## 1.21 Improving pesticide regulation by use of impact analyses: A case study for bees

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### Abstract

When changes to regulatory guidance for risk assessment are proposed it is necessary to undertake an impact analysis to assess whether they bring the desired improvement to a risk assessment and reliability of the outcomes to inform decision making. In particular impact analyses should estimate the chances of getting both false negative (concluding low risk where more research is needed) and false positive outcomes (concluding high risks where the product is of low risk). Such analyses are also used to inform on future product development costs and workload for regulatory authorities.

In this paper, we present the findings from an impact analysis conducted on the proposed EFSA bee guidance document (2013) and discuss whether the proposed guidance would provide for a cost effective and tiered approach toward the protection of bees due to the potential risks posed by the use of plant protection products. Following on from this a second impact assessment is presented based on new data generated by ECPA member companies regarding the assessment of chronic risk to bees. Critical areas are discussed and suggestions for the improvement of assess the risk assessment for plant protection products (PPP) to bees are presented.

**Keywords:** Honeybee, risk assessment, impact analysis, pesticide

## Introduction

When significant changes to regulatory guidance for risk assessment are proposed it is necessary to undertake an impact analysis to assess whether they bring the desired improvement to a risk assessment and reliability of the outcomes to inform decision making. In particular impact analyses should estimate the chances of getting both false negative (concluding low risk where more research is needed) and false positive outcomes (concluding high risks where the product is of low risk). Such analyses are also used to inform on future product development costs and workload for regulatory authorities.

In July 2013 EFSA released their guidance document on the risk assessment of pesticides on bees and considerably updated it in 2014 based on feedback from a workshop with European Union member states. The document demanded a more thorough approach for the testing and risk assessment of plant protection products (PPP) for bees.

## Material and methods

In 2013 industry undertook a detailed evaluation of the impact of the proposed screening and tier I risk assessments on the pass/fail rate of currently available active substances on the EU market using honey bee endpoints. The analysis considers 151 active substances covering 163 uses: 52 were herbicides, 52 fungicides, 51 insecticides or acaricides and 8 other uses like plant growth regulators. Solid applications were also considered with 20 active substances representing 36 uses (not shown). At the time not all data on all substances were available as test methods were yet to be developed; consequently it was necessary to estimate some endpoints.

Acute contact and oral toxicity: reported $LD_{50}$ values used (µg a.s./bee).

Chronic oral toxicity ($LDD_{50}$): Estimated as 1/5th acute oral toxicity endpoint based on advice from EFSA e.g. acute oral $LD_{50}$ = 100 µg a.s./bee was converted to chronic oral $LDD_{50}$ = 20 µg a.s./bee.

Larval toxicity (NOED, no observable effect dose): Estimated as 1/10th of adult's acute oral $LD_{50}$ corrected for mean larval body weight (83 mg, e.g. acute oral $LD_{50}$ = 100 µg a.s./bee was converted NOED = 8.3 µg a.s./larva.

The screening level risk assessment according to EFSA 2013 was conducted for all 163 uses according to the following formulae:

$HQ_{contact} = AR / LD_{50}$ contact

$ETR_{oral} = AR \times SV / LD_{50}$ oral

$ETR_{chronic} = AR \times SV / LDD_{50}$ oral

$ETR_{larva} = AR \times SV / NOED$

Where: AR = application rate in g a.s./ha for $HQ_{contact}$ and kg a.s./ha for all other ETR values.

SV = short cut value.

Following on from this a second impact assessment was conducted using the real-life endpoints from 10 day chronic studies with honey bees using the same procedure as above based on new data generated by ECPA member companies. Data from 85 uses including 32 herbicides, 32 fungicides and 17 insecticides were evaluated. In addition to the screening assessment a tier I evaluation was also conducted using the tier I S.V.s and accounting for dissipation in pollen and nectar over time using a default half-life ($DT_{50}$) of 10 days.

## Results and discussions

The number of uses passing or failing the screening risk assessment for the original impact analysis is presented as percent in table 1. The pass / fail rate of the EFSA proposal for acute risk (HQcontact and ETRacute adult oral) was very similar to the current risk assessment proceeded using HQ values for both contact and oral routes of exposure and the Annex VI trigger of 50 indicating that possibly there will be no overall significant changes in the risk assessment outcome

for acute risk assessment for foliar applied products, i.e. the overall protection level is similar. Consequently, based on the sample of 163 uses, 26% of all uses would require evaluation at a higher tier for acute risks to adult bees. This would include at least 60% of insecticides.

The risk to larvae based on the calculated $ETR_{larvae}$ values indicated that less than half of the uses will pass the screening tier risk assessment with 56% of uses indicating higher tier evaluation, including 74% of insecticides. This pass rate is similar to that based on real-life data from 22 day repeated dose studies (Becker *et al* 2018).

The chronic risk to honey bees as measured by calculation of $ETR_{chronic}$ adult oral was remarkably different to the acute risk. In this case only 18% of uses were observed to have passed the screening level trigger of <0.03. For this assessment 79% of all herbicide uses failed as well as 75% of fungicide uses and all 92% of insecticide uses. Overall this would mean that in 82% of all cases a higher tier risk assessment would be required which may necessitate the generation of higher tier data (e.g. field residue tests, semi-field and field tests).

The distribution of screening level $ETR_{chronic}$ adult oral risk is presented in Figure 1. It can be seen that the majority of substances do not pass the risk assessment. A tier I risk assessment only gives a moderate improvement (less than a factor of 10). The $ETR_{chronic}$ for many herbicides and fungicides require a refinement level of 2 – 3 orders of magnitude and for insecticides of 5 – 6 orders of magnitude. This means that risk assessment refinement methods such as used of measured residues in treated crops, generation of higher endpoints pose significant challenges even for herbicides and fungicides. As this was based on extrapolated values from acute studies to check if these findings were realistic and predictive industry undertook a follow-up analysis using endpoints and data obtained from several years of practical experience with 10 day adult testing. It was found that the overall pass rate was similar to that predicted with 18% predicted by the impact analysis and 24% based on real-life data. The number of uses passing for herbicides based on real data was slightly higher than predicted (31% vs. 21%) and this can be accounted for by the fact that in the impact assessment endpoints were often extrapolated from limit tests where no toxicity was observed. The number of fungicides uses passing based on real-life data was very close to the predicted level (28% vs. 21%). The impact analysis predicted that 8% of insecticides would pass the screening risk assessment however in real-life the actual value was 0%.

**Table 1** Risk to honey bees: Percentage number of uses passing the screening risk assessment for foliar (based on 163 uses) from impact assessment 2013.

| Chemical group | Acute risks to adult honey bees | | | | Chronic risk to Adult honey bees* | Larvae** |
|---|---|---|---|---|---|---|
| | $HQ_{contact}$ (current HQ<50) | $HQ_{contact}$ (new HQ <42 or 85) | $HQ_{oral}$ (current HQ<50) | $ETR_{acute\ adult\ oral}$ (<0.2) | $ETR_{chronic\ adult\ oral}$ (<0.03) | $ETR_{larvae}$ (<0.2) |
| Herbicides | 96 | 94 | 94 | 88 | 21 | 50 |
| Fungicides | 98 | 100 | 96 | 92 | 25 | 58 |
| Insecticides | 47 | 47 | 40 | 40 | 8 | 26 |
| Other | 100 | 100 | 88 | 75 | 13 | 25 |
| All | 81 | 82 | 78 | 74 | 18 | 44 |

* 10 day $LD_{50}$ for adults estimated as 1/5 of acute $LD_{50}$
** NOEL for larvae estimated as 1/10 of adult's $LD_{50}$ corrected for body weight (83 mg/bee)

**Table 2** Chronic risk to honey bees: Percentage number of uses passing the screening and tier I risk assessment for foliar (based on 81 uses) from industry data collection of real-life endpoints 2015.

| Chemical group | % uses passing honey bee chronic risk assessment | |
|---|---|---|
| | Screening level | Tier I |
| Herbicides (n=32) | 31% | 47% |
| Fungicides (n=32) | 28% | 44% |
| Insecticides (n=17) | 0.0% | 18% |
| All (n=81) | 24% | 36% |

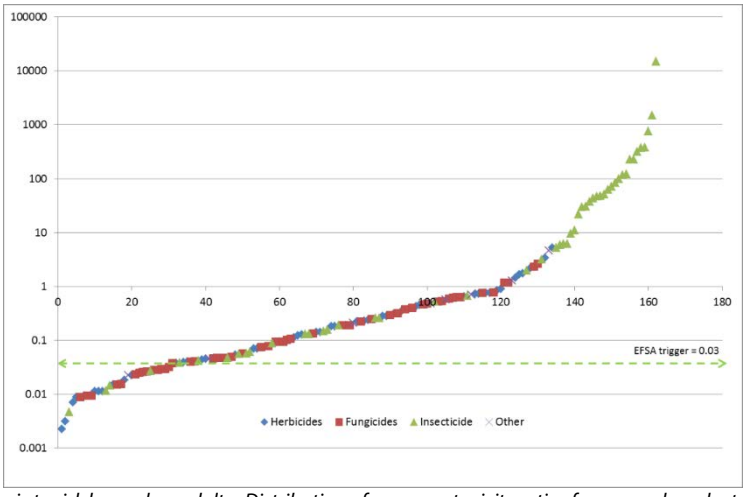


***Figure 1*** *Chronic to risk honey bee adults: Distribution of exposure toxicity ratios for sprayed products. Values below the dashed line pass the EFSA trigger of 0.03.*

## Conclusions

The impact analysis and the follow-up work by Becker *et al* 2018 on larvae and with chronic adult data in this paper highlight the problem of releasing new guidance without proper consideration of the impact on all users and stakeholders. The impact analysis allowed researchers to focus on key challenges such as appropriate triggers (Miles *et al*, 2018a), better ways to estimate bee exposure taking into account real-life bee feeding behaviour by use of models (Miles *et al* 2018b; Miles and Preuss, 2018) and additional consideration of the relative sensitivities of honey bees and non-*Apis* bees (Dinter *et al* 2018).

The EFSA 2013 guidance for bees is unworkable in its current form and will lead to systemic failure for almost all substances without providing workable higher tier options. Levels of screening and tier I refinement needed are large; 2 to 3 orders of magnitude for low toxicity compounds and 5 to 6 orders for insecticides. New guidance should be designed to work within current regulatory testing frameworks and be built on existing guidance. Before implementation any new guidance with potential to impact innovation should be subject to a testing phase and modified if needed to create workable processes.

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