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Environmental scenarios for ApisRAM version 3, a honey bee colony model for pesticides risk assessment

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Abstract

Environmental scenarios were established for ApisRAM, a honey bee colony model currently under implementation towards version 3, i.e. for its regulatory use in the risk assessment of pesticides. These scenarios need to represent the diversity of European environments in terms of risks for honey bees, addressing the regulatory question as outlined in the problem formulation (i.e., the risk characterisation for bees following individual pesticide uses) and taking account of the specific protection goals as defined by EFSA for honey bees. The scenarios are composed of a *baseline scenario*, defining the ecological quality, and the *case scenarios*, where pesticide application related aspects as defined in the GAP are given. The ecological quality is defined in typical "landscape windows" and classified along two dimensions, i.e. the *floral resource diversity*, as a proxy for the number of floral plant species, and the *floral resource quality*, as a proxy for the amount of nectar, sugar, and pollen produced by the respective plants. The scenario definition is closely related to ALMaSS, a dynamic landscape model and the platform on which ApisRAM runs, that is operating on landscape windows of 10x10 km with information on weather, crop and non-crop phenology, land use and landscape structure. Based on landscape information, three levels (low, medium, high) each of floral resource diversity and quality are defined, resulting in a factorial design of 9 baseline scenarios in 3 scenario groups (most, moderately and least favourable). For the assessment of risks, the use of a "risk matrix" is suggested, where for each of the 3 scenario groups, and for a given GAP, the respective case scenario will be evaluated. Further, by using exposure modification factors, the margins of safety can be determined. In conclusion, potential applications of those environmental scenarios in a broader context are suggested along with some specific recommendations.

Key words: ALMaSS, ApisRAM, ecological quality, environmental scenarios, floral resource diversity and quality, honey bee model

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Summary

This report describes the selection of environmental scenarios for the use of ApisRAM, a honey bee colony model, for the risk assessment of pesticides in honey bees.

In the introduction (section 1), background information is provided on the vision (**section 1.1**) and design (**section 1.2**) of ApisRAM, a honey bee colony model. ApisRAM was designed by an EFSA working group in 2016, as part of the EFSA MUST-B project which is developing a framework for the implementation of a holistic and integrated environmental risk assessment of multiple stressors in bees. The formal model was outsourced by EFSA, developed by Aarhus University and published in 2022. The next phase is the implementation of the model by building blocks (modules): the core colony with in-hive products (version 1), exposure to stressors such as biological agents (version 2) and pesticides with the influence of beekeeping management practices and beekeeper experience (versions 3 and 4). Version 3 is expected by 2025 to comply with the regulatory risk assessment of chemical pesticides for single substance/single product as foreseen under Regulation EC No 1107/2009[3], while version 4 is expected by 2027 and goes beyond the current regulation, incorporating invasive species and chemical mixtures (**Figure 1**).

The terms of reference and their Interpretation are defined in **section 1.3**. The environmental scenarios described in this report are meant for the use of ApisRAM version 3 and need to represent the diversity of European environments in terms of ecological quality, climate and colony status (infestation/infection levels and strength). The working group clarified that the scenarios assume good management practices, both for farming and beekeeping. However, in case the end-user wants to test the influence of the beekeeper experience on the overall assessment, the model will still have this option available.

The definition of an environmental scenario in environmental risk assessment (ERA) has been historically linked to environmental and crop-related aspects (e.g., as in FOCUS, 2001[4]), with aspects such as the application patterns of the pesticides or their physical-chemical processes being outside this paradigm. The MUST-B WG took up the underlying approach by FOCUS (2001) and further considered aspect which may specifically characterise the scenario definition for complex effect models, such as ApisRAM. For such a purpose, the EFSA scientific opinion on good modelling practices and the definition provided in the recent literature[5] on exposure and ecological scenarios for model use in pesticides risk assessment were considered. According to the MUST-B WG paradigm, environmental scenarios are considered to be at the interface of the abiotic and biotic processes which may influence risk characterisation. While not moving away from the FOCUS approach, the WG acknowledged the importance of aspects which have not historically been considered part of the scenario definition. Specifically, as part of the "case scenario" definition (which is specifically related to the use conditions, as explained under section 3.2), the WG acknowledged the influence of the application patterns of pesticides (as defined by the Good Agricultural Practice also referred as GAP) and the physicochemical properties influencing the behaviour of the active substance under assessment (**Figure 2, section 2.1**).

[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] FOCUS (2001). "FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC". Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2. 245 pp.
[5] E.g., outputs of the SETAC Working Group on Model Acceptability, version control and scenario Development (MAD).

Environmental scenarios define the characteristics under which the model will be used, and are linked to the specificities of the system (i.e. the organism under evaluation and the environment in which it operates) and to the risk assessment and decisions to be made by end-users, i.e. risk managers and risk assessors, on the way they will apply the model, within the Europe Union and at Member State level.

Environmental scenarios are designed to best support the regulatory questions as laid out in the problem formulation. For honey bees, these scenarios should therefore reflect the spatial and temporal dimensions of the specific protection goals as defined under the revised EFSA guidance published in 2023 for the risk assessment of plant protection products on bees (**Table 1, section 2.2**). The assessment endpoints used in ApisRAM and their alignment with the corresponding regulatory framework are described in **Table 2** (**section 2.3**).

The definitions and description of scenarios for ApisRAM are found in **section 3**. Baseline and case scenarios were developed for ApisRAM to support the risk assessment of pesticides on honey bee colonies. A baseline scenario provides the baseline conditions for colony status (baseline values for the presence of *Varroa*, *Nosema*, Deformed Wing Virus, Acute Bee Paralysis Virus and Sac Brood Virus and their corresponding infestation levels, each in the absence of clinical sign of disease) and environmental attributes (a gradient of environmental settings from most to least favourable conditions, in terms of diversity and quality of resources for foraging activity and ultimately for colony development) (**section 3.1**). A case scenario is a baseline scenario with the addition of pesticides in different proportions (exposure modification factors), for comparison with a control scenario (baseline without pesticide) and, ideally, a scenario with a toxic standard (**section 3.2**).

Baseline scenarios are partially informed by ALMaSS (the Animal Landscape and Man Simulation System), which is the platform on which ApisRAM runs, to simulate landscape dynamics (land use and structure, and crop phenology simulated with weather conditions over time) within 10x10 km landscape windows (so-called "ALMaSS windows"). The remaining information needed to define baseline scenarios refer to specific colony attributes (location of the colony, initial colony size, food stores, levels of infectious agents which do not induce any clinical signs, and pesticides residues set to 0 at the start of the simulation) and environmental attributes (geographic location of the assessment and input variables which are already informed by ALMaSS such as weather, and landscape structure). More information can be found in **section 3.1.1** (colony attributes) and **section 3.1.2.** (environmental attributes). Nine baseline scenarios are suggested to be defined after categorising ecological quality in ALMaSS in two dimensions (**Figure 3, section 3.1.3**). The first dimension relates to "floral resource diversity" which is expressed in terms of the number of floral plant species coming from crops (both focal and non-focal) and non-crop habitats. The second dimension relates to "floral resource quality" which is expressed as the total amount of pollen and sugar (from nectar) produced from these plants. In each of these dimensions, three quality levels (high, medium, low) are selected, representing different environmental conditions from the most favourable (high diversity and quantity of the foraged plant species) to the most unfavourable (low diversity and quantity of the foraged plant species) for honey bee colonies. From the resulting distributions of floral resource diversity and quality across the entire landscape of interest, the 5^{th}, 50^{th} and 95^{th} percentiles for each landscape will be calculated corresponding to low, medium and high proportions of floral resource diversity and quality. For each of the baseline scenarios, ALMaSS windows (of 10x10 km size) will be identified and selected._During the subsequent risk assessments, ApisRAM simulations will be performed for the selected ALMaSS windows, thereby creating model outputs across the baseline scenarios.

Case scenarios are informed by the GAP (selection of the crop/product and use which are regionally and temporally specific), and the critical GAP (worst-case for exposure scenario) should be selected. Exposure modification factors (obtained by multiplying application rates or mass of an active substance in the case of seed coating) are proposed to determine "margins of safety" for a GAP (**section 3.3)**.

Finally, a risk matrix can be established after first grouping the 9 baseline scenarios into three scenario groups (most favourable, moderately favourable, least favourable). The risk matrix presents simulations from case scenarios with different exposure modification factors (EMFs) according to the gradient of ecological quality (combinations of floral resource diversity and quality) as represented in the most favourable, moderately favourable and least favourable scenario groups. This matrix will help to identify "margins of safety" for a given GAP (**section 3.4** and **Figure 4**).

Conclusions and recommendations on how to further apply these environmental scenarios are made in **sections 4 and 5**, respectively.

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1. Introduction

1.1. Towards ApisRAM version 3: a tool for the risk assessment of pesticides

EFSA initiated an EU-wide project called MUST-B in 2015 to ensure preparedness for future risk challenges in the area of honey bee health, and to move towards a more holistic and integrated environmental risk assessment (ERA) (Rortais et al., 2017). In 2018, following a request from the European Parliament, this project was formalised with a mandate for the preparation of a scientific opinion on a more holistic risk assessment for bees, integrating multiple stressors and landscape aspects within the risk assessment. In 2021, the EFSA Scientific Committee published an opinion laying down the vision and methodology for a systems-based approach that would allow both predictive (prospective) and post-authorisation (retrospective) risk assessments of pesticides in honey bee colonies (EFSA SC, More et al., 2021). The system is composed of two parts (modelling and monitoring) interlinked by data flows coming from both modelling and monitoring outputs. While the approach was still in a conceptual phase, EFSA has already deployed efforts to implement the modelling part with the development of ApisRAM, an agent-based model for honey bee colonies. ApisRAM was conceptualised by the MUST-B Working Group (WG) (EFSA, 2016) in line with the Good Modelling Practices Scientific Opinion (EFSA PPR Panel, 2014) and the EFSA Scientific Opinion and Guidance Document on the risk assessment of plant protection products (PPPs) on bees (*Apis mellifera*, *Bombus* spp. and solitary bees) (EFSA PPR Panel, 2012; EFSA, 2013; EFSA et al., 2023). ApisRAM was recently formalised and published by Aarhus University as version 1 (Duan et al., 2022), and field data collection, specifically designed by the MUST-B WG for the calibration of ApisRAM (EFSA, 2017), was conducted in Denmark and Portugal (Dupont et al., 2021). Further data will be collected from other sources with the goal to design a tool for the risk assessment of pesticides (single product/use in possible interaction with biological agents) by 2025 (version 3) and later for the cumulative risk assessment of pesticides in interaction with other stressors (e.g. invasive species) by 2027 (version 4) (Figure 1).

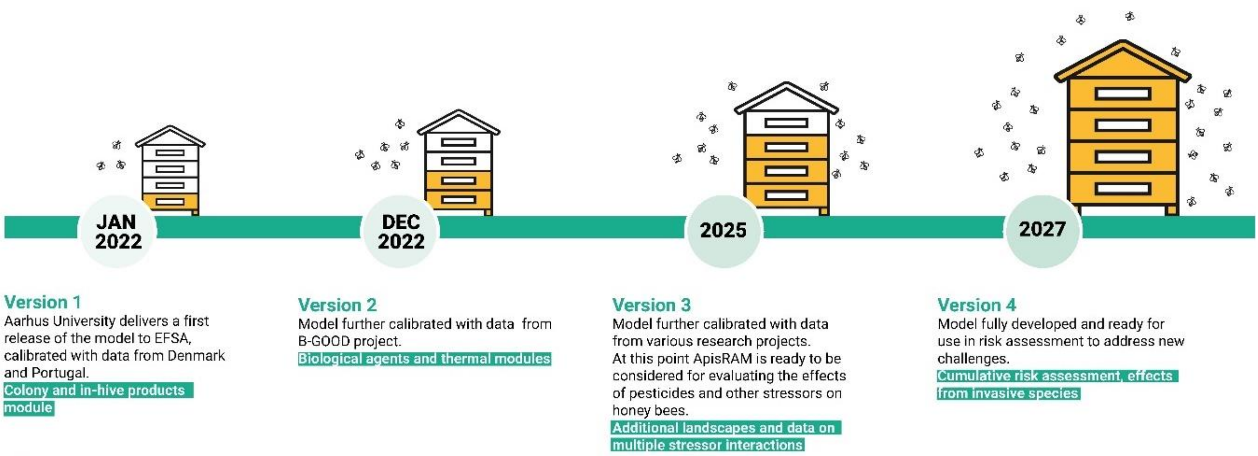

Figure 1: Timeline for the implementation of ApisRAM

In the environment, pesticides applications can be made individually, simultaneously or sequentially, which can result in oral or contact exposure of honey bees over time and space (e.g., individual or mixture of insecticides, fungicides and herbicides). In line with the regulatory framework, ApisRAM version 3 is designed to assess individual uses (in the sense of individual

Good Agricultural Practices (GAPs), as explained in Regulation (EC) No 396/2005[6]), which may include sequential applications of a product comprising one or more substances (e.g., as in the case ofPPPs containing more than one active substance (a.s.); a tank mixture of multiple PPPs; or the a.s. and its metabolite). In addition, ApisRAM version 3 will be able to simulate various types of pesticides applications (i.e. spray, granule and seed treatment), as well as exposure from drift of the PPP from the treated crop to adjacent areas. When drift is included, a minimum of two a.s. can be modelled.

ApisRAM Version 3 will comply with the current regulatory framework, i.e. with Regulation (EC) No 1107/2009[3] for the risk assessment of PPPs whereas version 4 will go beyond it, making risk assessments more holistic and context-dependent, as foreseen under the system-based ERA approach.

1.2. ApisRAM design

The model is a mechanistic exposure and effect model for the risk assessment of pesticides. The model is based on the dynamics of the honey bee colony, the in-hive products and their interactions with biotic and abiotic environmental and anthropogenic factors (i.e. including landscape structure and dynamics, pesticide applications, biological stressors, and beekeeping practices). It simulates the dynamics of a single honey bee colony over time in a complex and spatially-explicit landscape, where interactions between colonies are not considered.

ApisRAM includes the following modules, which individually and interactively influence colony dynamics:

- The “Pesticides” module comprises aspects related to pesticide exposure and effects. It describes the fate and behaviour of pesticides in the environment, their degradation and distribution in the beehive products and the patterns and routes of exposure (contact and oral) of the various bee life stages of a honey bee colony. The pesticides module takes into account lethal effects and may incorporate sub-lethal effects when appropriate experimental data are available.
- The “Biological Agents” module comprises the effects on colony and in-hive products of *Varroa destructor* with its two associated viruses, the Deformed Wing Virus (DWV) and the Acute Bee Paralysis Virus (ABPV), and *Nosema* spp. In addition, it was recently suggested to also include the Sacbrood virus (SBV) because it displays a different mode of infection that is of interest for ApisRAM and it also presents available data for its calibration.
- The “Beekeeping Management Practices” (BMP) module comprises a selection of 5 Beekeeping practices (namely “change in the number of workers”, “chemical control”, “replacement of combs with brood”, “replacement of combs with feed sources” and “supplementary feeding”) and beekeeper experience and their impacts on the other modules (see section 1.3. on how BMP are included in ApisRAM version 3).

1.3. Interpretation of the Terms of Reference

EFSA self-tasked the implementation of ApisRAM towards versions 3 and 4 with the launching of a framework partnership agreement (Grant Agreement GP/EFSA/SCER/2021/02) that was

[6] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC (Text with EEA relevance) (OJ L 70, 16.3.2005, p. 1)

signed between EFSA and Aarhus University for a period of 4 years starting in November 2022. Under this new mandate, the MUST-B WG was renewed, with the WG composition matching the scientific expertise required to undertake this mandate.

The new WG (MUST-B 2) is requested to support the implementation of ApisRAM with the following terms of references (TORs):

TOR 1: The WG will provide support in the definition and selection of environmental scenarios for ApisRAM.

These scenarios need to be realistic in the sense that they need to represent the diversity of possible EU environments, in terms of:

- Landscape (structure and composition) and climate
- Colony status (infestation/infection level and strength)

For these scenarios, the WG will consider the different spatial scale(s) (i.e. Zonal, Member State, Regional, Provincial, field, etc.) according to the uses under assessment (i.e. the GAP).

For risk assessments, BMPs need to comply with good beekeeping practices (see FAO et al., 2021 for Varroa control and supplementary feeding and Kulhanek et al., 2021 for Varroa control) and therefore, the selected environmental scenarios will not cover the diversity of BMPs found in Europe. ApisRAM will retain the ability to simulate the effects of beekeeper' experience (a continuous number ranging from 0 for inexperienced to 1 for experienced beekeepers). This will be modelled in ApisRAM as events (practices) that either align with good beekeeping practices (for experienced beekeepers) or are delayed or even omitted (for inexperienced beekeepers). The time delay in days will be randomly generated based on the beekeeper's experience (with less experience leading to a longer delay).

The influence of the beekeeper's experience will be made available in ApisRAM (as an option; not per default).

TOR2: The WG will support an expert knowledge elicitation (EKE) protocol on the scenarios for ApisRAM. The WG will act as a steering group, reviewing and assessing the evidence (see TOR1), identifying the areas and parameters (through specific questions; maximum 5 questions) that need further expert knowledge input (through an EKE) as well as the required expertise for the EKE workshop (maximum 10 experts). The WG will participate in the EKE exercise and review the results.

TOR3: The WG will support an external expert who will test ApisRAM (parameter/codes) by conducting sensitivity and uncertainty analyses. The external expert will report regularly to the WG on the results of these analyses. The WG will review the work of the external expert and provide input as needed.

This report covers TOR1. The steering group concluded that the need for an EKE (TOR2) was not needed for TOR1 and therefore was not conducted.

Under TOR1, it is noted that the WG developed scenarios at a conceptual level. The underlying assumptions made by the WG when defining these scenarios will need to be tested and validated by the model developer (Aarhus University) or by external users when new data become available. It is therefore clarified that testing does not fall under the remit of this WG. It was also clarified that the definition of environmental scenarios for the model and risk assessment using the model are two separate exercises. Where the scenario definition is framing the conditions for the assessment to be conducted, the implementation of this scenario framework for specific applications and contexts will require further development and may vary across regions or applications. In addition, while the environmental scenario framework developed here emphasizes variation in floral resources (in terms of quality and seasonality – see below), for certain scenario applications, other factors as outlined in the text below (section 3.1.3) may be of particular interest and importance for assessing risks.

2. Methodology for the set-up of environmental scenarios for ApisRAM

2.1. Definition of an environmental scenario

Environmental scenarios need to be defined when developing mechanistic effect models for the regulatory risk assessment of pesticides. Those scenarios are composed of exposure and ecological scenarios (EFSA PPR Panel, 2014) and the modelling framework for their use in risk assessment was described by van den Berg et al. (under review), but can be summarised as follows:

- *The exposure scenario* relates to the aspects of the abiotic conditions (e.g. weather and temperature). Aspects such as the application patterns, and physicochemical properties influencing the environmental fate and behaviour of the active substance (a.s.) under assessment will be taken into account in the case scenario (See 3.2)
- *The ecological scenario* relates to how the abiotic (e.g. weather, temperature, soil properties and pH) and biotic (e.g., food availability, food quality, predation pressure, competition, habitat quality) conditions and the spatial context of the landscape interact. Landscape aspects include configuration and connectivity characteristics of locations within a given ecosystem, such as habitat connections, availability, distance between refugia and heterogeneity (but not all these characteristics are relevant to managed honey bees).

Other aspects defining the environmental (case) scenarios are those related to the agricultural practice of the pesticide application, such as the crop and accordingly the choice of a PPP, application patterns in space and time as given by the GAP and, consequently to the general agronomic practices. Agronomic practices may provide information on e.g. weed removal, soil tillage, crop rotation, pesticide risk mitigation measures (e.g., buffer strips), and the use of pesticides other than the focal PPP. However, as previously described in section 1, ApisRAM version 3 will simulate the application of one pesticide a.s. applied according to the representative use in one crop of the simulated landscape. According to Regulation (EC) No 396/2005[6], a.s. uses are described by the GAP table, which provides information on the geographical area of use, the methods of application, the treated crop(s), the plant phenological stage (i.e. BBCH) at application, the number and frequency of applications, the application rate and any particular conditions of PPP use. This provides background information for the problem formulation and frames the regulatory question to be addressed. Additionally, the GAP provides information on the relevant exposure scenario for bees (see Figure 2).

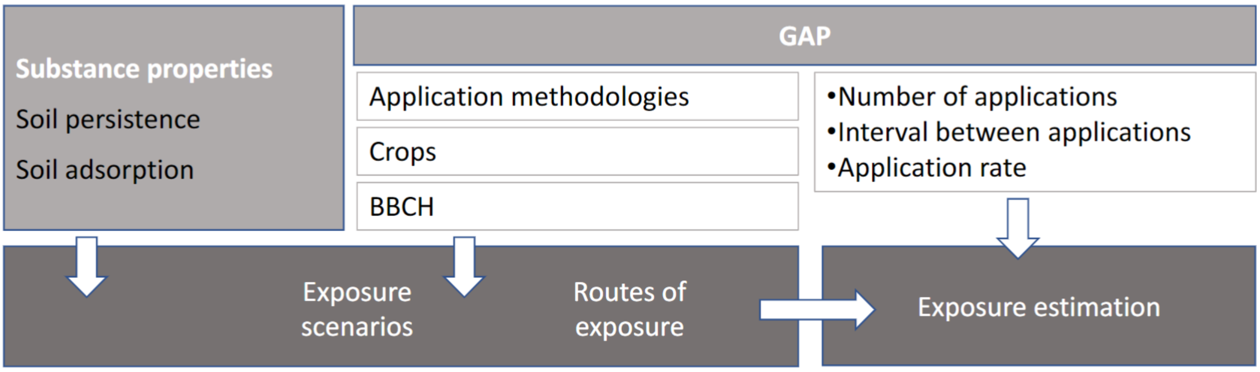

Figure 2: A conceptual diagram of how the GAP, physico-chemical properties and behaviour of the a.s. in the environment influences bee exposure to PPPs (from EFSA et al., 2023)

As mentioned above, the GAP uses, which describe in detail the pesticide application, are central to the problem formulation. The implementation of the GAP in ApisRAM version 3 may be summarised as follows:

- ApisRAM will support the application of PPPs via spray, seed treatment and granule, and may also support less common application methods such as drip irrigation.
- The crop types modelled by ApisRAM are class identifiers created in ALMaSS (the Animal Landscape and Man Simulation System), this being the dynamic landscape simulation model in which the colony is modelled. Therefore, identifiers/grouping in ApisRAM will be linked to specific codes of the European and Mediterranean Plant Protection Organization (EPPO, https://gd.eppo.int/taxonomy), with special attention to the list of attractive crops described in the EFSA guidance (EFSA et al., 2023).
- Crop phenology in ApisRAM relies on metrics simulated in the ALMaSS model such as biomass, leaf area index and flowering as a function of degree-day. However, crop phenology in GAP is normally expressed according to the BBCH scheme[7]. Moreover, the time of pesticide application in GAP is related to specific BBCH stages of the focal crop (and not the degree- or calendar day). Therefore, a model/algorithm needs to be developed linking the degree-day model to the BBCH coding system (see section 5). Such a tool, when available should ideally allow modelling the phenology of individual crops (See 'appendix A' of EFSA et al., 2023 for a list and categorisation of agricultural crops). For development of a tool linking BBCH phenological stages to the degree-day model in ApisRAM, it is advised that existing sources of information on EU crop phenology (e.g., Templ et al., 2018; Huges et al., 2023) are considered.

The ApisRAM formal model (Duan et al., 2022) currently assumes that the fate of a pesticide is determined by the dissipation and transfer rates of the parent compound or metabolites across environmental compartments (i.e., soil, crop, non-crop plant in and off-field, nectar, pollen and in-hive stores). The parameterisation of such a fate scenario might require data which is not necessarily readily available in the context of the regulatory assessment. Therefore, realistic, worst-case assumptions will inform the exposure assessment, which is in conceptual agreement with the EFSA guidance (EFSA et al., 2023) whenever data outside the context of Commission

[7] Julius Kühn-Institut (JKI). 2018. Growth stages of mono- and dicotyledonous plants, BBCH Monograph. DOI: 10.5073/20180906-074619

Regulations (EU) 283/2013[3] and 284/2013[8] are required. More specifically, the processes and routes of exposure of the fate model will be conceptually aligned to the underlying assumptions of the exposure assessment in the EFSA guidance (EFSA et al., 2023).

Environmental scenarios define the characteristics under which the model will be used, and are linked to the specificities of the system (i.e. the organism under evaluation and the environment in which it operates) and to the risk assessment and decisions to be made by end-users, i.e. risk managers and risk assessors, on the way they will have to apply the model, within the EU and at Member State level.

For ApisRAM version 3, the definition of a specific problem formulation is linked to various biological, temporal and spatial dimensions and aspects that the model is using. Some of those dimensions and aspects were already defined during the design of the formal model, as described in section 1 (e.g. the mechanistic principles of the physical/biological characteristics of the various modules composing ApisRAM), while other aspects (e.g. landscape and colony attributes) need to comply with the new risk assessment scheme (EFSA et al., 2023) and the risk assessment needs. The definition of environmental scenarios requires the consideration of those specific model dimensions and aspects as well (e.g. What are the modelled entities? Which spatial and temporal scales are used? What model outcomes are possible?) and is required before the model can be used in the regulatory framework. However, the definition of a specific problem formulation is likely to impact also the definition of the environmental scenario. After the definition of a specific problem formulation and the required input model parameters (which are specific to biological, temporal and spatial dimensions and aspects that the model is using), the environmental scenarios can be defined in detail. The fundamental structure of the environmental scenario definition for ApisRAM is laid out in the following sections.

2.2. Generic and specific problem formulation

2.2.1. Generic problem formulation

The definition of the regulatory question, related to the (specific) protection goal (SPG), has a major influence on scenario setting. Therefore, it is important to define *a priori* some related questions: What are the temporal and spatial dimensions of the ERA to be performed with ApisRAM? What are the questions which the model application aims to answer ultimately? How will the modelling results be used in the risk assessment?

The environmental scenario should be designed to best support the regulatory questions as laid out in the problem formulation. The definition of scenarios for use in a complex model such as ApisRAM is a novel process, noting that there are currently no other examples available within the EU.

Ecological models such as ApisRAM are here being suggested for use as a higher-tier risk assessment tool. In that context, ecological models can support and generalise the interpretation of higher-tier effect studies by e.g., extrapolating the exposure observations to untested scenarios. However, models are always a simplification of reality. Acknowledging this, a

[8] Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L93/85-152, 3.4.2013

modelling study may not face the same constraints of experimental effect studies, such as reliance on a limited number of selected situations for regulatory risk assessment conclusions. Instead, ecological models are ideally used by considering their simplification bias and at the same time exploiting their main advantage: screening larger numbers of environmental scenarios, thereby reducing the uncertainty in the ERA. In that sense, it is generally recommended that environmental scenarios are defined to encompass a diversity of ecologically conditions, ranging from favourable to unfavourable (but still realistic) (Van den Berg et al., under review). In addition, the use of exposure modification factors is suggested. Following these suggestions, the definition of environmental scenarios could include the use of a "risk matrix" (see section 3.4), which combines the variation of ecological quality, defined in a set of baseline scenarios, with exposure modification factors. This approach intends to provide margins of safety when applying pesticides under particular application scenarios in landscapes of varying ecological quality for honey bees.

2.2.2. Specific problem formulation

Relating to the approval of PPPs, Regulation (EC) No 1107/2009[3] stipulates that an a.s., safener or synergist shall be approved only if, under its intended use, "it will result in a negligible exposure of honey bees or has no unacceptable acute or chronic effects on colony survival and development, taking into account effects on honey bee larvae and honey bee behaviour". This is a generic protection goal which was further translated into specific and operational protection goals (EFSA, 2013) from which the "magnitude" dimension was recently reviewed (EFSA et al., 2021) and agreed by Member States (Table 1). The environmental scenario should reflect the spatial and temporal dimensions of the SPGs (EFSA et al., 2023) and is summarised under Table 1.

Table 1: SPGs for honey bees (adapted from EFSA et al., 2023)

Dimension	SPG
Ecological Entities	Colony (queen, drones and workers)
Attribute	Colony strength (the number of adult bees that forms the colony or colony size; operationalized as colony size reduction)[(a)]
Magnitude	≤ 10% (the maximum permitted level of colony size reduction following pesticide exposure)
Temporal scale	Any time (duration of tolerable effects)
Spatial scale	Edge of field (location of colonies in higher field studies)[(b)]

(a): Field effect studies may foresee assessments of brood development which is deemed informative of colony strength

(b): The spatial scale defines the various exposure scenarios from foraging in treated crops, in-field flowering weeds, in succeeding crops, in-field margins and adjacent crops

The implementation of the SPGs is followed by specific exposure/effects assessment goals which provide a basis for the definition of environmental exposure, type, duration and the toxicity endpoints. This will take account of the potential differences in field studies due to the inherent variation in the levels of exposure of colonies placed at the edge of the treated field. Effects should be investigated at an exposure level in line with the exposure assessment goal of the EFSA GD on the risk assessment of pesticides to bees (EFSA et al., 2023). For the oral exposure route, this is the 90th percentile worst-case exposure for the compound under evaluation, considering the spatio-temporal distribution of the exposure concentrations entering a hive .

2.3. Assessment endpoints

ApisRAM version 3 will simulate endpoints which are required under Regulation EC No 1107/2009[3] and EFSA (2023) (Table 2).

Table 2: Description of assessment endpoints that are covered by ApisRAM and their alignment with the regulatory framework

Endpoints #	ApisRAM[9]	Regulation EC 1107/2009[3] and EFSA (2023)
1	Daily colony size, defined as the (disaggregated) number of adult bees (i.e., drones, queen, in-hive adult bees and foragers) and in-hive pre-imaginal stages (i.e., eggs, larvae and pupae assessed from number of capped cells)	Daily colony size, defined as the (combined) number of adult bees (i.e., in-hive adult bees and foragers together) and number of capped brood cells
2	Daily adult and brood mortality, referred to the definition of adult and pre-imaginal stages described above	In tier one, when the driver is the contact exposure, at higher tier, semi-field tests can be conducted to measure foragers' mortality
3	Daily average vitality, for all simulated bees in the colony, used as a health indicator[10]	Not applicable
4	Homing failure (daily number of foragers failing to return to the hive)	Under the sublethal scheme, there are several steps and the homing test is one of them
5	Daily honey stores (in mg)	Not applicable
6	Daily pesticide residues in nectar/pollen of contaminated plants (i.e., crop and non-crops in and off-field) and in food stores (nectar/honey and pollen/beebread in the hive and nectar/pollen entering the hive) (in ng/g)	Standard risk assessment (RA) and "summer bees": maximum daily pesticide residues (for acute) and time weighted average (for chronic) over 10 days (for standard RA) and 27 days (for "summer bees") in nectar/pollen entering the hive (i.e., from the landscape) – the concentration in nectar/pollen of treated crops can be used as a surrogate. for "winter bees": average pesticide concentration over winter in stored honey
7	Ratios of pollen and nectar from the treated crops as a measure of the exposure from the treated field	Ratios of pollen and nectar from the treated crops as a measure of the exposure from the

[9] ApisRAM includes a unique approach to integrate, at the individual level, the effects of the various stressors and their modulators affecting bees (i.e. pesticides, infectious agents, nutrition, and body temperature). This is done by attributing a variable (v_b), which defines a vitality rate, to each bee. This vitality ranges from 0 to 1. A vitality rate of zero will indicate a dead bee whereas a vitality rate of 1 will indicate a bee in optimal health state. This vitality rate is the likelihood of survival and can be used as the bee's health indicator. Another variable (i_b) is used to represent the immune system strength of each bee. The immune system strength can be modulated by infectious agents (e.g. Nosema, DWV, ABPV and SBV which are modelled individually whereas Varroa is modelled as a virus vector). Further, pesticides can modulate model bees' immune system strength.

treated field and an indicator of the landscape factor (LF)

3. SCENARIOS FOR APISRAM

The focus of the ApisRAM model is to inform risk assessors and risk managers for the ERA of PPPs. In addition, it could also inform researchers and field practitioners (e.g. beekeepers and farmers). This could be done by running simulations under various scenarios that are representative of specific situations (in terms of colony health status, management, and environment). In this way, ApisRAM could be used to determine the relative influence of various anthropogenic and environmental stressors and of management decisions on honey bee colony health. For example, based on scenario definitions, specific landscape management (e.g. toxicity of pesticides used, choice of crops and, land homogenization and intensification with increased size of fields/farm) could be simulated to determine their effect on colony dynamics. The same could apply with environmental factors/stressors such as climate, exposure to infectious diseases and pests, or the combination of anthropogenic and environmental stressors. The influence of those stressors could also be simulated at various spatial (local/individual level or landscape level) and temporal (short *versus* long terms) scales and eventually provide insights into the mechanisms behind honey bee colony failure. Those results could inform field practitioners and risk managers on best practices and mitigation measure options.

Baseline and case scenarios need to be established when performing simulations to support the ERA of PPPs. For the purpose of this work, the following definitions of baseline and case scenarios are used:

- **A baseline scenario** provides the baseline conditions in terms of colony status and environmental attributes. For ApisRAM, this means an initially healthy colony (with baseline values for the infestation levels with Varroa, Nosema, DWV, ABPV and SBV, but without clinical signs of disease) in a gradient of ecological quality that spans from most favourable to the most unfavourable conditions for colony development (in terms of floral resource diversity and quality and weather conditions for foraging activity).
- **A case scenario** is a baseline scenario (considering floral resource diversity and quality) with the addition of a pesticide (the a.s. under assessment, for individual intended or representative use conditions).

For the case scenarios for the risk assessment of PPPs, consideration of exposure modification factors is suggested, plus ideally a scenario with a toxic standard (EFSA PPR Panel, 2014).

It is likely that ApisRAM will be used both within and outside the context of pesticide risk assessment; therefore, it is important to clearly distinguish baseline and case scenarios. However, this distinction will be influenced by aspects of problem formulation that drive the specific regulatory question under assessment when ApisRAM is used in the context of the ERA of pesticides. For instance, the representativeness of the specific regulatory question to be addressed at a given geographical location and on a specific cropping system may be primarily informed by the uses under assessment (GAPs). Therefore, the selection of appropriate landscape dimensions for the "baseline" scenario may be inherently linked to the GAPs. These aspects are further discussed below.

3.1. Baseline scenarios

When defining the baseline scenarios, several parameters need to be considered which are related both to the colony itself and the environment, as outlined in section 3.1.1 below. These parameters need to be defined in the context of the provisions and conditions set by the regulatory framework for the RA of PPPs (Regulation EC No 1107/2009[3]) and the revised Guidance for the RA of PPP in bees (EFSA et al., 2023).

In contrast, other aspects of the scenario definition in ApisRAM, such as those related to the landscape and climate, are informed by the ALMaSS dynamic landscape model. This model has a spatial resolution of $1m^2$ with daily updates for landscape characteristics and hourly updates for weather conditions (Topping et al., 2016). Landscapes within ALMaSS are represented by 10x10km areas (also called 'ALMaSS windows'). The various landscape elements within each area are organised in polygons containing field-level information on their vegetation and management at farm level.

The use of ApisRAM relies on available landscape models within ALMaSS with the requisite quality of pollen and nectar data. Current availability across EU is only partial with 10 landscapes for Denmark, Germany, Finland, France, The Netherlands, and Poland available. The French landscapes come from the Rhone-Alpes region, and the German landscapes from Lower Saxony and Brandenburg regions. The other four countries are nationally mapped. These are the countries and regions mapped in sufficient detail to currently generate ALMaSS model landscapes. Thus, in the nearest future, landscapes will need to be selected within these boundaries.

ALMaSS includes information on landscape heterogeneity (fields, fields margins, roads, buildings at farm level), landscape dynamics (associated vegetation growth models for pollen and nectar production with weather conditions) and farm activities (soil cultivation, fertilisers and pesticides) over time, which can be related to weather, crop growth, soil type or previous farming activities. However, the values defined for landscape dynamics (from model parameterisation to calibration, including input variables) might be associated with high uncertainties (e.g. the vegetation growth model can vary greatly among locations and over time). To address these uncertainties, the most sensitive environmental factors could be identified through a sensitivity analysis, for potential inclusion in the baseline scenarios.

The way ALMaSS is used in ApisRAM might need some adjustments (e.g. correspondence between degree day used in ALMaSS for the vegetation growth model and the BBCH used in GAP as already mentioned in section 2.1) to comply with the regulatory requirements for the model to be used for the regulatory RA of PPPs.

3.1.1. Colony attributes

The following colony attributes need to be defined from the start of the simulation, for the definition of a baseline scenario:

i. The location of the colony in the landscape and across geographical locations (relative to the GAP region and at the local and field scales);
ii. The colony size, defined as the disaggregated number of adult bees and in-hive pre-imaginal stages (i.e. eggs, larvae, pupae);
iii. The food stores in the hive;
iv. The within-colony infestation levels of infectious agents (Nosema, Varroa, DWV, ABPV, SBV);
v. The level of pesticide residues in the colony across different matrices (pollen/bee bread and nectar/honey) set at 0.

Many of the above requirements (i-v) are described in the revised EFSA Guidance, in particular on exposure/effect higher field studies (Annex G in EFSA et al., 2023). The reference to (iv) is only described in terms of the requirement for the use of good beekeeping practices. The colony will be placed in the centre of a 10x10 km (ALMaSS) landscape. In line with the SPGs as outlined in the revised EFSA guidance document (EFSA et al., 2023), the colony placement should be at the edge of a treated field.

(ii) and (iii) The colony needs to contain adult bees and brood in all stages (larger in summer than in early spring and fall) with initial stores of food resources. Food stores (honey and pollen) and colony size vary according to:

- Forage area characteristics;
- Season (in line with the GAP uses);
- Region in EU.

Data on population dynamics (distributions) for a honey bee colony are available in the literature and shall be used in ApisRAM to set the initial conditions of the colony demographics (i.e. the numbers of adult bees and brood cells) (Dupont et al., 2021; EFSA et al., 2021; Requier et al., 2016; Hatjina et al., 2014).

(iv) At the start of a simulation, the colony needs to be free of clinical signs of disease, which does not necessarily mean that the colony is free of infectious agents.

(v) The colony should be free of pesticides in food stores (no colony treatment 4 weeks prior testing and good beekeeping practices to be applied).

A reduction in bee vitality/immunity depends on the size and intensity of the stressor(s), such as infectious agents, background pesticide exposure (for ApisRAM version 4), temperature and nutrition (Breda et al., 2022). For example, appropriate food availability will increase and/or help to recover vitality, whereas poor nutrition will contribute to a decreasing vitality. Disease prevalence varies over time and space. Nonetheless, it is acknowledged that the implementation of these interactive processes in ApisRAM may be currently biased towards the availability of data on particular subsets of agrochemical classes (e.g., the widely studied neonicotinoid insecticides, as highlighted by Siviter et al., 2021). The resulting extrapolation of this body of evidence to other chemical classes may create uncertainties which may need to be taken into account while drawing any risk assessment conclusion.

Based on the literature, we can propose the following threshold-levels of infectious agents under which there is no clinical sign of health issue for colonies.

Varroa infestation level:
It was found that Varroa infestation levels above 3% and 7% in the fall (Alaux et al., 2017; Schüler et al., 2023) and winter (Liebig, 2001), respectively, were associated with a significant risk of colony collapse over the winter. We therefore recommend to keep Varroa infestation levels at the colony level below 3% during the fall in the baseline scenarios of ApisRAM simulations.

DWV infestation level:
Colonies that exhibited DWV infestation levels above 1×10^6 copies per bee were diagnosed with clinical sign of health issues by veterinarians or beekeepers (Schurr et al., 2019). Similarly, DWV infestation levels above 1×10^6 copies per bee during the fall was associated with a risk of colony

collapse over the winter (Dainat et al., 2012). Infestation levels below 1 x 10^5 DWV copies per bee should then be used in the baseline scenarios of ApisRAM simulations.
The prevalence of DWV within colonies has also been investigated but it remains difficult to set a threshold-value under which there is no clinical sign of health issue for colonies. Natsopoulou et al. (2017) notably found that DWV-B prevalence was significantly linked to colony decline over the winter (number of bees in the fall *vs*. in next the spring). In colonies exhibiting a population decline above 50% the average DWV-B prevalence reached 33% (Standard Deviation SD = 21%), while in the remaining colonies (population decline below 50%) the DWV-B prevalence was of 14.4% (SD = 16.1%). However, a low prevalence (<20%) could still lead to 70% adult mortality, indicating that it may be difficult to use prevalence alone and that the virus load should also be considered.

<u>ABPV infestation level:</u>
Colonies that exhibited ABPV infestation levels above 1 x 10^5 copies per bee were diagnosed with clinical sign of health issues by veterinarians or beekeepers (Schurr et al., 2019). Infestation levels below 1 x 10^4 DWV copies per bee should then be used in the baseline scenarios of ApisRAM simulations.

<u>SBV infestation at individual level:</u>
A threshold of 10^{10} SBV genome copies per bee was found to be related to an overt disease (Blanchard et al., 2014). However, colonies that exhibited SBV infestation levels above 1 x 10^9 copies per bee were also diagnosed with clinical sign of health issues by veterinarians or beekeepers (Schurr et al., 2019). Infestation levels below 1 x 10^8 SBV copies per bee should then be used in the baseline scenarios of ApisRAM simulations.

<u>*Nosema* infestation level:</u>
By analyzing a 15-year data set comprising data on more than 3000 honey bee colonies in Germany, Schüler et al. (2023) found that less than 10% of colonies were positive to *N. ceranae* in the fall. Although *N. ceranae* infections was significantly correlated with colony losses, determination of the effect size revealed that *N. ceranae* infections was of little or no biological relevance. *N. ceranae* infection only contributed significantly to colony mortality when the colonies did not harbor detectable *V. destructor* mites or very few mites (1-7 per 100 bees) in October (Schüler et al., 2023). Since, it was recommended to keep Varroa infestation levels below 3% during the fall in the baseline scenarios of ApisRAM simulations, colonies should concomitantly not exhibit any *Nosema* infection.

3.1.2. Environmental attributes

The following environmental specificities need to be defined for the baseline scenarios:

i. The location(s) at which the PPP will be assessed (country/state level; number of sites and landscape/field configuration/arrangement at the sites);
ii. The landscape structure, in terms of diversity of crops (both focal and non-focal) and non-crop habitats and field sizes, as given by ApisRAM or alternative landscape data;
iii. The weather, which could be implemented in ALMaSS by using historical or predicted data. Mean hourly (local/regional) weather data conditions (temperature, humidity and solar radiation for foraging window) would be used to be representative of the three EU regulatory zones where the PPP will be tested and simulated within the ALMaSS landscapes;
iv. An inventory of production of nectar, sugar from nectar, and pollen per plant species (see Filipiak et al., 2022);

v. All parameters, input variables and assumptions that are specific for the considered location within ALMaSS (e.g. vegetation models, phenology of crops and non-crop landscape elements, etc.) as described in EFSA (2016).

For the location of the assessment, a baseline scenario has to be defined for each of the 3 EU regulatory zones (to be in line with Regulation (EC) No 1107/2009[3]). The selection of a location should be informed by the regulatory question to be addressed, which is framed by the uses under assessment (i.e., the GAP table). The GAP specifies the area of use of the PPP under assessment (i.e., with a level of granularity corresponding to the regulatory zone or member state level). Therefore, the area of assessment should be an adequate representation of the use conditions represented by the GAP. Note however that the landscape availability by ALMaSS may currently limit full coverage across EU regulatory zones and Member States. Nevertheless, once full EU coverage has been achieved, the area of assessment should be representative of the geographical distribution of the crop under assessment within the area of use established in the GAP. Additionally, a sufficient number of locations should be selected so that heterogeneity is adequately represented (see further description in section 3.4), including worst-case landscape configurations (e.g., area of intense cultivation in the EU, where monoculture might be a reality).

Across geographical areas, real and representative landscapes are selected across the 10x10 km 'ALMaSS windows'. Landscapes should be selected at various locations in the EU, representing the 3 regulatory zones (or, where relevant, across the regulatory zones indicated in the GAP). Those landscapes should represent the heterogeneity in ecological quality. Landscape classes should then be identified according to a gradient of ecological quality. We suggest to define ecological quality of a landscape for honey bees in categories of floral resources diversity and quality (more details in the next section 3.1.3.). The range of (baseline) scenarios should cover conditions going from the most favourable to the most unfavourable for colony development in terms of resources over time and space.

For the regulatory use of ApisRAM, a representative EU coverage of ALMaSS landscapes is critical. In the short-term, it is proposed to select scenarios for three EU countries (i.e. Denmark, Germany and Poland) where ALMaSS landscape data are readily available and reliable (i.e. 10 ALMaSS landscapes of 10x10 km are made available per each of those countries, and there is sufficient data to define and test pollen/nectar production over time in ALMaSS). In the medium-term (i.e. by 2025), additional landscapes will be made available for Finland, Netherlands and France (restricted to one region representing the Central EU zone and gathering data from mostly arable crops).

3.1.3. The concept of ecological quality for scenarios

The concept of ecological quality for the setup of environmental scenarios for ApisRAM is based on the typical "ALMaSS windows" (10x10 km), describing the landscape that ApisRAM represents. Heterogeneity in ecological quality is intended to represent the possible range of landscapes across the EU.

Ecological quality of landscapes for baseline scenarios in ApisRAM is related to floral resources, specifically those species visited by honey bees, in light of their critical importance for patterns of exposure and colony health. Such a classification is reliant on landscape data, more specifically on habitat mapping and floral compositions (see landscape data availability in section 3.1). In particular, the baseline scenarios are suggested to be selected to represent various levels of floral resource diversity and quality, as defined by two metrics: (1) Floral resource quality (FQ) is determined by the levels of resources (pollen and sugar sources from nectar) provided for honey bees; (2) Floral resource diversity (FD) is determined by the diversity of floral plant species from the crops (both focal and non-focal) and non-crop habitats that can be used by honey bees in a landscape. The aim of using these two categories for the definition of the ecological quality is to consider the overall potential of pollen and nectar provision (FQ) and the diversity of these resources (FD), which can serve as a proxy for stability of floral resources over time. Under such a paradigm, it is assumed that floral resource diversity and quality are each relevant to the timeframe and locations of the modelling simulation. Within these spatio-temporal boundaries, a high diversity of floral resources decreases the probability of having gaps in floral resources, that might occur in a monotonous landscape consisting only of one or two floral resources and can negatively affect honey bee colony growth (Dolezal et al., 2019). Previous work has shown that the viability of the colony depends on the availability of food over time (pollen and nectar) (Horn et al., 2021). A high diversity of the resources increases the likelihood of availability of nectar and pollen over time for colony growth.

The emphasis on overall quality and diversity of floral resources in the suggested scenario definition does not comprehensively capture all environment factors that could impact ecological quality for honey bees. For example, spatial configuration of landscapes can have important effects on bees and colony health. Previous work has shown that increased edge density within landscapes can benefit pollinators (Martin et al. 2019) and that highly patchy landscapes result in larger foraging ranges in honey bees going predominantly beyond 6 km away from the hives (Beekman and Ratnieks, 2000). Using the BEESCOUT/BEEHAVE models, it was found that areal proportion, spatial distribution, and the quality of the flower strips (i.e. availability of nectar and pollen as determined by plant-species composition) all have significant effects on the size of honey bee colonies in agricultural landscapes. However, interactions were identified, and flower strips of high quality were of benefit to honey bee colonies, whereas those of low quality were not (Baden-Böm et al., 2022). These findings demonstrate that honey bee foraging behaviour and range depend heavily on the surrounding landscape (number and quality of floral resources) and reflect the complex interactions between floral quality, foraging behaviour, and spatial configuration within the landscape. While the typical size of an ALMaSS windows (10X10 km) covers the typical foraging range of honey bees and the factors emphasized here (FQ and FD) are likely to capture important axes of ecological quality, other aspects (e.g, spatial configuration and weather) could have important effects, and may be especially important for particular regions or risk assessment applications using the ApisRAM model. The definition of environmental baseline scenarios needs to be informed by regional agricultural landscapes and practices, to ensure that the simulation is representative of the intended uses (GAP) in terms of geographic location and relative presence of crops in the landscape.

Within the ALMaSS landscapes with the most reliable data (i.e. Denmark, Germany and Poland), scenarios need to be checked on a case-by-case to ensure they are realistic.

Floral resource diversity and quality consider all possible floral resources in a landscape, i.e. the crop under assessment (focal crop), the non-focal crops and non-crop elements that can provide pollen and/or nectar. The primary use of these scenarios is thought to be for a single compound, single use risk assessment, but the approach developed here could be easily adaptable to also evaluate multiple crop types within agricultural areas, or the effects of particular exposure scenarios within these crop types.

3.1.3.1. Definition and levels of floral resource diversity for environmental baseline scenarios

The diversity of floral resources in space and time will have important effects on the foraging behaviour of bees and thus emergent patterns of exposure and colony health. Floral resource diversity is suggested to be quantified based on the Shannon diversity index denoted as:

$$FD = - \Sigma p_i * ln(p_i)$$ [11]

where p_i quantifies the proportion of a single floral species i in the entire community and noted as "FD". For example, the proportion of a single floral species, p_i, could be quantified based on the area that this species covers in a given ALMaSS window. The temporal dimension of floral diversity is omitted here, as it does not currently seem possible to expect time series of floral diversity or a complete record of the phenology of all plant species. The implicit assumption here is that the higher the diversity, the greater the chance of a continuous supply of nectar and pollen resources.

For the definition of environmental baseline scenarios, it is suggested to select landscapes (ALMaSS windows) with three levels of floral resource diversity: low, medium, and high floral resource diversity. The selection could be done by quantifying the diversity of resources within the target region, e.g. a larger region within a country, or a whole country, to quantify the respective Shannon diversity, and then to select from the resulting distribution ALMaSS windows containing landscapes with "low" floral resource diversity equivalent to the 5th percentile, "medium" to the 50th percentile, and "high" to the 95th percentile of floral resource diversity within the target region.

3.1.3.2. Definition and levels of floral resource quality for environmental baseline scenarios

Currently, in ApisRAM/ALMaSS landscape definition files, information on habitat mapping and floral composition are available. Additional information on the volume of nectar, the quantity of sugar in the nectar of crops (which is a proxy of nectar quality) and the quantity of pollen produced by the crops is required. This information could come from simulations with the ApisRAM resource model, and probably as well from additional data sources. Data on pollen quality of the crops (i.e. protein and lipid contents in pollen) is currently not available, but more data could be made available under various (past and ongoing) EU research projects (e.g. BiodivERrsA, PoshBee, B-Better, INSIGNIA, etc.)[12].

In the definition of the environmental baseline scenario, we refer to floral resource quality mainly in the sense of the quantity of nectar and pollen provision and sugar content in nectar.

Crop and non-crop habitats can vary significantly in quantity of resources for honey bees, with subsequent impacts on both foraging behaviour and colony nutrition. For each habitat type, the floral resource quality (FQ) is expressed as cumulative available sugar (from nectar) and pollen mass, in units of mg per square meter ($\frac{mg}{m^2}$). We suggest balancing the importance of nectar and pollen into a single metric of floral resource quantity per species i, while accounting for the differential mass of sugar (from nectar) and pollen consumed by *Apis mellifera* colonies:

$$FQ_i = Q_{sugar} + k*Q_{pollen}$$

The mass of pollen is here suggested to be scaled by a factor k that represents the ratio of the total amount of sugar (from nectar/honey) over the total amount of pollen required by

[11] The higher the value of FD, the higher the diversity of species in a particular community. The lower the value of FD, the lower the diversity. A value of FD = 0 indicates the whole landscape is covered by a single species.
12 https://www.biodiversa.eu/, https://poshbee.eu/, https://www.better-b.eu/, https://www.insignia-bee.eu/

honeybees over time (it could be averaged at the colony level over a season or at the individual level over a single day).

For example, for a flower species producing 100 mg of sugar and 8 mg pollen per m^2:

$FQ = 100 + k \cdot 8.$

If honey bees are not known to collect either nectar or pollen from a particular flower species, these resources are not considered for floral quality calculations.

This value can be used to quantify the potential resources available for honey bees in a landscape, calculated as cumulative value per area, by summing up the potential provision of pollen and sugar from nectar for each flowering plant species (FQ_i), weighted by the respective area:

$$FQ = \frac{1}{A}\sum_{i=1}^{n} FQ_i \cdot A_{FR,i}$$

with *n* as overall number of flowering plant species in the landscape, $A_{FR,i}$ represents the area covered by flowering species *i*, and *A* is the total area of the landscape. FQ thus represents a total estimate of floral resource quantity per unit area across all flowering species within a certain landscape window, accounting for the relative production of nectar/sugar and pollen, as well as the relative coverage of each flowering plant species within the landscape. FQ does not include a temporal dimension, but it provides an estimate of the potential for pollen and nectar/sugar production based on average values.

As in 3.1.3.1, for environmental baseline scenarios, three levels will be defined: low, medium, and high floral resource quality. These levels will be defined by quantifying the floral resource quality in a representative sample within the target region, e.g. a larger region within a country, or a whole country, and then to select from the resulting distribution landscapes with "low" floral resource quality equivalent to the 5th percentile, "medium" to the 50th percentile, and "high" to the 95th percentile of floral resource quality for all habitat types (focal and non-focal crops and non-crops) within the target region.

3.1.3.3. Definition of baseline scenarios as combinations of floral resource diversity and quality

When conducting the risk assessment for PPPs, a set of baseline scenarios along a gradient of ecological quality will be defined by combining the classes of floral resource diversity and quality for the selected geographical location of use in a factorial design (Figure 3). The following scheme (see Figure 3) shows the factorial composition of quality classes concerning floral resource diversity and quality, when the corresponding low, medium, and high values are representative of the respective 5th, 50th, and 95th percentiles within the target region:

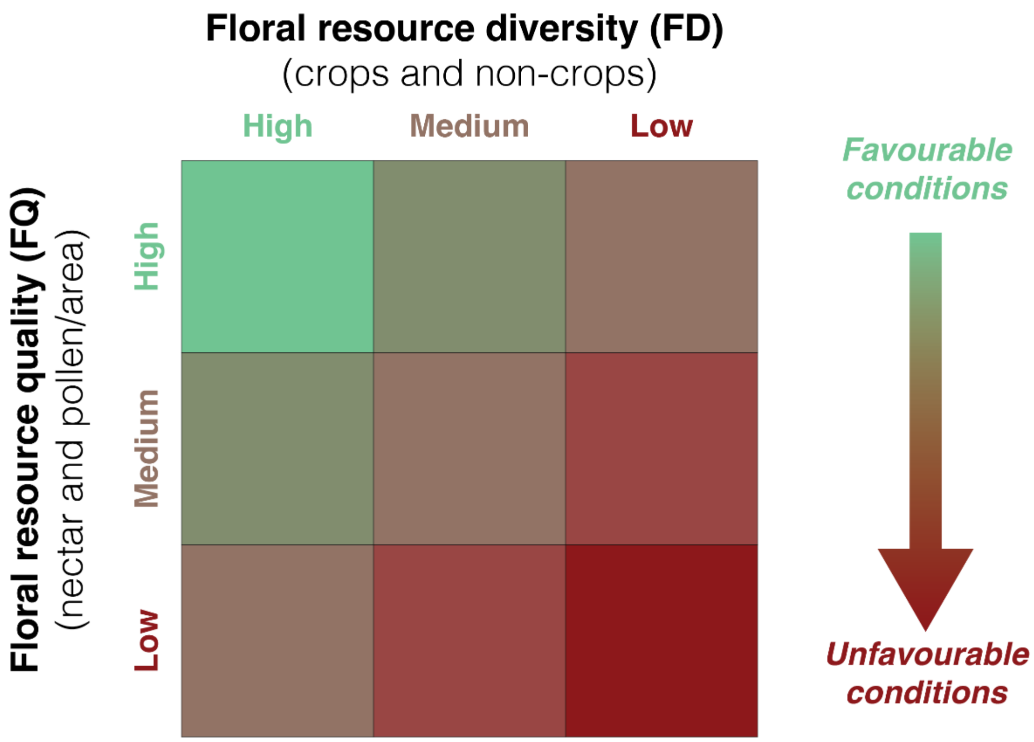

Figure 3: Figure 3. Overview of the 9 baseline scenarios along a gradient going from the most favourable to the most unfavourable conditions (i.e. in terms of floral resource diversity and quality)

The definition of these scenarios is thought to be based on realistic geodata, hence landscape conditions that should allow a honey bee population to survive and grow. Nevertheless, it is expected that honey bee colonies will perform differently in landscapes of different floral resource diversity and quality, so that the baselines scenarios will provide a gradient of ecological quality.

The following steps are proposed to operationalise this approach:

- Available ALMaSS/ApisRAM landscape definition files, including information on habitat mapping and floral compositions, from a target region, e.g. a larger region within a country, or a whole country, will be analysed concerning the floral resource diversity and quantity. From the resulting distributions of ALMaSS/ApisRAM landscapes in the two-dimensional space spanned by axes of floral resource diversity and qualities, landscapes according to the 5^{th}, 50^{th} and 95^{th} percentiles in each of the categories will be selected, corresponding to low, medium and high proportions of floral resource diversity and quality. This approach will result in 9 baseline scenarios which consist each of an ALMaSS/ApisRAM window (of 10x10 km size).
- During the subsequent risk assessments, ApisRAM simulations are performed for the selected ALMaSS windows, thereby creating model output for each of the baseline scenarios (from BS1 through to BS9).
- In order to address the variability in exposure conditions due to landscape configurational heterogeneity, we suggest conducting multiple simulations in which the positioning of the colonies in the landscapes (but always at the edge of the field/treated crop) is varied. Consideration of foraging range will be important when considering colony location.

3.2. Case scenarios

The case scenarios correspond to the conditions set for the testing of specific PPPs/use. The case scenarios correspond to the baseline scenarios as defined in section 3.1, and describe how the tested pesticide is applied. Therefore, the treated crop and pesticide use would be defined as follow:

i. For the selection of the crops, the crop in the GAP should be used. Each use and, therefore, all crops in the GAP should be addressed individually. It is important that the critical GAP (e.g., highest dose and minimum application interval on the most attractive crop resulting in the highest predicted residue/theoretical intake) is covered. Depending on the assumption within ApisRAM about crop attractiveness, it may be reasonable for regulatory risk assessment purposes to select a surrogate, worst-case crop to be treated according to the critical GAP. Crop rotation may be implemented if regionally realistic.
ii. For the pesticide to be tested, the type of application(s) per year (for spray, granule, seed treatment) at given time(s) related to the representative use at each zone are described in the GAP (the accompanying exposure and toxicity information should be substance specific or realistic worst-case). There is no background pesticides contamination.

In agreement with section 2.2.1, the definition of the regulatory question, related to the (specific) protection goal (SPG), has a major influence on scenario settings when scenarios are being developed for the purpose of assessing the environmental risk of pesticide uses. The problem formulation for the 'case scenario' - hence, the specific regulatory question to be addressed - is directly informed by the uses under assessment. Such uses, which are defined in the GAP, are regionally and temporally specific and defined by a unique combination of application regimes, crops and their phenology. The assessment of such uses may follow a risk matrix approach, whereby use conditions resulting in worst-case risk situations may cover more favourable risk scenarios.

In terms of the pesticide application regime defined in the GAP, the definition of a worst-case risk scenario is a result of the following aspects:

- the intrinsic characteristics of the treated crop, such as those related to the attractiveness of the treated crop under assessment;
- the pesticide application pattern, which is defined by the application method, the dose per hectare, the number and interval of the applications and the crop;
- the characteristics of the non-crop plants in and off-field which may be contaminated;
- the phenology of the plants which may be contaminated by the pesticide application;
- special conditions of use;

Exposure in realistic scenarios is a result of the complex interaction of biotic, abiotic, ecological and landscape-specific aspects. Therefore, the range of use conditions within a given GAP use may, in reality, result in a range of risk situations. To account for such unexplained or unmeasurable variability, and to determine the margin of safety of a GAP it is proposed to use Exposure Modification Factors (EMFs) in the risk assessment.

3.3. Exposure modification factors

Exposure modification factors seek to determine "margins of safety", i.e., the determination of the distance of a GAP in a specific landscape from having non-negligible effects. As with the use of safety factors in other contexts of the environmental risk assessment, EMFs have been used in the context of TK/TD models to quantify margins of safety for a GAP and hence they have helped providing greater confidence in the outcome of the risk assessment. In the same application, EMFs have also been used to provide insights into the sensitivity of the system to detect effects. Exposure modification factors are practically implemented by applying increasing multiplication factors to the application rates (or mass of a.s. in, e.g., seed coating). It should be noted that the use of EMFs in the context of the regulatory use of complex effect models such as ApisRAM has not yet been explored. Therefore, the WG acknowledged their potential usefulness, while noting that the sheer scale of potentially influential parameters in ApisRAM may make their use interpretation more challenging than for simpler mechanistic effect models (e.g., TK/TD).

3.4. Definition of the risk matrix

For a comprehensive ERA, a risk matrix could be defined by the combination of the baseline scenarios (representing a gradient in ecological quality, with different combinations of floral resource diversity and quality) and case scenarios with increasing EMFs in a factorial design. To aid interpretation, the 9 baseline scenarios as outlined previously could be grouped, from most favourable to least favourable, potentially as follows:

- Scenario group 1 *(most favourable)*, including the following baseline scenarios:
  - High FD + High FQ
  - Medium FD + High FQ
  - High FD + Medium FQ
- Scenario group 2 *(moderately favourable)*
  - Low FD + High FQ
  - High FD + Low FQ
  - Medium FD + Medium FQ
  - Low FD + Medium FQ
  - Medium FD + Low FQ
- Scenario group 3 *(least favourable, which could be considered as a realistic worst-case)*
  - Low FD + Low FQ

Modelling endpoints relevant to regulatory decision-making could be generated and provided in a form of a lookup table, where for example the rows could represent variations in ecological quality as defined by the scenario groups (most favourable, moderately favourable, least favourable), and the columns represent case scenarios with increasing EMFs. The simulations using the case scenario without exposure modification, i.e. the original GAP, are labelled as EMF1 (Figure 4).

If the results were generated and presented in this manner (see Figure 4), it would be possible to identify margins of safety in landscapes of different ecological qualities. For applications in landscapes of low ecological quality (least favourable scenario group), as for example in intensively cultivated areas, the hypothesis would be that the margin of safety is lower compared to applications in landscapes of higher heterogeneity. In that sense, these landscapes would provide a realistic worst-case scenario. By systematic variation of EMFs per scenario group, it would also be possible to determine at which EMF the transitions, from no to small transient, and from large transient to large irreversible impacts, could occur per landscape.

Accordingly, the simulation results provided by ApisRAM could inform risk assessment decisions, and in addition could provide useful management information.

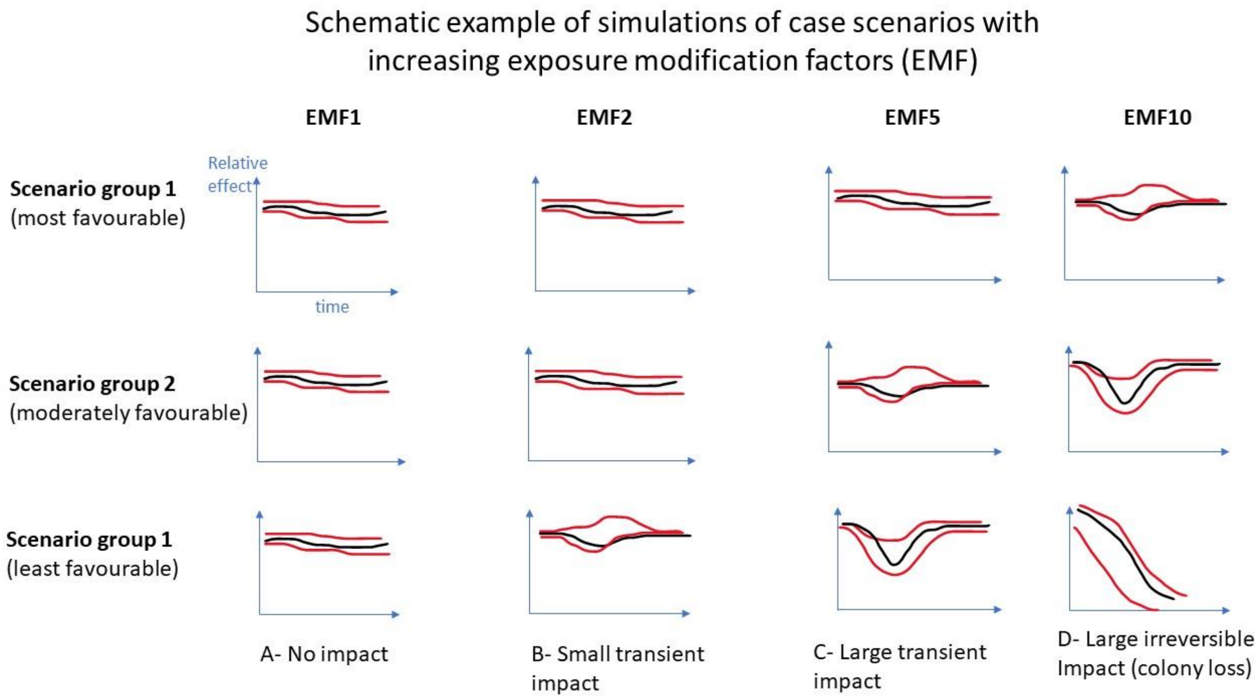

Figure 4: A risk matrix in support of a comprehensive ERA. The matrix presents simulations from case scenarios with different exposure modification factors (EMFs) according to the gradient of ecological quality (combinations of floral resource diversity and quality) as defined in the most favourable, moderately favourable and least favourable scenario groups.

4. CONCLUSIONS

The baseline scenarios were defined based on ecological quality. This classification is reliant on landscape data, more specifically on habitat mapping and floral compositions. Data compiled within ALMaSS/ApisRAM landscapes could be used when defining these scenarios, however, the number of ALMaSS-compiled landscapes is currently limited. In the short-term, this represents a limitation of the application of the proposed baseline scenarios. As an alternative, the processing of appropriate data in any other suitable way could be an option for consideration during scenario definition.

The environmental scenarios described in this report are to be used in ApisRAM to support ERA and higher tier effect studies (by describing specific sets of experiments) and to test different environmental conditions and risk mitigation measures.

The identified scenarios and the approach taken to define them were shared with the contractor developing the model ApisRAM (Aarhus University), and with other EFSA experts (i.e. Panels of the Scientific Committee, on Plant Protection Products and their Residues and on Plant Health) and representatives of EU Member States (i.e. Standing Committee on Plants, Animals, Food and Feed) who would be the end-users of the model. This process was followed to ensure that the scenarios are relevant and, in a regulatory context, also fit for purpose.

The proposed environmental scenarios are originally designed for ApisRAM, a honey bee colony effect model. However, these scenarios could be applied to other species effect models by adjusting the concept of ecological quality to the requirements of the relevant species (i.e. different species may have different resource preference leading to different ranking of a landscape in term of ecological quality).

The proposed risk matrix approach allows the margin of safety to be estimated in landscapes of differing ecological quality for honey bees, thereby providing information to support differentiated ERA decisions.

The proposed environmental scenarios represent ecological quality based on two dimensions: floral resource diversity and floral resource quality. This is a simplification whereas for example spatial configuration (other than spatial dimension) is a third dimension that was not considered in this report because of its complexity for scenario definition. However, landscape configuration and as well temporal dynamics, which could not be considered for the definition of the scenarios are considered and integral parts of the final ApisRAM simulations that are performed for risk assessment.

One important aspect which may not be directly addressed by the 'ecological quality' paradigm is how crop diversity alone may influence exposure of a bee colony in the ApisRAM simulation. The assessment of what is a realistic proportion of a focal crop relative to other crops in a landscape may require case-specific consideration of agronomic practices at the local scale. To ensure that risk assessment conclusions can be extrapolated to worst-case use conditions (e.g., monoculture), it may be particularly important to justify whether the presence of the focal treated crop relative to other untreated crops may be representative of realistic use conditions.

As clarified in the terms of reference, ApisRAM version 3 was designed for a specific purpose which is to test applications of single chemical pesticide a.s. applied according to the representative use in one crop of the simulated landscape. Those applications include spray, seed treatment and granules, and drip irrigation.

The gradient of environmental quality provides insights into those processes - other than application rate - that may influence honey bee colony health. It can be regarded as an implicit way to account for the uncertainty of model parameters of a complex model like ApisRAM, and, in that sense, the variation of ecological qualities across the baseline scenarios aims to implicitly cover parameter uncertainty.

5. RECOMMENDATIONS

For the baseline scenarios to be applied in a broader context and be more representative of the diversity of EU landscapes, the number of ALMaSS-compiled landscapes will need to be increased. This will require resources but also improved access to landscape data.

Before these scenarios can be used to support ERA and higher tier effect studies, they need to be tested when ApisRAM is fully developed, calibrated and evaluated for its use in the regulatory risk assessment of pesticides. An area that needs further exploration before the case scenarios can be implemented in ApisRAM is the linkage between the degree days used in ALMaSS phenological model and the BBCH scale used to quantify crop phenology in the GAP.

When the scenarios are formally tested with the implemented ApisRAM model, a new series of communications and consultations with end-users would be needed.

The approach used to define environmental scenarios for honey bee colonies could form a good basis for further development on other organisms such as non-target arthropods, in particular for the new EFSA project on the collection, generation and analysis of data to develop environmental scenarios for the advancement of the environmental risk assessment (ERA) of plant protection products (PPP) under Regulation No 1107/2009[3] (OC/EFSA/PREV/2023/02)

As conceptualised by the MUST-B WG, the risk matrix approach detailed in section 3.4 would allow accounting for key aspects of environmental quality conditions when exploring from least- to most favourable conditions of the pesticide use risk characterisation. Therefore, by using the risk matrix, in the case scenarios, in combination with EMFs, it would be possible to effectively characterise the margin of safety of the assessment for each environmental quality level. Consistent with existing regulatory approaches (e.g., EFSA PPR Panel, 2018), this could be practically done by estimating the multiplication factor to be applied to each case scenario in order to reach a certain level of colony-level effect (i.e., as outlined in the SPGs in Table 1).

However, one important step for the application and use of these scenarios will be conducting preliminary testing of the model to explore the potential influence of environmental and landscape factors beyond what was conceptualised in this report. These tests may be tailored to further exploring the spatial effects of hive placement within the landscape on colony growth and health. If such preliminary testing demonstrates important effects of hive placement and/or spatial configuration of non-crop habitat (e.g., edge density), some additional environmental scenarios based on configuration could be defined (including a range of hive placement and/or spatial configurations) and added to the ones presented in this report.

It is advised that end-user pay particular attention ensuring that the relative presence of the focal crop in the simulated landscape is a realistic worst-case. This would allow ensuring that key aspects such as the influence on the exposure of predominant, contaminated mass flowering crops are not overlooked. Therefore, no single recommendation across the geographical area of the EU assessment may be possible.

Other types of pesticides (e.g. micro-organism pesticides), pesticide mixtures and naturally occurring compounds produced by plants or other contaminants could be considered for implementation in the model at a later stage, when data and guidance on their risk assessment are made available.

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Glossary and abbreviations

Glossary on the definitions of (environmental, baseline) scenarios

Scenarios are representations of possible futures for one or more components of a system, particularly, in this assessment, for drivers of change in nature and nature's benefits, including alternative policy or management options (IPBES, 2019). An environmental scenario is defined with a combination of abiotic, biotic and agronomic parameters of the environmental context in which the model is run.

A baseline scenario (also known as 'reference' or 'benchmark' or 'non-intervention' scenarios) depict a future state of society and/or environment in which no new environmental policies are implemented apart from those already in the pipeline today; or in which these policies do not have a discernable influence regarding the questions being analysed (EEA, https://www.eea.europa.eu/help/glossary/eea-glossary/baseline-scenario). It provides the baseline conditions in terms of colony status and environmental attributes. For ApisRAM, this means an initially healthy colony (with baseline values for the presence of Varroa, Nosema, DWV, ABPV and SBV, but without clinical signs of disease) in a gradient of ecological quality that spans from most to least favourable conditions for colony development (in terms of floral resource diversity and quality for foraging activity).

A case scenario is a baseline scenario with the addition of a pesticide (the a.s. under assessment for a set of intended or representative use conditions).

Abbreviation:

ABPV	Acute Bee Paralysis Virus
ALMaSS	Animal Landscape and Man Simulation System
a.s.	Active substance
BBCH	Biologische Bundesanstalt, Bundessortenamt and CHemical industry
B-GOOD	Giving beekeeping guidance by computational-assisted decision making
BMP	Beekeeping Management Practices
BS	Baseline scenario
DWV (DWV-A or DWV-B)	Deformed Wing Virus (strain A or B)
EC	European Commission
EKE	expert knowledge elicitation
EPPO	European and Mediterranean Plant Protection Organization
EU	European Union
EFSA	European Food Safety Authority
ERA	Environmental risk assessment
EMF	Exposure modification factor
FAO	Food and Agriculture Organization
FD	Floral resource diversity
FQ	Floral resources quality
GAP	Good Agricultural Practices
MUSTB	EU efforts towards the development of a holistic and integrated approach for the environmental risk assessment of multiple stressors in bees
PPP	Plant protection products
PPR	Plant protection residues
RA	Risk assessment
SBV	Sacbrood virus
SC	Scientific committee
SD	Standard deviation

SPG	Specific protection goal
TOR	Terms of reference
WG	Working Group