Workshop on the development of a fit-for-purpose approach for assessing the risk of low-concern active substances

Vryzas Zisis[1], Arts Gertie H.P.[3], Dalakouras Athanasios[6], Fragkoulis Georgios[1], Guijarro Belén[5], Karazafeiris Emmanouil[1], Karpouzas Dimitrios[2], Menkissoglu-Spiroudi Urania[1], Papadakis Emmanouil Nikolaos[1], Papadopoulou Kalliope K.[2], Patino-Ropero María José[5], Polst Bastian[3], Alonso-Prados José Luis[5], Steenbergh Anne[4], Tsaloumi Sofia[2], Tsampoula Aggeliki[1]

[1]Aristotle University of Thessaloniki

[2]University of Thessaly

[3]Wageningen Environmental Research

[4]Dutch board for the Authorisation of Plant Protection Products and Biocides

[5]National Centre National Institute for Agricultural and Food Research and Technology

[6]Hellenic Agricultural Organization – Demeter

Abstract

The workshop, co-organised by EFSA and the consortium of the project on 15-16 January 2025 in Thessaloniki, was part of the project titled "Develop a stepwise approach for a fit-for-purpose risk assessment, particularly for low-concern active substances and uses". The main objectives of the workshop were to: i) Gather feedback from Member States (MS) on the current risk assessment of low concern active substances (LCASs); ii) Introduce the use of problem formulation in risk assessment for LCASs and present the proposed approach developed by the consortium in collaboration with EFSA; iii) Present the application of the Pathways to Breach the Protection Goals (PBPG) approach to LCASs; and iv) Facilitate discussions and acquire feedback through parallel Breakout Groups (BGs). The event included three discussion sessions: Session 1 focused on identifying gaps in current practices, considering participants' expertise and perspectives; Session 2 addressed specific questions regarding the particularities of LCASs and their respective PBPGs; Session 3 involved a follow-up from Session 2, with general questions and recommendations to address the gaps identified in Sessions 1 and 2. Participants were

divided into four BGs based on their expertise and engaged in discussions on the following topics: BG 1: Fate and exposure aspects; BG 2: Ecotoxicology aspects; BG 3: Fit-for-purpose risk assessment methodology; BG 4: Fit-for-purpose risk assessment/risk management. A plenary at the end of Day 1 summarised the outcomes of Session 1. The plenary at the end of Day 2 provided an opportunity for group chairs to present the key findings from their breakout group discussions (Sessions 2 and 3), including identified gaps and suggestions for improvements. This report provides a detailed summary of the outcomes from the breakout discussions, which will be considered to finalise the proposed scheme for a fit-for-purpose risk assessment of LCASs to be presented in the final report of the project.

Keywords: (problem formulation, pathways to breach the protection goals, low concern pesticides, fit-for-purpose risk assessment, waiver criteria, data requirements, qualitative risk assessment)

Correspondence: any enquiries related to this output should be addressed to plants@efsa.europa.eu

Acknowledgements: We kindly acknowledge all the parties involved in the project for their help and interesting discussions. In particular, we thank Aude Kienzler, Rachel Sharp, Domenica Auteri, Christopher Lythgo, Roberto Lava, Franco Ferilli and Marco Binaglia from EFSA for the valuable discussions, meetings, input and feedback.

Suggested citation: Vryzas Z, Arts GHP, Dalakouras A, Fragkoulis G, Guijarro B, Karazafeiris E, Karpouzas D.G, Menkissoglu-Spiroudi U, Papadakis EN, Papadopoulou K, Patino-Ropero MJ, Polst B, Alonso-Prados J-L, Steenbergh A, Tsaloumi S, Tsampoula A, 2025. Fit-for-purpose and innovative risk assessment for low-concern pesticide active substances and uses.

Table of contents

1 Introduction

Project background information

Six partner institutions, encompassing regulatory agencies, academic centres, and research institutes with expertise in pesticide risk assessment, environmental fate, ecotoxicology, and specialized knowledge of low-risk/low-concern substances are leading the project in response to **EFSA's call (GP/EFSA/PLANTS/2023/04)**. This call seeks a stepwise, science-based approach to assess pesticide "low concern active substances" (LCASs) in a manner more flexible than the frameworks commonly used for conventional synthetic pesticides.

The **consortium** includes:
1. Aristotle University of Thessaloniki (AUTH, Greece) – Project coordinator
2. University of Thessaly (UTH, Greece)
3. Wageningen Environmental Research (WR, The Netherlands)
4. Dutch Board for the Authorisation of Plant Protection Products and Biocides (Ctgb, The Netherlands)
5. National Centre, National Institute for Agricultural and Food Research and Technology (CSIC-INIA, Spain)
6. Hellenic Agricultural Organization – Demeter (ELGO, Greece)

Conventional risk-assessment methods and data requirements, as set out in Part A of Regulation (EU) No 283/2013, generally target synthetic chemical pesticides with clearly defined toxic modes of action. However, many low-concern active substances, such as semiochemicals, botanicals, microbial metabolites, peptides, dsRNAs, and certain inorganics, exhibit properties that may not align with traditional "toxic mode of action" testing, particularly when hazard or exposure is inherently low. Thus, there is a need to develop appropriate risk-assessment strategies for low concern substances that remain rigorous, ensuring safety standards are maintained, while simultaneously reducing unnecessary data demands and accelerating the approval process for substances with lower environmental and health risks.
To accomplish this, a structured "**problem formulation**" approach is proposed which systematically examines how harm could occur, identifying only the data and most appropriate tests needed by mapping out relevant hazards, potential exposure routes, and resulting risks to assess if the protection goals are met. This targeted process brings flexibility, focusing the assessment on relevant risks, plus efficiency and transparency by clarifying when data can be waived, and precising which evidence is required to support waiver criteria. "**Pathways to Breach the Protection Goals**" (PBPGs) guide the process by listing the step-by-step events which must all take place in order for effects to be severe enough to breach the protection goal. This means that if any of the events in the pathway can be demonstrated not to take place, the protection goal is not breached and thus a low risk can be concluded. In general, this situation will occur if there is an absence of a specific hazard or of exposure. In cases where neither hazard or exposure is absent, the approach aims to assess the likelihood of breaching the protection goals. This fit-for-purpose risk assessment strategy of LCASs, helps safeguard public health and the environment, and supports the introduction of more sustainable pesticide technologies under EU regulation.

Introduction to the workshop

In January 2025, EFSA and the project consortium co-organised a two-day workshop in Thessaloniki. This workshop is part of the project entitled "Develop a stepwise approach for a fit-for-purpose risk assessment, particularly for low-concern active substances and uses". The workshop was attended by total 53 participants from different stakeholders. The workshop aimed

to advance the development of an innovative risk assessment framework tailored specifically for Low Concern Active Substances (LCASs).

The workshop was designed with four main objectives in mind:

- To gather critical feedback from Member States on existing risk assessment methodologies applied to LCASs, highlighting gaps and challenges in current practices.
- To introduce the application of problem formulation in the risk assessment of LCASs and present a proposed approach developed by the consortium.
- To showcase the use of the Pathways to Breach the Protection Goals (PBPG) framework in the context of LCASs, illustrating its potential for streamlining decision-making processes.
- To facilitate discussions through structured breakout sessions, enabling experts to exchange views on fate and exposure, ecotoxicology, risk assessment methodologies, and risk management strategies.

A background document was provided to workshop participants that that describes the fundamentals and the application of problem-formulation approach via PBPGs for LCAs. The agenda was structured over two intensive days (see the agenda in Appendix B). Day 1 began with a series of introductory presentations—including overviews of the project, problem formulation in risk assessment, and the PBPG framework. This was followed by presentations of case studies on LCAS, setting the stage for two breakout group sessions. Participants were divided into four breakout groups according to their areas of expertise. The groups explored topics ranging from environmental fate and exposure assessments to ecotoxicological effects, the integration of non-standard data into a weight-of-evidence framework, and methods to enhance communication between risk assessors and managers. Session 1 provided a platform to identify overarching challenges in the current regulatory framework—such as unsuitable data requirements, inadequate testing methodologies, and the need for more robust guidance on waivers and expert judgment. Session 2 then delved into the particularities of LCASs, examining specific issues related to the use of background levels, adaptation of exposure models, and the applicability of traditional endpoints. The day concluded with a plenary session summarising the discussions of Session 1 and a networking event, providing an opportunity for further informal exchange amongst participants.

Day 2 opened with a summary of the previous day's discussions and featured stakeholder experiences. This was followed by breakout group session 3, which built on the outcomes of Sessions 1 and 2 by focusing on refining exposure assessment approaches and exploring additional methodological improvements. Group chairs presented the key points raised in each breakout group and recommendations from sessions 2 and 3 in a plenary session. The workshop concluded with a final session on conclusions and next steps, ensuring that all insights and suggestions would inform the revision of the proposed risk assessment scheme for LCASs.

This report provides a detailed summary of the workshop. A summary of the discussions during the breakout sessions is given in Section 2. The conclusions from these breakout sessions have been included in Section 3. The minutes from the plenary sessions have been included in Appendix A, while the agenda has been included in Appendix B. The information in this report reflects the input from participants during the workshop; this information does not necessarily represent the opinion of the consortium. The insights captured here will contribute to the ongoing revision of the proposed risk assessment scheme for LCASs.

2 Highlights from the discussion

2.1 Session 1 - General approach of the risk assessment

Objective: Stakeholder input on the current situation and overall approach
Goal: Gather insights from stakeholders based on their experience with LCASs.
Expected Output: A detailed list of challenges were discussed and they were related to:

- ✓ the environmental fate and exposure (group 1);
- ✓ hazards others than toxicity, ecotox (group 2);
- ✓ risk assessment methodology (group 3);
- ✓ risk management and risk communication (group 4).

Break-out group 1: Fate and exposure aspects	
QUESTIONS	**INPUTS**
Question 1: What is your view on / experience with the current regulatory framework to be applied to the risk assessment of LCASs?	Current challenges • Submission of incomplete dossiers that do not provide sufficient supporting information to justify waivers; • Inconsistent requests from different authorities and lack of consensus during peer reviews lead to delays in approval and renewal; • Requesting a waiver without expert advice is quite challenging. Conflicting conclusions from different experts, leading to a lack of harmonisation for LCASs; • More expertise is required to conduct a RA for LCASs. Due to lack of expertise, there may be a tendency to revert to default or overly conservative approaches, using inappropriate surrogates. It is important to choose more relevant and suitable surrogates. We need to gather more information and decide whether to guide applicants more proactively.
Question 1.1: Can you reflect on the hazards relevant for LCASs compared to hazards of 'conventional' substances?	Current challenges • Lack of methodologies to explain the fate of LCASs (mixture of compounds are excluded before pre-submission); • Traditional tests are often not appropriate for LCASs; • Need for specific ecotox studies (e.g. for oily substances); • Need for New Approach Methodologies (NAMs).
Question 1.2: Do you agree that the testing guidelines and risk assessment schemes are not appropriate for hazards other than toxicity?	• Yes.

Question 1.3: Do you agree that a quantitative approach is mostly not possible for LCASs?	• A quantitative approach is possible if we have the necessary information (e.g., e-fate and ecotoxicological data); • For leaching, a quantitative approach can be used only for specific substances due to the 0.1 threshold.
Question 1.4: Pros and cons of the current quantitative approach	<u>pros</u> • A quantitative approach helps reduce uncertainty; • There are existing guidelines to follow; • Expert judgement is less important. <u>cons</u> • Current quantitative approach cannot be applied to some LCASs due to lack of data, unsuitable exposure models, and inadequate ecotox studies for specific hazards. Moreover, relying on default values often leads to overestimations of risk.
Question 2: Do you consider the proposed approach useful to make the risk assessment more fit-for-purpose and efficient (pros and cons)?	<u>pros</u> • Fate and exposure are crucial for effective risk characterisation; • It provides a tool to harmonise communication and a framework for peer review; • It is a transparent process and an easy-to-follow approach; • Offers a more comprehensive understanding of various modes of action-hazards; • Identifies more pathways for harm scenarios; • Supports consensus during peer review. <u>cons</u> • The final decision remains unclear due to ambiguous terminology (e.g., "likely," "unlikely"); • It is not clear how reliable are the conclusions when data is missing?
Question 3: What would you change in the proposed approach? This could include anything you would suggest to make it more appropriate or more complete (i.e. additional waiving criteria? Additional hazards that are not captured?)	<u>Participants' perspectives - suggestions for improvement</u> • Simplify terminology (Low concern active substances may not always be of low concern, particularly for inorganics and certain types-metabolites of microorganisms); • Better define the agricultural practices followed and specify what constitutes risk mitigation measures; • Develop specific exposure scenarios (case-by-case use pattern) as part of the process for analysing and addressing exposure questions; • Clarify qualitative 'scoring' of likelihood as far as is practicable; • Incorporate the intrinsic nature of substances as a line of evidence (including for fate). In addition, the nature of substances and their past uses (e.g., feed, food, fertilizer) could be integrated into the PBPG (analysis plan) as evidence of no (or negligible) harm.
Break-out group 2: Ecotoxicology aspects	

QUESTIONS	INPUTS
Question 1: What is your view on / experience with the current regulatory framework to be applied to the risk assessment of LCASs? Question 1.1: Can you reflect on the hazards relevant for LCASs compared to hazards of 'conventional' substances?	Current challenges • Current regulatory framework and data requirement are not appropriate to the risk assessment of LCASs, mainly because the Mode of Action (MOA) may be different. In some cases, conventional endpoints are not suited for standard assessments. Role of co-formulants might be higher with LCASs compared to conventional substances. Tests are not fitting and are not adequate since they might not capture effects due to particular MOA; • Classic chemical analytical methods are not always fitting. Data requirements are not appropriate and there is a lack of specificity. Current data requirements (DR) are not all necessary for LCASs (depending on the type of LCASs, need for a case-by-case approach). LCASs approach leaves uncertainties and room for wrong interpretation. Also, sublethal effects need to be considered. It might not be possible to perform field studies for all types of LCASs.
Question 1.2: Do you agree that the testing guidelines and risk assessment schemes are not appropriate for hazards other than toxicity?	Current challenges • For the majority of participants, the current approach is not appropriate to assess LCASs ; one person pointed out that for the majority of substances the current approach could still be appropriate, but not in the case of substances with a non-typical MOA; • Test protocols/guidelines are missing to capture effects from other MOA than toxicity and protocols for analytical methods for LCASs are missing as well.
Question 1.3: Do you agree that a quantitative approach is mostly not possible for LCASs?	Participants' perspectives - suggestions for improvement • A quantitative approach would still be preferable, even for LCASs (maybe after a qualitative approach) or it will need to be as quantitative as possible. Without clear thresholds, there is a higher uncertainty on the outcome of the regulatory process. However, the opinion was also that a quantitative approach is not always needed or possible and a qualitative approach could in some case be sufficient; • If there is a qualitative risk identified, even with a low risk, the risk must be quantified. In addition, a quantitative assessment is needed to account for risk mitigation. Stronger communication and agreements with authorities are required and it is needed to establish early on when the risk is assessed in a sufficient way; • It was mentioned that categorisation of likelihood needs boundaries and consequences for data requirements etc.; • What to do in case of high qualitative risk? Could it be refined? • In case of a qualitative approach, a better definition of the quantitative term is needed to avoid different interpretation. (Would we need to make it quantitative in the definition?).

Question 2: Do you consider the proposed approach useful to make the risk assessment more fit-for-purpose and efficient (pros and cons)?	<u>pros</u> • Potentially quicker and less time consuming; • Harmonised; • Uses similar language & approach for applicant & authorities; • More clarity on what can be waived, and focus more on what data is really necessary, i.e. fewer studies needed; • Transparent; • Using the events that are relevant for a given scenario will simplify the assessment; • Tailored for specific MOA/case-by-case. <u>cons</u> • Categories of Likeliness (Likely/unlikely etc…) are not well defined; • The approach, should be further developed and become more specific e.g. when pathways can be used and the need for a fit-for-purpose analysis plan; • Applicant needs to predict reliably the outcome of a RA before investing in the development of a substance (more expert judgement, so more uncertainties); • Absence of information, identified in the literature, does not mean there is no effect; it means it was never investigated, and unexpected effects might be missed; Necessary additional information is accounted for in the analysis plan, where experiments, literature search, modelling etc., depending on the type of information that is needed, is explained to be required. • Test methods are needed (ring-tested validated); • Propose an efficient PBPG: It is not efficient to handle data requests one by one, therefore the data information should be requested at the same time. The analysis plan sheds more light on the data needed.
Question 3: What would you change in the proposed approach? This could include anything you would suggest to make it more appropriate or more complete (i.e. additional waiving criteria? Additional hazards that are not captured?).	<u>Participants' perspectives - suggestions for improvement</u> • Provide guidance to increase transparency to all stakeholders; • Include explicit and additional waiving criteria while providing more descriptive detail; • More focus is needed on the MOA in combination with efficacy; • Some aspects need to be further specified, i.e. criteria/clear definition for the evaluation of likelihood; • Options should be included to cross-refer to information in other dossiers/similar LCASs; • Include a clear indication of when quantitative approach is triggered; • In case of a physical MOA perhaps the absence of toxicity should also be demonstrated; • Include more specific test methods; • Include methods of risk assessment for short persistence products;

	• Work on guidance/ guidelines for when to use the proposed approach; • The analysis plan (NAMs, Experiments) needs to be fit-for-purpose depending on different hazards; • Need for development of NAMs and guidance for Quantitative Structure Activity Relationship (QSAR) use; • Include tiered testing to avoid unnecessary field studies; • A definition is needed of which open literature is acceptable to use; • For social insects there is a need for inclusion of behavioral effects and welfare; • Requires investment on the planning of relevant pathways; • Good documentation of the conclusion to avoid becoming questionable afterwards.
Break-out group 3: Fit-for-purpose risk assessment methodology aspects	
QUESTIONS	**INPUTS**

Question 1: What is your view on / experience with the current regulatory framework to be applied to the risk assessment of LCASs?	• All agreed that the current situation is not ideal and needs to be improved.
	• Major issues with current situation:
	  • Lack of guidance for testing non-standard organisms that might be necessary for LCASs;
	  • No clear way to assess the background (natural) level and how to use / interpret information to be compared with the Predicted Environmental Concentrations (PEC); lack of proper guidance on this topic.
	Participants' perspectives - suggestions for improvement:
	• Definition of LCASs needs to be clarified/reconsidered;
	• A new EU expert group could help to act as a sounding board to discuss overall approach at pre-submission stage.

Question 2: Do you consider the proposed approach useful to make the risk assessment more fit-for-purpose and efficient (pros and cons)?	<u>pros</u> • Useful if clearly defined roles of actors are implemented; • Helpful for the applicant to present the RA approach to be followed at pre-submission meetings; • More fit-for-purpose; • Easier way to consider substances with a favourable ecotoxicological profile; • More transparent and comprehensive; • Identifies additional hazards and inclusion of other MOA beyond toxicity which is very useful; • Harmonised; • Potentially applicable for both conventional pesticides and LCASs. <u>cons</u> • Difficulties in the assignment of likelihood, e.g. how to differentiate likely from very likely? This brings uncertainty in the process;

	• Generic approach which might not be appropriate for all LCASs; • Intense procedure for risk assessors with qualitative approaches having higher uncertainty than quantitative approaches; • Interpretation of the outcomes of the evaluation is not always very clear (e.g., when no harm is acceptable?); • Wide margin for expert judgement, the risk assessors do not feel comfortable to take this on without detailed guidance. <u>Participants' perspectives - suggestions for improvement:</u> • More information and guidance on how to handle events with unknown likelihood in the PBPG is needed, along with a clear guidance on study planning for unknown likelihood events; • DA detailed guidance on how to apply and take decision is needed; • Terminology and definitions to express likelihood need to be provided.
Question 3: What would you change in the proposed approach? This could include anything you would suggest making it more appropriate or more complete (i.e. additional waiving criteria? Additional hazards that are not captured?)	<u>Participants' perspectives - suggestions for improvement:</u> • Terminology and definitions to express likelihood need to be provided and clarified to reduce uncertainty; • Recommendations for what to do (analysis plan) when the PBPG indicates 'unknown' are necessary; • Clear and detailed guidance is required; • Might fit to a more generalised approach that could be used when the quantitative approach is not acceptable. It was made clear that some risk assessors feel more comfortable with what they know like the quantitative approach and they feel out of their comfort zone when they have to apply a qualitative approach that entails a lot of expert judgment.
Break-out group 4: Fit-for-purpose risk assessment/ risk management	
QUESTIONS	**INPUTS**
Question 1: What is your view on / experience with the current regulatory framework to be applied to the risk assessment of LCASs?	• All agreed that the current situation is not ideal and needs to be improved. • Major issues with current situation: ▪ Lack of appropriate effect testing; ▪ Difficult to give advice at pre-submission stage; uncertainty on whether the proposed approach for the risk assessment will be accepted; ▪ Lack of harmonisation; ▪ Complex; ▪ Lack of data in the dossier (for different reasons – either smaller businesses with less experience or oversights from larger companies). <u>Participants' perspectives - suggestions for improvement:</u> • A better definition of LCAS is needed to indicate which substances are eligible for the proposed approach;

	• A new EU-expert group could help to act as a sounding board to discuss overall approach at pre-submission stage.
Question 2: Do you consider the proposed approach useful to make the risk assessment more fit-for-purpose and efficient (pros and cons)?	<u>pros</u> • Harmonised, systematic approach which can be applied to many types of LCAS; • Seems to be a fit-for-purpose approach; • The approach allows for expert judgement and encourages common sense and is as a result more realistic and helps to focus on key issues; • The approach leads to more transparency; • The approach is also suitable for the assessment of physical effects; • The approach encourages a more integrated approach for the assessment by linking exposure to effect; • Using the approach justifications for waivers can be better substantiated and assessed; • Improved dossier quality expected. <u>cons</u> • Scepticism on whether this approach will lead to solutions; • Indirect effects are not explicitly included in the approach; • Other cons are mostly related to the implementation, not the principle: ▪ Difficulties in harmonisation for completing PBPG; how to ensure consistency (for likelihood, expert judgement, weight of evidence); ▪ Could lead to need for higher tier studies as lower tier studies for effects other than toxicity are not available; ▪ Lack of agreed test guidelines for non-toxic effects. <u>Participants' perspectives - suggestions for improvement:</u> • Provide more information on how data on the proposed use can be used in the problem formulation approach (e.g., on the mode of action, the properties of the active substance, risk mitigation, conditions of use); • More information on how to handle events with unknown likelihood in the PBPG are needed; • A discussion is needed on whether physical hazards need to be included in the risk assessment of PPP (for all types of active substances – not only LCASs);
Question 3: What would you change in the proposed approach? This could include anything you would suggest to make it more appropriate or more complete (i.e. additional waiving criteria? Additional hazards that are not captured?)	<u>What is missing (for the proposed approach):</u> • Indirect effects and a specific consideration for biodiversity are not included in the approach. <u>Participants' perspectives - suggestions for improvement:</u> • Provide waiver criteria for: ▪ easy parts/quick wins; ▪ for situations where exposure is lower than background level; ▪ for situations where consumers are already exposed via diet;

	• Terminology and definitions to express likelihood need to be provided; • Definition of LCASs needs to be clarified/reconsidered; • A discussion is needed on whether physical hazards need to be included in the risk assessment of PPP (for all types of active substances – not only LCASs); provide criteria for when physical effects should be accounted for (to avoid triggering additional studies for all types of active substances); • More guidance is needed on what to do when the outcome of the likelihood assessment of a PBPG is 'unknown'; • The data requirements should be amended to be fit-for-purpose for every type of active substance; • Legal procedures: reassure the assessors that this approach would comply with the current regulation.

2.2 Session 2: Specific questions regarding particularities of LCASs and respective PBPGs

- **Break-out group 1: Fate and exposure aspects**
  Objective: Input on Fate and Exposure Aspects.
  Goal: Gather input on the use of background levels in the analysis plan and considerations for specific uses.
  Expected Output:
  - ✓ Key areas of concern for fate and exposure assessment of different LCASs types (e.g. mixture of compounds in botanicals, distribution of oil-type compounds in water bodies, use of default DT50 values or presence of background concentrations);
  - ✓ Identified factors to be considered in the analysis plan of exposure assessment for the different types of LCASs and specific uses.

Break-out group 1: Fate and exposure aspects	
QUESTIONS	**INPUTS**
Question 1: Which particularities of different types of LCASs (mixture of compounds in botanicals, semiochemicals, microbial metabolites, inorganics, peptides and dsRNA) and uses (e.g. dispensers, injection and precision application) should be considered in fate and exposure assessment of the analysis plan?	<u>Participants' perspectives - suggestions for improvement</u> • General uses and application techniques (not just for LCASs) models need to be adapted for different application methods, dose expression (dose / unit area, vertical, horizontal, spot treatment, ratio treated to untreated); • Consider endpoints from individual components in a mixture, focusing on lead components and applying read-across from those lead components; • Address how to handle endpoints when mixtures have been investigated, including how to use data such as ready biodegradability, adsorption, volatility, and uncertainties related to these properties;

Question 1.1: Are all necessary endpoints available to be used as input parameters for PEC calculations?	• For water-immiscible oils and products containing surfactants, ensure proper expression of exposure (e.g., mg/m² of water surface instead of mg/L); • All the aforementioned considerations contribute to defining the structure of the scenarios that should be addressed in the analysis plan. More specific and well-defined scenarios reduce uncertainty in qualitative approaches and enhance the robustness of the PBPGs.
Question 2: How to consider variability in background levels i.e. does it need to be a worst case or only representative? Question 2.1: Availability and reliability of data (scientific papers/monitoring data/other sources?)	Participants' perspectives - suggestions for improvement • Understanding the context of available information on background levels is crucial. This includes considering factors such as location, timing, whether the data is limited to farming environments (or not, other ecosystem compartments) or includes other anthropogenic activities; • While representative values are generally preferred, environmental properties can be significant. For example, factors like pH and sulfate levels can influence outcomes. The context (specific realistic scenario) is important; best and worst cases can also, in some cases, be applicable; • It should be evidenced that the information was collected in an unbiased systematic way from available published data sources (i.e. to avoid cherry picking preferable data).
Question 3: How to consider and communicate uncertainty in the exposure assessment. Should imperfect data be used with a clear indication of the associated uncertainty?	Participants' perspectives - suggestions for improvement • Yes, imperfect data should be used, but data is always imperfect so the importance is to know the "additional" uncertainty of the available information compared to the "usual" uncertainty; • It should be explicitly stated that the data/model was not fully applicable to the specific context; • Assessing uncertainty in the qualitative RA framework is complex but essential; • To ensure transparency and assess the reliability of conclusions, it is essential to report uncertainty at each step of the assessment process. This practice allows for a comprehensive understanding of the robustness of the final conclusions.
Question 4: Any other points in the analysis plan that would need to be discussed based on your experience, in relation to the fate and exposure aspect?	Participants' perspectives - suggestions for improvement • Highlight the most relevant exposure scenario to focus on for each specific PBPG i.e. different scenarios to indicate species needing consideration based on compartment where they reside (e.g. soil, water, plants, air) and not each indictor taxon listed in the data requirements; • Consider substance properties (e.g. oils which are immiscible with water, volatile substances) and description of agricultural practices, application methods, and on top of this potential exposure mitigation options.

- **Break-out group 2: Ecotoxicology aspects**
  Objective: Fit-for-Purpose Effect Testing
  Goal: Identify cases where standard test guidelines may not fully capture the effects of LCASs due to their specific properties.
  Expected Output:
  - ✓ List of tests deemed unsuitable for LCASs hazard assessment and potential alternative methods;
  - ✓ Considerations for testing LCASs that act via a physical MOA.

Break-out group 2: Ecotoxicology aspects	
QUESTIONS	**INPUTS**
Question 1: What type of LCASs require non-standard testing?	<u>The general consensus was that this holds for:</u> • LCASs acting via a physical MOA (oil-type (for aquatic & non-target arthropods (NTAs)); inorganics); desiccation and suffocation and when the predominant route of exposure is inhalation, the latter in the case of volatile substances; • Semiochemicals, attractants; • Silicate/kaolin; • Rapidly degrading peptides; • Ds RNA, RNAi; • Substances with a non-toxic MOA; • Organic acids: already existing in the environments of the organisms (at similar concentrations); they are not toxic to the organism they are applied to but are toxic to their enemies. They should not be overlooked.
Question 2: What type of consideration are needed when testing LCASs acting via physical MOA? Question 2.1: In particular, how a 2 Dimensions (2D, i.e. at the water surface thereby calculations being expressed at the deposition area) effects on aquatic organisms could be captured in a test? E.g. for immiscible substances (e.g. oils): would a 2D assessment be preferable, by applying the oil at the surface of the test vessel if PEC is agreed to be better expressed in terms of mg a.s./m^2 due to substance properties (density, low solubility in water)?	• The consensus was that it depends on the chemical behaviour. Both scenarios should be addressed under different circumstances: 2D if a persistent layer is expected at water surfaces (new, or amended, Test Guideline needed), 3D to address species in the water column when toxicity and exposure in the water column cannot be excluded (existing Test Guideline could be used or adapted). The decision should be based on the chemical behavior of the substance, as assessed by the fate assessment. In some case, both the 2D and 3D approach might be needed. <u>Participants' perspectives - suggestions for improvement</u> • When co-formulants of concern are present, toxicity in the water column should be considered; • 2D approach might only be relevant for invertebrates, less for fish. Consider if oxygen measurements in the water are sufficient to assess hypoxia. • Floating plants (Lemna) should be tested with overspraying (new, or amended, Test Guideline needed);

	• Reflection might be needed on specific cases, such as when substances might have different effects at different concentrations, i.e. an acid that might be corrosive at high concentrations and acidifying at lower concentrations?
Question 2.2: How should tests for bees and NTAs for substances with a physical effect and 'low' toxicity profile (overspray / contact exposure) be designed? Could we accept semi-field studies, or give indication of adapted laboratory studies?	<u>Participants' perspectives - suggestions for improvement</u> • Overspray tests: ▪ For terrestrial organisms direct overspray is particularly important for LCASs with a physical MOA instead of exposure to dry residues and instead of an acute contact test; consider how to express the endpoints (per cm^2?); • Develop specific test methods: ▪ Specific tests for bees/NTAs: apply the a.s. in a volatile solvent; after evaporation of the solvent we have an oily layer; ▪ Explore a test approach with contact to a high volume of oil on a glass plate; ▪ There is a need to consider the biology of the NTOs to assess the effects (e.g. presence of tracheae); • Tiered approach: ▪ For bees and NTAs first tier laboratory studies at relevant concentrations are necessary; ▪ Depending on the GAP and application rate and where refinement is needed, a tiered testing is recommended: laboratory, overspray and then semi-field studies only if effects are demonstrated in the lower tiers; ▪ Semi-field studies could be useful for these types of substances, e.g. contact tests for bees, semi-field studies for NTAs, use of volatile solvent for bees in case of oils; • Product information: the formulation is also important to consider, to distinguish between effect of active substance and co-formulants; • Pollen/honey might absorb volatile substances. So, this quality might be a concern.
Question 3: What about MOA such as desiccation, suffocation, hypoxia, mass trapping etc. (e.g.: paraffin oil, rapeseed oil)? How to consider hypoxia?	• The following needs for information and testing were raised by the group: <u>Participants' perspectives - suggestions for improvement</u> • A ring-tested Test Guideline for each hazard (i.e. suffocation/desiccation and volatile substances) should be developed on agreed NTOs species; • Evidence in the literature can be sought that the MOA actually causes an effect in reality and that these MOA are really an issue; • Body of knowledge can help in the Risk Assessment for example in case of peptides; • When evaluating pheromones for mass trapping, special consideration should be given to their inherent high specificity, which can be considered to refine the risk assessment; • Desiccation: NTAs and bees should also be tested by overspraying;

	• A quantitative method for hypoxia is needed; • The test organisms should be really exposed to relevant amounts by the relevant pathway; the duration of exposure should be relevant; • Endpoint should be observed, and a suitable recovery period could be included; • MOA should be considered when testing.

- **Break-out group 3: Fit-for-purpose risk assessment methodology aspects**
  Objective: Strengthening the collection of evidence for Weight of Evidence (WoE) Analysis
  Goal: Clarify expectations for applicants regarding evidence collection and integration into the analysis plan.
  Expected Output:
  - ✓ List of relevant databases, keywords, literature search strategies, and data justification/validation methods;
  - ✓ Suggestions to streamline and enhance the evidence collection process in the dossier.

Break-out group 3: Fit-for-purpose risk assessment methodology aspects	
QUESTIONS	**INPUTS**
Question 1: What are the reasonable expectations for the Applicant to ensure that data collected from the literature are done in an unbiased manner?	What is working well: • Current EFSA guidance on data collection seem sufficient Current challenges: • Qualitative criteria for literature review in general for all type of substances • Not much literature is available for some new LCASs; • In some cases, there is misuse of read-across based on improper and superficial literature review; • Maybe a need for specific criteria for LCASs where the literature review should be more extensive (e.g. higher quality criteria). Participants' perspectives - suggestions for improvement : • Use Klimisch score for reliability of papers used in literature review; • Independent body/certified organisation to run the literature verification for independent analysis and transparency (but might delay the process)
Question 2: Within the proposed approach, how to extract and present evidence from other sections of the assessment (residues, efficacy, etc..) to be used in a WoE approach?	What is working well: • Data from efficacy and residues testing are already used by risk assessors in other parts of the risk assessment. Current challenges: • Guidance on how to use these data is lacking; • EFSA does not have access to all the relevant data (i.e. biological assessment dossiers submitted for the efficacy assessments of products) and that might be a problem for WoE;

	• Modifications in experimental setups of the residue section could provide valid information for other sections of the RA (i.e. persistence, background levels), this should be taken into account by the applicants or upon consultation at the pre-submission meeting. Participants' perspectives - suggestions for improvement : • Data extracted from other sections of the dossier that are deemed useful for parts of the risk assessment should be included in a table easily accessible to risk assessors (e.g. like in the ED section).
Question 3: Is the role of RM, MS risk assessor, Applicant, clear in the proposed scheme? e.g. the applicant should complete the PBPG at the time of dossier drafting?	What is working well: • The role of the MS risk assessor and the applicant is clear; • The proposed approach fits well with the timing of a pre-submission meeting. Current challenges: • Specific guidance is needed for applicants to draft the PBPG. Participants' perspectives - suggestions for improvement : • Applicants should propose the PBPG approach, to be used before the drafting of the dossier, i.e., at early stage, just after the testing of the efficacy of the proposed a.s. This is considered beneficial also for the applicant saving time and resources; • RMS to intervene in an earlier stage to identify the correct application of the PBPGs; • Importance to give the applicant the opportunity to discuss the proposed risk assessment scheme before the drafting the dossier, to avoid in a later stage identifying the wrong application of the approach.

- **Break-out group 4: Fit-for-purpose risk assessment/ risk management**
  Objective: Enhancing Risk Communication with Risk Managers
  Goal: Improve how risk assessment outcomes are communicated to risk managers.
  Expected Output:
  - ✓ List of actions to improve communication of the outcome of the risk assessment with risk managers.

Break-out group 4: Fit-for-purpose risk assessment/ risk management	
QUESTIONS	**INPUTS**
Question 1: Give pros and cons of the proposed approach regarding communication on the outcome of the risk assessment with risk managers.	Pros: • The approach will result in less unnecessary data gaps and better explanation for the reason for identifying a data gap or issue not finalised (more transparent);

	• The approach could increase consistency and improve the justification of conclusions for risk management; • In some cases, the approach could lead to lighter dossiers and faster assessments. <u>Cons:</u> • Sceptical if approach will indeed increase transparency; • 'Unknowns' may be misinterpreted as 'high risk', while it just means that more information is needed for the assessment; • Integration of risk mitigation measures are not included in the approach; • To be able to use common sense you need a lot of experience (which may be difficult for assessors who are not specialised in the assessment of LCASs). <u>Participants' perspectives - suggestions for improvement:</u> • Risk assessors could flag options for risk mitigation; • To provide a better overview, the output of risk assessment could include the PBPG schemes instead of free text; • Precautionary RMM which are introduced to address uncertainties should be clearly distinguished from specific RMM (especially relevant in the context for risk managers to decide on whether the substance is low risk).
Question 2: Give ideas for solutions on how to communicate to risk managers in case of an inconclusive assessment.	<u>Participants' perspectives - suggestions for improvement :</u> • Provide evidence to justify the possibility of low risk (e.g., from literature search); • Provide clarity on the real 'need to know' data; • Provide information on already approved, similar substances.
Question 3: Propose solutions to reaching a conclusion for situations of low toxicity (e.g. > values) but high application rates. Standard RA is not sufficient to exclude a risk (e.g. TER value fails, and it is not possible/recommended to test higher rate).	<u>Participants' perspectives - suggestions for improvement :</u> • In case a study is feasible at the appropriate concentration/dose, it should be performed; • If study is not feasible, a case-by-case approach should be followed, for example by including information on the DT50 of the substance, the longevity of the effect to the target organism and on the mode of action of the substance; • Higher tier studies can be performed.

2.3 Session 3: Follow-up from break-out session 2 and general questions

Break-out group 1: Fate and exposure aspects	
QUESTIONS	**INPUTS**
Question 1: Are there available tools to adapt fate models to the needs of exposure assessment of different types	• A document for accepted adaptations would be useful. Post approval issues group may have more examples that have been used for product authorisation than can be retrieved from EFSA conclusions;

of LCASs (mixture of compounds in botanicals, semiochemicals, microbial metabolites, inorganics, peptides and dsRNA)? If yes, give examples.	• The adaptation of the FOCUS Steps for oils immiscible with water (not using Step 3 and typical step 4, spray drift mitigation on Step 2) is an agreed approach. TOXSWA might have new equations for this situation if a large number of actives with these properties would be commercialised (technically possible but the investment might not be justified); • Post processing tools are available for multi component actives (e.g. plant extracts) when substance properties would be available for each component. • Participants noted that methodologies, such as metabolomic and bioinformatic approaches, are available for evaluating environmental footprints; • Some application methods are not easily supported by current tools. This could be improved by developing best practice guidance (as mentioned in the first point above). Additionally, alternative ways to express doses may also be needed; • The PPR statement on transition metals[1] includes models related to speciation and bioavailability and discusses the incorporation of data on background levels.
Question 2: Are there available technologies to calculate the exposure due to precision application or specific application technique (e.g. dispenser)? If yes, give examples.	• PERSAM for PEC soil in and between rows; • Experimental release rate data are needed for very specific application techniques (e.g., semiochemicals); • Spray drift reduction due to specific drift reduction technology, compared to standard hydraulic sprayers, is available; • Different environmental compartments must be treated separately when it comes to precision applications.
Question 3: Can the fate models be used / adapted?	• Yes, fate models can be used/adapted if we have relevant information (e.g. release mechanism for pheromone dispensers); • New tools will be needed for specific type of LCASs (e.g. formulated dsRNA, as not formulated active degrades too quickly to have efficacy); • Environmental scenario descriptions (e.g., FOCUS scenarios) should not be updated for LCASs as the exposure assessment goals and subsequent protection goals should be the same for all substances.
Question 4: Any other ideas for possible solutions for fit-for-purpose exposure assessment for LCASs to be further investigated?	• Descriptors for likelihood (table 1 page 11 to background document) request to refine / update wording so the gradation becomes clearer;
Break-out group 2: Ecotoxicology aspects	

[1] EFSA PPR Panel (EFSA Panel of the Plant Protection Products and their Residues), Hernandez-Jerez A, Adriaanse P, Aldrich A, Berny P, Coja T, Duquesne S, Focks A,Marinovich M, Millet M, Pelkonen O, Tiktak A, Topping C, Widenfalk A, Wilks M, Wolterink G, Conrad Aand Pieper S, 2021. Statement of the PPR Panel on a framework for conducting the environmental exposure and risk assessment for transition metals when used as active substances in plant protection products (PPP). EFSA Journal 2021;19(3):6498, 88 pp

QUESTIONS	INPUTS
Question 1: How to use read-across hazard data and waiver criteria in the analysis plan? Question 1.1: Discuss the surface tension and if this could be used as a waiver criterium?	Participants' perspectives - suggestions for improvement • Species models predicting the effects of LCASs should be developed respectively made available; • Active substances versus formulated products matters a lot in this context, since it would highly depends on product / a.s. properties; • Different thresholds for NTAs and Aquatics might be needed; The group agreed that using the surface tension as a waiver criterium could be accepted, but it should be based on experimental data and on a case-by-case approach depending on the chemical and the data. A question was raised whether QSAR approaches could be used for this?
Question 1.2: For substances with a physical effect to NTAs and readily biodegradable and/or short DT50 in soil (<14 days?), can it be assumed that there will be recovery of in-field NTA within 1 year (i.e. analogous to the assumption that an aged residue study is sufficient to show potential for recovery), considering also multiple applications.	Participants' perspectives - suggestions for improvement: • Tier 1 study for testing the physical MOA would still be needed. *A priori* generalised waivers are not appropriate. This could be assumed in the context of a refinement; • It could make sense for soil dwellers; however, it should be combined with other indications (low toxicity for bees?). Rate, number of applications, and intervals between the applications should be taken into consideration; • Multiple applications should be taken into consideration since they could deplete the off-field population; • Consider criteria such as ratio between the number and interval between the applications; • There could be an effect on reproduction. This could lead to too much uncertainty; • Mortality rate should also be taken into consideration; • In case of multiple MOA the most hazardous MOA should be considered in the analysis plan; The conclusion is that the assumption might hold only for specific species, also depending on the DT50 and the number of applications plus the mortality rate. It would be helpful if there are examples/data available from the past (and a model) that could be used to predict if the statement is correct.
Question 1.3: For substances that are present in nature, can a period of time be defined for 'returning to background levels' which can be assumed not to pose a risk to NTAs and soil organisms (i.e. analogous to the assumption that an aged residue study is sufficient to show potential for recovery).	Participants' perspectives - suggestions for improvement: • Route of exposure and way the NTAs are exposed might differ, an overspray study would still be needed at Tier 1; • Time needed for recovery might depend on species. Further, recovery might occur but with a change in species composition; • Could be used for soil organisms as a refinement;

	• Depends on the data available and should be considered on a case-by-case basis. It also depends on the persistence of the substance in combination with the type of application. The group concluded that it is difficult to say this upfront.
Question 2: (not only related to physical MOA): Are you aware of specific New Approach Methods that could be used under a regulatory framework to assess potential hazards from LCASs?	• NAMs are mainly developed for Human Health Toxicology and there is not enough pressure to develop NAMs for ecotoxicology. There are studies available, but the limiting factor is the lack of data, and that there is a lack of standardized tests. <u>The following NAMs were mentioned:</u> • For NAMs, especially fish cell lines and other cell-line studies, could be useful; • Cell Painting could be an approach; • A DNT testing battery could be developed; • Developmental neuro activity/toxicity could be a potential NAM; • QSARs for LCASs were considered useful; • ED studies using NAMs (respectively to replace fish/vertrebrate studies); • Skin sensitisation could be relevant for NTAs.
Question 3: Any other ideas for possible solutions for fit-for-purpose hazard assessment for LCASs to be further investigated?	<u>Participants' perspectives - suggestions for further investigations are:</u> • Understand limitations of tests and thereby the conclusions; • Discussion regarding the co-formulants (per se available for risk assessor but not to public); • Consider the DT50 as an important parameter in the risk assessment; • Consider mortality in the hazard assessment; • Investigate the prediction of MoA for the risk; include other MoA (e.g. physical, suffocation etc); • Establish publicly approved background levels; • Develop fit-for-purpose validated test guidelines; • Make use of eDNA for background levels and effects; • Need for clear definitions; • Need for protocol development; • Need for more robust and more clear methodology.

Overall conclusions Group 2
• LCASs acting via a physical MOA (e.g. oil-type; inorganics); desiccation and suffocation and when the predominant route of exposure is inhalation & volatiles substances would require non-standard testing;
• Aquatic: If toxicity and exposure in the water column cannot be excluded, for invertebrates both 2D and 3D approaches are required, except for if supported by fate properties of the substances;
• Appropriate Tier 1 test guidelines are needed (2D for invertebrates in water; overspray for NTAs ad bees, etc…);
• Waivers are acceptable and are needed, however:
  • should be based on experimental data
  • should be used on a case-by-case basis (generalised waiver might not be appropriate) considering other information and the GAP	

Break-out group 3: Fit-for-purpose risk assessment methodology aspects	
QUESTIONS	**INPUTS**
Question 1: How to better describe how to evaluate the evidence? (evaluation of non-standard information, extraction of information from studies not designed to be used in risk assessment; consideration of the uncertainty of the evidence).	Participants' perspectives - suggestions for improvement: • Data from non-standard methods are not disregarded by default; • Data from non-standard methods could be considered if the experimental setup and methodology is well described and it is clearly validated (e.g. statistically sound); • Data from studies not designed for RA could be used, as long as they were assessed properly and found to be robust and reliable, to support the evaluation but not to be used for deriving endpoint values; • Uncertainty should be always identified, even for non-standard tests where common statistical analysis is not usually available; • Qualitative RA increases uncertainty in the case of LCAS. Given the figures presented regarding the definition of the likelihood, even highly unlikely events could be regarded as leading to high risk (highly unlikely 2 – 5 %, thus there is still effect).
Question 2: Any other ideas for possible solutions for fit-for-purpose RA for LCAS?	Current challenges: • The current RA (both for synthetic and LCASs) does not properly consider the impact on microbial community; • Good and clear guidance for the identification of the most critical steps in the process (i.e., it is not necessary to go through all the steps or start from the first step). Participants' perspectives - suggestions for improvement: • The definition of likelihood should be clarified in a better way, especially when negligible or very unlikely effects are concluded; • Clear guidance on where to start and where to stop in a PBPG.
Break-out group 4: Fit-for-purpose risk assessment/ risk management	
QUESTIONS	**INPUTS**
Question 1: How to finalise the conclusion based on WoE and the entire PBPGs?	What works well? • The PBPG assessment will force the assessment to be more contextualised. Participants' perspectives - suggestions for improvement: • Additional details to be included in EFSA conclusions would be useful for risk managers and risk assessors at product level (including information on diverging opinions); • The uncertainty assessment should be meaningful and contextualised. This is important for both the exposure and effect assessment. The uncertainty

	assessment is more relevant to be done in both the exposure and final risk assessment; • Uncertainty in the assessment should be balanced and taken into account in a WoE approach and explained in the final conclusion; • In certain cases, it may be needed to reiterate the approach for separate scenarios which are part of a single use, for example by applying the approach for bees to flowering, pre-flowering, and post flowering growth stages; • Risk managers have a desire for clear conclusions of the risk assessments which include uncertainty; • A WoE approach should also consider unquantified risk mitigation options.
Question 2: Any other ideas for possible solutions for fit-for-purpose RA for LCAS?	<u>Participants' perspectives - suggestions for improvement:</u> • Develop a way of identifying early on, in the regulatory process, which LCASs are really of low concern and which need a more detailed risk assessment. For example, consider whether the MOA is broad spectrum or specific; • Include information on the overall environmental impact in the conclusion on the risk assessment, for example to demonstrate that the overall impact profile is preferable compared to alternative plant protection products or other farming techniques; • Qualitative likelihood descriptors should be used as such (as currently proposed); using numbers instead of qualitative descriptors for a qualitative likelihood assessment may be questionable; • It should be avoided that an outcome of a likely breach of the protection goal is interpreted as being a high risk. If the conclusion of the assessment of a PBPG is that it is likely that the protection goal will be breached, it is important to contextualise that this outcome is based on the available information and expert knowledge. The outcome can be different in case more information becomes available.

3 Conclusion

Below is a summary of the discussion, along with a grouping of the points from participants for each session:

SESSION 1

1. **The current regulatory framework is considered to be unsuitable for most LCAS**
    - **Incomplete submissions and inconsistent requirements:**
        - Many dossiers are incomplete.
        - Considering the nature and characteristics of LCAS, data requirements might not be fully aligned across dossier and might be inconsistent.
    - **Expertise and Guidance Deficits:**
        - There is a need for clearer guidance to support the acceptance of appropriate waivers, including a more proactive role for experts during pre-submission.
2. **Limitations of conventional testing and quantitative approaches**
    - **Unsuitability for some type of LCASs:**
        - Conventional tests and endpoints (especially those focused solely on toxicity) are not well suited for LCASs, which often involve unique modes of action and mixtures of compounds.
        - Inadequate analytical methods and data requirements lead to uncertainty, particularly when addressing hazards other than toxicity (e.g., desiccation, suffocation, hypoxia, mass trapping, and sublethal effects).
    - **Challenges with a quantitative approach:**
        - While quantitative methods can reduce uncertainty when sufficient data exist, they are often not suitable to LCASs due to insufficient or inappropriate data and models.
        - There is a need to balance quantitative and qualitative methods, ensuring that even when a high risk identified through a qualitative approach, it is subsequently quantified to support decision-making.
3. **Merits and shortcomings of the proposed risk assessment approach**
    - **Positive aspects:**
        - The proposed approach is viewed as a promising tool that could harmonise communication, support transparent decision-making, and provide a systematic framework for risk assessment of LCASs.
        - It offers a more comprehensive understanding on how to assess pesticide with diverse MOA on a case-by-case basis.
    - **Participants' perspectives - areas needing improvement:**
        - **Terminology and definitions:**
            - Clear definitions to express the likelihood are needed.
            - The term LCASs should be better defined.
        - **Guidance and implementation:**
            - A detailed hands-on guidance on applying the approach is needed.
            - Guidance is needed on how to handle situations with missing data or "unknown" likelihood outcomes.
        - **Need for specific adjustments:**
            - Additional criteria for waiving certain data requirements (for example, when exposure levels are minimal or when NTOs are already exposed through other routes without adverse effects) should be provided as part of the analysis plans.
4. **Participants' perspectives - suggestions for moving forward**

- **Develop clearer guidance and terminology:**
  - Establish detailed guidelines and definitions to reduce reliance on subjective expert judgment.
  - Clarify when and how to apply both quantitative and qualitative approaches.
- **Enhance Communication and Harmonisation:**
  - A more harmonised and transparent process is needed, one that involves all stakeholders (potentially including a new EU expert group) early in the process, particularly at the pre-submission stage.

SESSION 2

1. Fate and exposure aspects

- **Tailored exposure models:**
  - Different LCASs types (e.g., botanical mixtures, semiochemicals, microbial metabolites, inorganics, peptides, dsRNA) and various application methods (dispensers, injection, precision application) require exposure models adapted to their specific usage.
  - Models must account for different dose expressions (e.g., dose per unit area, vertical *vs*. horizontal application, spot treatment) and the characteristics of individual mixture components—focusing on lead compounds and applying read-across where appropriate.
- **Defining endpoints and scenarios:**
  - Endpoints such as ready biodegradability, adsorption, and volatility should be considered, including associated uncertainties.
  - For substances like water-immiscible oils, exposure should be expressed in relevant units (e.g., mg/m² on water surfaces).
  - Well-defined and specific exposure scenarios in the analysis plan can reduce uncertainty and strengthen the qualitative assessment.
- **Handling background levels and uncertainty:**
  - Variability in background concentrations should be understood in context; while representative values are preferred, both worst-case and realistic scenarios may be applicable depending on factors like location, timing, and environmental context.
  - Data used must be unbiased and systematically collected from reliable sources.
  - Imperfect data should be transparently used, with clear indications of the additional uncertainty at each step of the assessment process.
- **Overall recommendation:**
  - Focus on the most relevant exposure scenarios per PBPG, integrating substance-specific properties (e.g., immiscibility, volatility) and realistic use conditions (including agricultural practices and potential mitigation options).

2. Ecotoxicology aspects

- **Identifying LCASs requiring non-standard testing:**
  - LCASs with physical modes of action (e.g., water-immiscible oils, inorganics, substances causing desiccation, suffocation, or hypoxia) and those acting via non-chemical mechanisms (e.g., semiochemicals, attractants, dsRNA) may not be adequately assessed using standard test guidelines.
  - Substances such as silicate/kaolin, rapidly degrading peptides, and organic acids (present naturally in the environment) also require special consideration.
- **Testing approaches for physical MOA:**
  - A two-dimensional (2D) approach (assessing deposition on water surfaces) might be preferable for substances likely to form a persistent surface layer. However, when effects in the water column cannot be excluded, both 2D and 3D assessments should be performed.

- For terrestrial organisms (e.g., bees and non-target arthropods), adapted laboratory overspray tests and tiered testing strategies are recommended to capture contact and exposure effects accurately.

- **Guidance needs:**
  - There is a need for ring-tested technical guidelines to address specific hazards (e.g., suffocation, desiccation, hypoxia) for agreed non-target species.
  - Testing strategies should ensure that organisms are exposed to relevant doses for appropriate durations, and endpoints (such as recovery after exposure) are clearly observed and documented.

3. Fit-for-Purpose Risk Assessment Methodology (Evidence Collection and WoE Analysis)

- **Unbiased data collection:**
  - There is a need for improved literature reviews of LCASs where data may be sporadic.
  - The use of reliability metrics (e.g., the Klimisch score) is recommended to ensure that literature and other data sources are robust and unbiased.
  - The possibility to involve an independent or certified body for literature verification to enhance transparency was proposed, even if it might extend the review timeline.
- **Integration of cross-sectional data:**
  - Data from other parts of the dossier (e.g., residues, efficacy) should be extracted and presented in accessible formats (such as summary tables) to support a comprehensive weight-of-evidence (WoE) analysis.
  - Clear guidance is needed on how to integrate and interpret evidence from various sections to support the overall risk assessment.
- **Clarifying roles and timing:**
  - While the roles of the risk managers, national risk assessors, and applicants are generally clear, applicants should be required to propose the PBPG at an early stage (e.g., after efficacy testing and before dossier drafting) to ensure that the risk assessment scheme is correctly applied from the beginning.
  - Early intervention by the RMS is advised to guide the proper application of the PBPG approach.

4. Fit-for-Purpose risk assessment/risk management (communication)

- **Enhanced communication of outcomes:**
  - The proposed approach promotes transparency by clearly documenting why specific data gaps exist and by providing detailed justifications for conclusions, potentially leading to more consistent risk management decisions and lighter dossiers.
- **Participants' perspectives - suggestions for risk communication:**
  - The final output should include structured PBPG schemes rather than free-text explanations, helping to distinguish precautionary risk management measures from those based on definitive evidence.
  - In cases of inconclusive assessments, communication should include what evidence is available to assess the risk.
  - For substances with low toxicity but high application rates, a case-by-case approach is recommended, which may involve conducting higher tier studies or providing supplementary data on persistence, exposure duration, and mode of action.

SESSION 3

1. Fate and exposure aspects

- **Adaptation of existing tools:**

- There are several tools and approaches available that can be adapted for LCAS exposure assessments. For example, the adaptation of the FOCUS Steps for water-immiscible oils (by skipping or modifying certain steps in tiered approach) and post-processing tools for multi-component actives have been successfully applied.
- Bioinformatic/metabolomic methods (e.g., environmental metabolic footprinting) and guidance (e.g., EFSA Guidances [2] are available for assessing mixtures, although not all application methods are currently well supported.

- **Precision application techniques:**
  - Tools such as PERSAM are available to estimate PEC in soil for precision applications (e.g., between rows), while experimental data (e.g., release rate information from granules or dispensers) and models describing spray drift reduction exist for specific application technologies (e.g. drift reduction nozzles,).
  - Fate models can be used—provided they incorporate relevant release mechanism information—while specific adaptations may be required for formulations like for products containing dsRNA, whose efficacy depends on formulation technology that to a certain extent reduces the rapid degradation of dsRNA.
- **Participants' perspectives - suggestions for improvement:**
  - Develop a documented list of accepted adaptations and best practices to support exposure assessment, including alternative ways to express doses for non-standard application methods.
  - Clarify descriptors for likelihood and ensure that the PBPG decisions (including how endpoints are weighed) are clearly presented in pre-submission and dossier documents.

2. Ecotoxicology aspects

- **Use of read-across and waiver criteria:**
  - The use of parameters such as surface tension as a waiver criterion is acceptable—but only on a case-by-case basis and when backed by experimental data. Since co-formulants may impact physical chemical properties, a consideration of both active substances and formulated products is crucial for consideration of waiver criteria such as surface tension.
- **Handling physical modes of action and recovery:**
  - For LCASs with physical MOA (e.g., causing desiccation, suffocation, or hypoxia) and with short DT50 values, a generalised assumption of recovery (e.g., within one year) cannot be made universally. Such assumptions depend on species-specific factors, application frequency, reproduction, and mortality rates.
  - For substances naturally present in the environment, defining a "return to background levels" timeframe is complex and must consider different exposure routes and potential shifts in species composition.
- **New approach methods (NAMs):**

[2] EFSA Guidance on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals. EFSA Scientific Committee, Simon John More, Vasileios Bampidis, Diane Benford, Susanne Hougaard Bennekou, Claude Bragard, Thorhallur Ingi Halldorsson, Antonio F Hernández-Jerez, Konstantinos Koutsoumanis, Hanspeter Naegeli, Josef R Schlatter, Vittorio Silano, Søren Saxmose Nielsen, Dieter Schrenk, Dominique Turck, Maged Younes, Emilio Benfenati, Laurence Castle, Nina Cedergreen, Anthony Hardy, Ryszard Laskowski, Jean Charles Leblanc, Andreas Kortenkamp, Ad Ragas, Leo Posthuma, Claus Svendsen, Roland Solecki, Emanuela Testai, Bruno Dujardin, George EN Kass, Paola Manini, Maryam Zare Jeddi, Jean-Lou CM Dorne, Christer Hogstrand https://doi.org/10.2903/j.efsa.2019.5634

- Although NAMs are more developed for human health, there is a need to further develop and standardize NAMs (e.g., fish cell lines, cell painting, QSARs) for ecotoxicological endpoints. This would help reduce reliance on standard tests that may not be fit for LCASs.

- **Participants' perspectives - Overall suggestions for ecotoxicology:**
  - Develop appropriate Tier 1 test guidelines (e.g., 2D and 3D approaches for aquatic invertebrates, overspray tests for bees and NTAs).
  - Use waivers based on experimental evidence and consider additional information (e.g., mode of action, GAP) on a case-by-case basis.
  - Enhance methods for understanding the impact on non-target organisms, including using ring tests and exploring eDNA for establishing background levels.

3. Fit-for-Purpose risk assessment methodology

- **Evaluation of evidence:**
  - Data from non-standard studies or those not originally designed for risk assessment should not be discarded if the experimental setup is well-described, robust and reliable. However, their uncertainty must be carefully evaluated and clearly communicated.
  - A more robust approach is needed for evaluating the WoE that incorporates uncertainty assessments even when qualitative methods are used.
- **Improving the process:**
  - There is a need for clear guidance on which steps of the PBPG should be followed and where to stop eventually the assessment process.
  - The current RA framework should be expanded to better address impacts on soil microbial communities and other endpoints that are currently under-considered in the whole risk assessment process including conventional chemical substances.

4. Fit-for-Purpose risk assessment/risk management and communication

- **Finalising conclusions using WoE:**
  - The structured PBPG approach forces a more contextualised risk assessment. Outcome of assessments should be detailed and include diverging evidence/opinions, and a balanced uncertainty assessment to help risk managers make better-informed decisions.
  - Risk communication should clearly state whether approval criteria are met, detail any data gaps, and explain the uncertainty surrounding the final conclusions.
- **Further communication enhancements:**
  - Develop methods to identify early on which LCASs are truly of low concern versus those that need a more in-depth assessment.
  - Include overall environmental impact comparisons (e.g., compared to alternative products or farming practices) in the final conclusions.
  - Avoid overinterpreting qualitative likelihood descriptors; if an outcome indicates a potential breach of protection goals, this should be presented as provisional, pending additional data.

Glossary

Term	Definition
AI	The adequate intake (AI) is a dietary recommendation used when there is no enough data to calculate an Average Requirement. An AI is the average nutrient level consumed daily by a typical healthy population which is assumed to be adequate for the population's needs.
Botanical	A substance derived from plants.
DNA	A complex chain-like molecule that carries the genetic material, present in living organisms and some viruses. DNA (deoxyribonucleic acid) is capable of copying itself and carries the instructions for all the proteins used to create and sustain life.
Ecotoxicology	The study of the adverse impacts of substances, particularly chemicals, in relation to the environment and public health.
Endocrine Disruptor	A substance that adversely affects the endocrine (hormone) system leading to negative effects for organisms and/or their offspring.
Endpoint	A physical or chemical outcome that can be assessed by a test; for example, blood pressure or levels of a potential toxin in the body.
Environmental Risk Assessment (ERA)	The process of assessing potential harm to the environment caused by a substance.
Exposure	Concentration or amount of a particular substance that is taken in by an individual, population or ecosystem in a specific frequency over a certain amount of time.
Exposure Assessment	One of the key steps in risk assessment, this relates to a thorough evaluation of who, or what, has been exposed to a hazard and a quantification of the amounts involved.
Genetically Modified Organism (GMO)	An organism which contains genetic material that has been deliberately altered and which does not occur naturally through breeding or selection.
GLP	Good laboratory practice (GLP) is a standardised way of planning, performing and reporting laboratory-based studies to ensure a high standard of quality and reliability.
Hazard	A substance or activity which has the potential to cause adverse effects to living organisms or environments.
Inorganic Compound	Chemical that does not generally contain carbon; for example, water, oxygen, sodium chloride.
Mode Of Action	A sequence of events, identified by research, which explains an observed effect.
Organism	A living thing such as humans, animals, plants and microbes (e.g. bacteria, viruses).
Pesticide	Substance used to kill or control pests, including disease-carrying organisms and undesirable insects, animals and plants.

Plant Protection Product (PPP)	Products used to protect, preserve or influence the growth of desirable plants or to destroy or control the growth of unwanted plants or parts of plants.
Population	Community of humans, animals or plants from the same species.
Problem Formulation	The process of defining the specific problem being addressed in, for example, an environmental risk assessment. It involves articulating a question and defining how it may be answered (e.g. by identifying the endpoints to be measured).
Risk Assessment	A specialised field of applied science that involves reviewing scientific data and studies in order to evaluate risks associated with certain hazards. It involves problem formulation, hazard identification, hazard characterisation, exposure assessment and risk characterisation.
Risk Management	The management of risks which have been identified by risk assessment. It includes the planning, implementation and evaluation of any resulting actions taken to protect consumers, animals and the environment.
RNA	A type of nucleic acid found in the body, similar to DNA but single stranded. The best-known function of RNA (ribonucleic acid) is transmitting instructions from DNA to the cellular machinery responsible for making proteins.
Threshold	A dose or exposure below which adverse effects are not detected.
Toxicity	The potential of a substance to cause harm to a living organism.
Uncertainty	A lack of full knowledge about a situation in, for example, risk assessment. Uncertainty can be reduced by carrying out more research.

Abbreviations

AUTH	Aristotle University of Thessaloniki
BGs	Breakout Groups
CSIC	Consejo Superior de Investigaciones Científicas
Ctgb	Dutch Board for the Authorization of Plant Protection Products and Biocides
DNT	Developmental Neurotoxicity
DOI	Digital Object Identifier
DR	Data Requirements
dsRNAs	Double-stranded Ribonucleic Acid
DT_{50}	Degradation Time
ED	Endocrine Disruptors
EFSA	European Food Safety Authority
ELGO	Hellenic Agricultural Organization - DIMITRA
ERA	Environmental Risk Assessment
EU	European Union
EUP	Experimental Use Permits
GAP	Good Agricultural Practice
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
GM	Genetically Modified
INIA-CSIC	Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria
INRAE	National Research Institute for Agriculture, Food and Environment
LCASs	Low Concern Active Substances
MOA	Mode of Action
mRNA	Messenger Ribonucleic Acid
MS	Member States
NA	Not Applicable
NAM	New Approach Methodologies
NTA	Non-Target Arthropods
NTO	Non-Target-Organisms
PBPGs	Pathways to breach the protection goals
PECs	Predicted Environmental Concentrations
PerSAM	Persistence in Soil Analytical Model
PF	Problem Formulation
PPP	Plant Protection Products
QSAR	Quantitative Structure–Activity Relationships
RA	Risk Assessment
RMM	Risk Minimization Measures
RNA	Ribonucleic Acid
UTH	University of Thessaly
WoE	Weight of Evidence
WR	Wageningen Environmental Research

Appendix A – Meeting minutes

Appendix B – AGENDA