REPORT OF PESTICIDES PEER REVIEW MEETING 28

GENERAL RECURRING ISSUES IN FATE AND BEHAVIOUR AND ECOTOXICOLOGY RELATED TO THE ENVIRONMENTAL RISK ASSESSMENT OF MICRO-ORGANISMS.

4. and 5. Fate and Behaviour and Ecotoxicology

Date: 25 October 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
EU statutory staff representing EU Institutions, agencies or other bodies (other than EFSA)	EC
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National Experts nominated by MS Belgium	Federal Public Service (FPS) Health, Food Chain Safety and Environment - BE
National Experts nominated by MS Czech Republic	The Central Institute for Supervising and Testing in Agriculture - CZ
National Experts nominated by MS Germany	German Environment Agency (UBA) – DE
National Experts nominated by MS Denmark	Ministry of Environment of Denmark - DK
National Experts nominated by MS Estonia	Agriculture and Food Board - EE
National Experts nominated by MS Greece	Benaki Phytopathological Institute - EL
National Experts nominated by MS Spain	National Institute for Agricultural and Food Research and Technology (INIA) - ES
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National Experts nominated by MS Ireland	Ministry of Agriculture Ireland - IE
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National Experts nominated by MS Lithuania	The State Plant Service under the Ministry of Agriculture - LT

National Experts nominated by MS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) - NL
National Experts nominated by MS Sweden	Swedish Chemicals Agency (KemI) - SE
National Experts nominated by MS Slovakia	Central Control and Testing Institute in Agriculture (ÚKSÚP)

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

4. and 5. Fate and Behaviour and Ecotoxicology

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Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Agenda cluster 1 Agree on basic criteria and suggestions to summarize and present the assessment of the information available in sections 1, 2, 3, 5, and 7 of the data requirements used in risk characterization for non-target organisms.	Some tabular templates were presented and proposed as methods for summarizing the available information. Overall, it was considered that providing a summary table of the available biological information would be advisable. This could be included as background information in the RAR. However, drafting such a summary table was not considered mandatory for the time being. As regards, summarizing the weight of evidence (WoE), the majority of experts agreed that it should be presented in a WoE/conclusion table, quantitatively weighing the point-by-point uncertainty and assessing the individual lines of evidence. The tabular form was considered a way to increase transparency and communication when the WoE approach is applied. Regarding the potential use of the QPS approach in the WoE, it was agreed that the QPS pre-assessment is potentially informative, despite acknowledging its limitations (e.g. normally it is for higher taxonomic level). As regards read-across (considering the microorganism, phylogenetic information was deemed important but not per se sufficient evidence for justifying/addressing read-across assessments. For such purpose, further experts` judgement was deemed key. There was agreement that read-across justifications would require consideration at the species (fate) or strain (ecotox) level. In case evidence suggesting potential adversity is available (e.g., suggesting adversity of a similar strain or anti-microbial

Subject	Conclusions Pesticide Peer Review Meeting
	resistance), sufficient information should be submitted allowing to exclude the occurrence of key adverse processes in the strain under assessment. For such purpose, consideration of e.g., virulence factors may be possible. Ideally, such information should address species or strain-level specificities related to the exposure routes and hazard to each specific NTO group.
Agenda cluster 2 Agree on basic criteria for the search strategy for the literature review and the strategy to summarise and evaluate the scientific literature and dossier studies in a harmonized manner	The following points were agreed: - The proposal of using CRED for the appraisal of the literature studies and the proposed modifications were supported. GLP should not be considered a reliability criterion for published studies (Lahr, 2023). - Literature searches for microorganisms may need to be produced in an iterative way in order to identify the relevant taxonomic levels for which information is available (e.g., starting with the strain level and broaden it out from there when needed). But a clear conclusion applicable to all situations and whether top down or bottom up approaches should be applied has not been reached. The search strategy may depend on whether the regulatory question could have been addressed with the search. The minimum requirement for the string search is, in addition the key words, the NTOs as considered by the data requirements (from 8.1 to 8.7). - It is agreed that a reliability assessment for not relevant studies is not necessary. - Separate literature searches should be performed for the metabolites (including of MoC). Studies should be considered if the metabolites of concern are produced by other species or strains. Relevant metabolites guidance should be followed (SANCO 2020-12258). - With respect to the studies that were performed outside Europe (or on non-European species) it is agreed that this is not necessarily a reason to exclude a study.
Agenda cluster 3 List, discuss and agree on crucial and essential issues with regard the test design for pathogenicity and infectiveness.	<u>General issues</u> *Study duration*

Subject	Conclusions Pesticide Peer Review Meeting
	The duration of the study should be adapted depending on the non-target species being tested and the biological properties of the micro-organism, as covered in the explanatory note. The test duration should be sufficiently long to enable infectivity and pathogenicity to be detected. Acute studies should not be accepted for pathogenicity. *Control treatments* A reference control with a chemical compound is not necessarily needed for studies with microorganisms although it may demonstrate that the test design can detect effects. A positive control for pathogenicity is also not routinely needed. Nevertheless, when it cannot be excluded that the microorganism may be pathogenic to the test organism, then, a positive control for pathogenicity could be considered. For all cases, the viability of the microorganism would need to be confirmed every time before dosing the test organism, which is in line with the Canadian test guideline(s). <u>Specific issues</u> *Terrestrial vertebrates* In the absence of testing guidelines with reptiles and amphibians and a risk assessment scheme, a systematic literature search should be the starting point of the risk assessment of these NTOs. In principle, the risk assessment could be conducted using a weight of evidence approach with robust lines of evidence and all available information (e.g., biological properties of the microorganism, mode of action, studies with other vertebrates). The absence of evidence might not be enough to conclude low risk and, in that case, it should be concluded that the risk assessment cannot be finalised for amphibians/reptiles. *Aquatic organisms* It was agreed that using nominal concentrations can be appropriate in aquatic tests with microorganisms only if confirmed at the beginning and at the end of the test as it is done for chemical testing. *Non-target arthropods other than bees* The relevant exposure route(s) in relation to the mode of action and biological properties should be considered for the study design. - When the oral exposure route is relevant, tier 1 - glass plate studies are not fully relevant and, therefore, should not be accepted.

Subject	Conclusions Pesticide Peer Review Meeting
	- When the contact route of exposure is relevant, glass plate studies could inform on the potential toxicity (not pathogenicity) of the test material. Extended laboratory studies with leaf discs would be preferred. For the selection of the test organisms, case-by-case consideration is needed, including a consideration on the intended use(s). The two standard species tested for chemical compounds (*Aphidius rhopalosiphi* and *Typhlodromus pyri*) might not always be suitable for microorganism and additional species, including soil-dwelling organisms, could be tested. IOBC test guidelines from Candolfi et al. (1998) are available for a number of non-target arthropod species other than the standard ones and should be used as a starting point although a drawback is that guidance for assessing infectivity and pathogenicity is not included in these guidelines. *Microorganism/MPCA-AM vs. formulated product (all groups of non-target organisms)* In the absence of negative effects on the non-target organism, studies with the formulated product could potentially address all the regulatory questions, such us pathogenicity, toxicity of co-formulants, and metabolites of concern (when present in the formulated product). However, when negative effects are observed in those tests with the formulated product, then, further studies might be needed to elucidate the cause of such effects.
Agenda cluster 4 In relation to Risk assessment: (e.g.) • Discussion on the potential use of the 'margin of safety' approach, maximum hazard concentration (MHC) approach • Qualified Presumption of Safety (QPS) approach • Quantitative vs. qualitative risk assessment and WoE. • The use of the summaries in the WoE	Regarding the microorganisms, the following points were agreed: - To calculate exposure PED values, it is appropriate assuming no degradation or interception following indications of the explanatory notes; - Using the Maximum Hazard Concentration (MHC) approach is a possible option (e.g., assuming 10-100 x field rate). In such case, the effect endpoint can come from studies conducted with MHC as in the US-EPA guidance or in OECD 67, if appropriate, or dose-response studies; - If a MoS < 1 is identified the risk is not necessarily concluded as high. Instead, it may be possible to further address it by e.g., using a WoE approach or effect and/or exposure refinement. For the metabolite of concern and PPP co-formulants, the following points were agreed: - Assessment factors of the TERs/HQs can be applied (the presence of MoC should be proven); - the same assessment factor as in part A of the Uniform Principles is also applicable to the assessment for NTTPs.

Subject	Conclusions Pesticide Peer Review Meeting
	As regards risk management, there was agreement with the proposed EU-level approach on off-field exposure quantification (i.e., quantification via standard Rautmann curves for spray drift, as outlined in the explanatory notes). Consistent with this approach, specific mitigation of the off-field drift by means of no-spray buffer zones was deemed appropriate for consideration at the national level. However, the quantification of the drift reduction off-field via drift-reducing nozzles was not unanimously considered appropriate for products containing MOs, due to the potentially different behaviour of the microbial PPP. Nevertheless, if similarity of PPP containing microorganisms to PPP containing only chemical is demonstrated, than MSs could consider this RMM option for the assessments for off-field. As regards the natural background level of the microorganism, the following points were agreed: - Background level info can be used as qualitative line of evidence in a WoE approach, noting the compartment- and scenario-specificity to such assessment (i.e., soil background level is not to be deemed informative of other compartments); - A definition of „natural" background is not relevant (in line with the data requirements), as agricultural environments are artificial. Further work/discussion needed before agreeing upon a quantitative use of background exposure levels in the ERA
Agenda cluster 5 Agree on proposals for: • testing strategy for terrestrial non-target organisms for metabolites of concern and MCPA. • approaches for soil exposure characterization for metabolites of concern, and for the microorganism .	<u>Testing metabolites (MoC):</u> If the applicant submits data of metabolites that can be synthesised or purified from a fermentation, Part A of the data requirements should be followed. However, if the metabolite cannot be obtained in relevant quantities (not having the molecule) and having the toxicity data (on NTOs) with analysis of metabolites in the tested material, the concern for the metabolites can be addressed. because information on toxicity (submitting the analytics) of metabolite(s) can be deduced <u>Characterization of level of Metabolite in the batch (Products):</u> In case the MoC plays a role in the effect then the risk from MoC maybe addressed by testing MPCA-AM/PPP. Tests with the mixture (PPP and MPCA-AM) should specify the amount of MoC in the mixture, by providing the analytics of MoC (how much of MoC is in the test material). Although, test design addressing just toxicity of MoC or only the pathogenicity of the microorganisms may need to be different,

Subject	Conclusions Pesticide Peer Review Meeting
	addressing both in one test may be possible however it may result in a very complex test design. <u>Monitoring Studies (Data Requirements 7.1.3 and 7.2.2):</u> It is not recommended to ask monitoring studies to the applicant. Applicant should submit monitoring and ecology studies from literature when available. Monitoring could normally contribute to a qualitative assessment only (example: have better understanding of MoC level produced by the closely related species) <u>Higher Tier Studies (Data Requirements 7.1.4 and 7.2.3):</u> Field studies are not generally recommended (too many variables playing a significant role). A model laboratory experiment is more preferable for deriving both exposure and/or effect endpoints. Analytical method to evaluate the level of strains/microorganisms as well as MoC in the test system. is needed to have characterised the test material and experimental matrices.
Agenda cluster 6 Create and agree on a list of definitions/abbreviations	The list of definitions presented in the meeting was considered valuable by the experts. However, most of the terms are already included and agreed in the explanatory notes. Therefore, the experts agreed that currently a new repository with definitions and abbreviations is not needed. In any case, the document presented in the meeting will be made available. Attention should be paid to ensure consistency in the definition of terms across the different documents. It was recognised that some of the terms might need to be revised in the future after some practical experience.
Agenda cluster 7 Among others, to agree on biological information to be provided on the micro-organism under evaluation e.g. naturally occurring background levels, mode of action, details of method of application, mobility and persistence, etc..	The MoA is generally a key source of information; therefore, the experts at the meeting agreed that it should be available (ideally as detailed as possible). However, it was acknowledged there can be cases when the MoA is not yet investigated and understood sufficiently, but an exposure assessment and consequent RA still can be performed. When the microorganism is effective by a direct MoA (infectivity, pathogenicity and / or toxicity) it needs to be described in detail.

Subject	Conclusions Pesticide Peer Review Meeting
	The experts at the meeting agreed that full details on the method how the PPP (GAP) is used in the field has to be available. Pending on certain circumstances, persistence and information on natural background level can be essential (not automatically for all assessments). The experts at the meeting discussed and agreed that when this information is needed, it should ideally be requested at strain level. However, assessment considering higher taxonomic level can also be accepted if similarity with the strain under assessment, in terms of biology and MoA is sufficiently justified and underpinned with some data (e.g. phylogenetic/molecular similarity, virulence). This is in line with the explanatory notes. The experts agreed that data from the literature should be considered in the Weight of Evidence (WoE) only if they address the right taxonomic level. The experts agreed that no general criteria can be set regarding when the MO should fall back to the natural background level after the application. Some may persistent or even increase. Nevertheless, it was agreed, that (in line with the DR and the explanatory notes) the test (as required by 7.1.4 when applicable) should last at least until clear decline is evidenced. If this is not seen, then no conclusion can be drawn on the persistence. It was acknowledged that, the mobility is not explicitly mentioned in the new DR for the MO (in section 7). It is however an important parameter to be judged. Two characteristics were particularly highlighted to be considered (usually information should be found under the biological properties and summarized in the fate section as appropriate): 1) it is important to understand if the MO produce spores (i.e. as part of the life cycle) and whether the spores are likely mobile e.g. by the air (or e.g. more likely immobile in the soil); 2) it is important to have a good understanding on the host range and the mobility/behaviour of the host organisms. Groundwater contamination by the MO is not a point that needs to be assessed. If MoC are identified, the mobility parameter (i.e. Koc) amongst others is essential to estimate the PEC values, as requested by the DR (i.e. Part A).