenarios, from which the 'treated crop' and 'weeds flowering in the field' were regarded as the most relevant. Calculations were conducted using the EFSA-tool, Version 3 (October 2015). As standardized test methods for non-*Apis* bees larvae are not available, RA for bumblebees (BB) and solitary bees (SB) were based on 1/10th of the HB endpoint as surrogate.

An alternative RA option proposed by ECPA [4] used a trigger value of 5 and calculated TER values dividing the NOEDD by an 'estimated theoretical exposure' (ETE). Total exposure ETE was calculated using worst-case consumption for larvae, an overall sugar content of 30% and the median default RUD values from EFSA [1].

In addition, endpoints obtained at different development stages after 8 and 22 days in OECD GD 239 studies are compared.

Adult chronic pass rates were taken from a current poster [5] for comparison with honey bee larval pass rates.

3. Findings

- The data comprised single and repeated dosing and generated 7/8 and 22 day endpoints. The resulting Tier 1 RA pass rates are shown in Table 1.
- The majority of fungicide and herbicide uses passed Tier 1 RA for honey bee larvae in the 'treated crop' and 'weed' scenario. As expected, pass rates for insecticide uses were distinctly lower.
- As standardized test methods for non-*Apis* bees larvae in the laboratory are not available, risk was based on 1/10th of the HB endpoint as a surrogate. In this case the overall pass rates in the Tier 1 RA for both scenarios substantially decreased for BB and SB to very low levels.
- Overall, D8 endpoint was equivalent to the D22 endpoint in approx. 66% of the studies, while in approx. 31% of the cases the D22 endpoint was lower (Tab. 2).
- The pass rates for the alternative ECPA RA approach only substantially differed for insecticides from those derived from EFSA Bee GD (Tab. 3). The RA based on real chronic adult honey bee data [5] resulted in lower pass rates for all compound groups compared to larval data.

Table 1: Overall pass rates of the EFSA Tier 1 RA for honey bee larvae

Use (n)	Pass rates [%] for					
	Treated crop			Weeds in the field		
	HB	BB	SB	HB	BB	SB
Fungicides (72)	94.4	4.2	9.7	97.0	11.9	10.4
Herbicides (91)	97.8	14.4	15.6	96.7	16.5	13.2
Insecticides (52)	42.3	9.6	13.5	42.9	1.9	1.9
All (215)	83.2	9.8	13.1	84.1	11.4	9.5

Table 2: Sensitivity comparison of D8 vs D22 endpoint in repeated exposure studies (OECD GD 239)

Studies (n)	Endpoint proportion [%]		
	D8 > D22	D8 ≙ D22	D8 < D22
Fungicides (22)	22.7	77.3	0.0
Herbicides (29)	31.0	62.1	6.9
Insecticides(11)	45.5	54.5	0.0
All (62)	30.6	66.1	3.2

Table 3: Pass rates in 'treated crops' for honey bee larvae compared with adult chronic data

Use	Pass rates [%] for		
	Larvae		Adults
	EFSA Tier 1	ECPA RA option	EFSA Tier 1, chronic exposure
Fungicides	94.4	98.6	56.9
Herbicides	97.8	100	75.0
Insecticides	42.3	53.8	18.6
All	83.2	88.4	53.8

4. Summary and conclusions

- **Risk assessments using real larval data confirm that the chronic risk for adults is the key driver of honey bee risk in the EFSA Bee GD as stated in the original impact analysis [2].**
- **Based on the data with different larval endpoints it can be concluded that larval tests providing D7/D8 endpoints can be used in the risk assessment for non-toxic compounds.**
- **For toxic compounds, the differences between sensitivity on D8 and on D22 will likely increase RA failure rates, if exclusively D22 endpoint would be used for the Tier 1 RA.**
- **Insecticide failure in the larval chronic Tier 1 RA triggers the need for higher-tier data to refine the risk. However there is still a lack of workable higher-tier study guidelines, agreement on endpoints or how they should be used to refine the RA.**
- **When basing the RA of bumblebee and solitary bee larvae on 1/10th of the honey bee endpoint, the majority of active substances and their respective products will fail the risk assessment. As valid larval laboratory methods for bumblebees and solitary bees are currently still not available and higher tier studies are long-term research projects, the risk assessment in these areas cannot be completed.**

[1] EFSA (2013): EFSA Guidance Document on the risk assessment of plant production products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees) (published on July 04, 2013, updated on 04 July 2014). EFSA Journal 11(7): 3295.
[2] Alix, A., Miles, M. & G. Weyman (2013): Sensitivity and impact analysis of the risk assessment for honey bees, bumble bees and solitary bees based on the guidance of the European Food Safety Authority. – ECPA, unpublished report.
[3] Becker, R., Lückmann, J., Miles, M. et al. (2018): Sensitivity of honey bee larvae to plant protection products and impact on EFSA bee guidance document. In Hazards of pesticides to bees, 13th International Symp. of the ICP-PR, Valencia, Spain 2017, ed. by Oomen, P. A .& J. Pistorius, Julius-Kuhn-Archiv 462: 69-71.
[4] ECPA (2017): Proposal for a protective and workable regulatory European bee risk assessment scheme based on the EFSA bee guidance and other new data and available approaches. Unpublished report.
[5] Lückmann, J., Miles, M., Becker, R. et al. (2019): Chronic oral exposure of adult honeybees to PPPs: sensitivity and impact analysis of EFSA Bee GD. – Poster, 29th Annual meeting of SETAC Europe 2019, Helsinki/Finland.

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