Sensitivity of honey bee larvae to PPPs and impact on 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 [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). The ECPA impact analysis [2] assessed whether the GD brings the desired improvement to the risk assessment on bees comprising bee larvae and reliability of the outcomes.

In the meantime, a number of larvae toxicity studies have been conducted according to the newly developed testing methods for single exposure (OECD test guideline 237) and repeated exposure testing (OECD guidance document 239). The objective of this poster is to summarize all available industry data, to assess the pass/failure rates according to the EFSA Bee GD and to compare the real data with to the original outcome of the impact analysis which used estimated endpoints. Available adult chronic test data were also considered.

2. Methods and data sources (honey bee risk)

The analysis from 2013 [2] considered 151 active substances covering 163 uses: 60 were herbicides comprising PGRs, 52 fungicides, and 51 insecticides comprising acaricides. Because at the time no data were available as test methods were yet to be developed, larval toxicity endpoint ($NOED_{larvae}$ – no observed effect dose) were estimated as follows: 1/10th of adult's acute oral LD_{50} corrected for mean larval body weight (83 mg), e.g. acute oral LD_{50} of 100 µg a.s./bee ≙ NOED of 8.3 µg a.s./larva.

For the current analysis, real experimental data from 114 active substances or formulated products were considered covering 166 uses: 58 were herbicides, 53 fungicides, 47 insecticides and 8 plant growth regulators (PGRs).

As study methods developed throughout the last years, studies on larvae were performed according to different methods resp. endpoints: single exposure studies until day 7 (reflected by OECD TG 237), repeated exposure studies until day 8 and repeated exposure studies until day 22 (reflected by OECD GD 239).

For the risk assessment, 'exposure-toxicity-ratios' (ETRs) were calculated based on the application rate (AR, in kg a.s./ha) and the $NOED_{larvae}$. Whereas for the 'screening step' RA only the application rate and an application-type dependent 'short cut' (SV) value was considered (ETRlarva = AR x SV /NOED), the tier 1 RA takes into account on the one hand crop dependent exposure factors (Ef) and on the other hand SV-values, which depend on default values for pollen and nectar consumption, sugar content in nectar, residues (RUDs) in pollen and nectar and crop attractiveness (ETRlarva = AR x Ef X SV /NOED) (for details see [1]). Moreover, it distinguishes the risk for bees being exposed to different scenarios, from which risk for being exposed to the 'treated crop' and 'weeds flowering in the field' were regarded as the most relevant. Calculations were done using the EFSA–tool, Version 3 (October 2015).

Adult chronic pass rates were taken from a previous poster [3].

Findings (honey bee risk)

Table 1: Overall pass rates of screening and tier I RA for honey bee larva

Use (n)	Pass rates from 2017 analysis [%]		
	Screening	Tier I	
		treated crop	weeds in the field
Insecticides (47)	21	40	43
Fungicides (53)	77	89	96
Herbicides & PGRs (66)	96	97	97
All (166)	69	79	82

Larval data evaluation analysis results:

- **The compiled data comprised single and repeated dosing as well studies with 7/8 and 22 day endpoints resulting in the overall screening step and tier I RA pass rates described in Table 1.**
- **In 43% of the cases the D8 endpoint is equivalent to the D22 endpoint, while in 48% of the cases the D22 endpoint is lower (Tab. 2).**
- **Higher potential failure rates have to be expected, at least for compounds showing toxicity, according to the requirements (repeated exposure, D22 endpoint) of the EFSA Bee GD (Tab. 2 and Tab. 3).**
- **The risk assessment based on real chronic adult honey bee data ([3]) resulted in lower pass rates for all compound groups compared to larval data, with the exception of insecticides using a D22 endpoint.**
- **As standardized test methods for larval non-*Apis* bees are not available, risk would be based on 1/10th of the HB endpoint as surrogate. In this case the pass rates of spray application uses would significantly decrease for bumble bees (< 5%, n = 162) and solitary bees (< 5%, n = 162).**

Table 2: Sensitivity of D8 endpoint in repeated exposure D22 in honey bee larvae studies

Endpoint relation	Proportion [%] (n_{ges} = 21)
D8 ≙ D22	42.9
D8 > D22	47.6
D8 < D22	4.8
D8 data not available	4.8

Table 3: Pass rates using endpoints of single (D7) and repeated exposure (D22) larvae studies as well as adult chronic studies

Use	Pass rates [%]			
	Honey bee larvae			Adult honey bees
	Screening (2013 [2]) (endpoint deriving from acute oral testing)	Tier I (2017)		Tier I (2017 [3]) chronic exposure
		single exposure (D7)	repeated exposure (D22)	
Insecticides	26	43	15	18
Fungicides	58	89	80	44
Herbicides & PGRs	47	100	100	46
All	44	71	62	36

4. Summary and conclusions

- **Risk assessments using real larval data confirm that the chronic risk assessment for adults is the key driver of honey bee risk in the EFSA Bee GD as stated in the original impact analysis.**
- **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.**
- **The high failure rate on insecticides for honey bees jeopardize their registration, as risks cannot be resolved by unworkable higher tier studies.**
- **Almost all compounds and their respective products will fail the bumble bee and solitary bee larval risk assessment, because valid laboratory methods on their larvae are not available and higher tier studies are long-term research projects.**
- **The need to develop internationally recognised guidelines remains. New guidance should be built on existing guidance, recent research results as well as experiences and recommendations of all stakeholders.**

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[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] Miles, M. et.al.: Improving pesticide regulation by use of impact analyses: A case study for bees – Poster SETAC 2017