CropLife EUROPE

Comments: "Business and food industry"

Review of the EFSA Guidance on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees)

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Virtual Workshop with risk managers, risk assessors and Stakeholders - 5th October 2022

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Conclusions

Introduction

- The revised version of the guidance document reflects a significant effort from the expert working group to address the questions raised on EFSA 2013 document
- The documentation shared by EFSA goes beyond the revised guidance document, as it seems to also include the content of a “scientific opinion”. Hence commenting the whole content within the timeline was a challenge
- This presentation was prepared in collaboration with Euroseeds and IBMA, to reflect the understanding, comments and proposals across the crop protection industry
- The comments were collated and uploaded – 77 pages of comments and a few additional technical input, prepared by ca 20 experts (bee health and bee testing, statisticians and modelers)
- EFSA’s feedback on these comments will be most welcome
- CLE would be very interested to learn if there will be a process to allow the possibility for further work involving the different stakeholders

Preliminary feedback on impact analysis

- 114 a.s./products (I/IGR: 24; F: 44; H/PGR/W: 46)
- 211 uses (I/IGR: 64; F: 68; H/PGR/W: 79)
- Results of the screening step for honeybees (overall effect equal or below 10%):
  - I/IGR: 2/64 (= 3%)
  - F: 54/68 (= 79%)
  - H/PGR/W: 55/79 (= 70%)
  - Overall: 111/211: (= 53%)
- All applications were assumed to be applied 1x during flowering.
- Where the endpoints were unbound LD(D)50 we used a correction of 4.6x and a slope of 1.43 for the acute studies (less than 10% effects) and 2.6 and a slope of 1.43 (10-20% effects) for the larvae and 10 day chronic.
- Where LD(D)50 were available they were used in the analysis and if a slope was available it was used (regardless of model).
- No consideration of effect of sublethal and TRT risk assessments

Specific protection goals

- Quantitative SPG not defined for bumble bees and solitary bees, which has led to more conservative assumptions in the low tier risk assessment, and hence will trigger a high number of high tier studies for BB and SB
  - Should studies requested in the regulatory context be the preferred way to build scientific knowledge, particularly where the absence of test guidance will be an issue for study acceptance?
  - Since the honeybee appears to belong to the most sensitive group according the revised guidance, we propose a tiered system be considered where additional testing on bumble bees and solitary bees is triggered based on the outcome of the honeybee risk assessment and to address specific questions where other bees might be exposed
  - If high tier are to be requested, we need a reliable consultation process on study protocols to address the concerns associated in the absence of guidance for these studies

Laboratory testing

- Several new parameters have been introduced for these to be addressed in the low tier studies, such as behavioral observations, TRT recommendations in chronic studies LDD10, LDD20 and LDD50
- This raises concerns on implementation timelines and the risk that dossiers currently under evaluation / finalization will be considered incomplete (see previous EFSA conclusions based on EFSA 2013)
  - Should chronic studies determining a NOEL be systematically repeated?
  - Will guidelines be updated before additional endpoints are expected?

Exposure

- Realism of applications positioning in default assumption
  - Eg Ndu and Nbe should reflect GAP table particularly as more precision applications will be recommended
- Realism of larvae exposure (BB and SB)
- Weeds in the treated field:
  - It would be more scientific to consider the relevance of flowering weeds on a crop-by-crop basis (presence of weeds and proportion of flowering weeds)?
  - As for succeeding crops, could a screening approach based on toxicity levels to decide on the need for a risk assessment be considered?
- Concentrations in pollen and nectar through soil:
  - Should the default assumption be to use the pore water concentration where data suggest systematically lower levels?
- Robustness of databases on which to base RUD:
  - RUD distribution for sidewards/upwards applications (3 studies)
- Options to refine field margin risk assessment (non cropped) through experimental data

Sublethal effects on honeybees in risk assessment

- The assessment of sublethal assessments in existing studies might lead to study repetitions – the need of these should be open to discussion
  - Exposure levels in laboratory studies are not aiming at representing GAPs but provide dose-effects responses – may have implications on sublethal effects
  - There is a need for alignment with current recommendations on the homing study so that to ensure meaningful parameters are measurable
- The setting of a 10% trigger for sublethal effects is arbitrary and not linked to the same level of effect on colony size
  - Are there examples of cases where a factor of 50 was observed between a LD(D) 50 and a LD(D)10?
- Questions of how the tiered approach will work for many low toxicity compounds
  - E.g. are effects presupposed?

    LD50 > 100 µg/bee (but no difference to control in behavior or food consumption)

    sublethal NOED = > 2 µg/bee or > 100 µg/bee?

Lower tier risk assessment

- The cumulated exposure assessment in lower tiers should be discussed in light with the fact that some exposure routes outweigh others
- Hypothesis of the 1:1 propagation from the individual to the colony level is highly conservative considering real data and more realistic options are needed e.g.
  - taking into account the actual ratio of foragers, hive bees, uncapped and capped brood (not being fed)
  - Beehave / modelling options
- Very high-level complexity of the approach taken for lower tier risk assessment e.g.
    - PFF
    - TRT – GUTS modelling
    - Sublethal effects
    - Multiple applications

Higher tier risk assessment

- On the discussion on the role of high tier studies categories to refine a risk assessment:
  - Need to discuss the decision criteria towards semi-field or field studies, since exposure routes might be very similar
  - Semi-field studies can also be useful for other bees than foragers
  - Colony feeding studies still consider pollen collection by foragers and could be a more integral part of the higher tier assessment along with semi-field tests
- Need standardized guidance for high tier studies on bumble bees and solitary bees before a systematic requirement
- Higher tier studies for honeybees:
  - Need to review conditions of validity of higher tier testing (e.g. rainfall events, variability vs uncertainty)
  - Merits of sampling methods for pollen and nectar (flower vs bees)
  - The concept of equalization of colonies is understood from a statistical point of view thought difficult to achieve in situ and unlikely to represent variability encountered between colonies and thus relate to actual field situations, even in healthy colonies

High tier studies design and statistics

- 90th percentile exposure goal may mean GAPs need to be exceeded for a valid study
- The proposed recommendations (Annex C) could be checked in light of existing data and a series of generic studies in order to confirm practicality and use in determining study endpoints (ICPPR working group? In cooperation with OECD?)

General comments on statistics

- There are several aspects of the draft guidance document which are either statistically flawed, not in line with modern statistical practice / other guidance documents or overlook a key aspect
- CLE has provided detailed comments and recommendations allowing the document to be updated to be scientific and give reliable conclusions E.g.
  - Dose response modelling
  - Equivalence testing

See detailed comments submitted

BEEHAVE

- CLE believes BEEHAVE is ready for regulatory use
- Since EFSA (2015) reviewed BEEHAVE there have been 20 publications using BEEHAVE
  - All the main issues raised by EFSA have been addressed: e.g. ecotox module, exposure, extensive validation using field, feeding and tunnel studies, case studies, scenarios
  - BEEHAVE is the most widely used and tested colony model (including by EFSA for setting SPG and calibrating tier I)
  - ApisRam is several years delayed

Use of BEEHAVE to set 1st tier triggers and refinements

- The BEEHAVE simulations show that while 1:1 between individual effects and colonies is worst-case, it also indicate that most of the time colonies are much more resilient
  - BEEHAVE should therefore be an option for higher tier refinements
- The 1:1 is very conservative because there is no consideration of colony resilience. However, social insects are super-organisms and a colony does not represent a population, but rather one reproductive unit
  - Colony "recovery" is more akin to damage repair in TKTD modelling than the ERO (ecological recovery option) and should be allowed if it takes place within a reasonable timeframe and as long as the effects do not exceed the SPG

Species extrapolation

- (See commenting table for detailed comments about the extrapolation factor of 228 for solitary and bumble bees)
- The exaggerated extrapolation factor of 228 is due to how uncertainty is handled in a non peer-review ad hoc statistical approach, which is not in line with best practice
- All CLE's analyses of the data of EFSA provided about the bee weight suggest that the extrapolation factor for solitary bees should be in the region of 10-18
- Details of this analysis (including R-code) was submitted

Time Reinforced Toxicity

- CLE agrees that GUTS is a suitable model to assess TRT and effects under time variable exposure
- EFSA proposes only to use only GUTS-SD (and not GUTS-IT)
  - the choice between GUTS-SD and GUTS-IT cannot be made *a priori*, because GUTS-IT can yield more conservative predictions (Nickisch et al. 2022, Ashauer et al. 2015)
  - Baas et al (2022) have calibrated and validated both GUTS-SD and GUTS-IT on a large dataset for honeybees demonstrating both GUTS-SD and –IT are fit for purpose
  - CLE recommends that EFSA follow EFSA's guidance on good modelling practice: "The level of conservatism is defined in the SPG and reflected in the scenario, but the model should be realistic." (EFSA 2015)
- CLE recommends that both GUTS-IT and GUT-SD should be calibrated and validated; model choice should depend on model performance criteria (e.g. from the EFSA TKTD (2018) Scientific Opinion)

IBMA: Specific points relating to biocontrol

- **Welcome the exclusion of micro-organisms** from the scope of the guidance as requested in our previous comments
- However, IBMA believes that the adoption of the bee guidance in its current form could reduce the EU's ability to authorise other type of biocontrol products, and so reach the objectives of the Farm to Fork strategy
- **Semiochemicals** (pheromones) and **Natural Substances**, and their specificities, have not been considered in the present EFSA review:
  - Are they excluded too?

IBMA: Specific points relating to biocontrol

- **IBMA believes that semiochemicals should be also excluded from the scope of the bee guidance:**
- Semiochemicals are substances emitted by plants, animals and other organisms which are used for intra- and inter-species communication, have a target-specific and non-toxic mode of action and are naturally occurring.
- According to:
  - Regulation (EU) No. 2017/1432: "*low-risk substances*"
  - OECD No. 93 & SANTE/12815/2014: *no need for risk characterization for non-target species when use in dispensers or exposure is similar to natural exposure levels*
  - EFSA Conclusion for Straight Chain Lepidopteran Pheromones (SCLPs): *even in case a risk is identified, the intrinsic properties of the substances lead to a low risk to bees*

IBMA: Specific points relating to biocontrol

- **IBMA asks for the exclusion of groups of Natural Substances (NS) based on their specific properties:**
- Consist of one or more components that originate from nature, including but not limited to: plants, algae/microalgae, animals, peptides and minerals.
- They represent a wide spectrum of substances, but they have in common that are relevant to the bee risk assessment: nature identicality, presence in the environment, known degradation pathways and a background exposure of pollinators.
- Should the bee guidance be approved in its current form, we expect that many natural substances and especially the ones with insecticidal properties could be rejected. **Careful consideration of the applicability of the guidelines should be made.**
- Several NS should be excluded such as fatty acids based on their properties.

Biologicals

- Biological pesticides other than microorganisms may trigger some data waivers depending on their nature (e.g. semiochemicals, botanicals)
- Biologicals are also identified as candidates to meet the criteria of the “uses of potential low environmental impact” according to the eponymous draft guidance document of the EU Commission
- Will the revised guidance document provide guidance on the risk assessment for these biologicals or will this be provided into ad hoc documents?

Conclusions

- The revised guidance addresses a number of issues identified in the EFSA 2013 document, and fills gaps from previous guidance
- Significant changes are needed before implementation
- Science is complex and the inclusion of that complexity in a guidance document is a challenge
- The proposed revised guidance shows areas where tiered approaches could be considered while still addressing the critical components of the risk assessment with a high level of safety
- A progressive implementation of the guidance is necessary to enable compliance of the dossiers