Outcome of the public consultation on the draft guidance on the assessment of the safety of feed additives for the environment

European Food Safety Authority (EFSA)

Abstract

The European Food Safety Authority (EFSA) carried out a public consultation to receive input from the scientific community and all interested parties on the draft guidance on the assessment of the safety of feed additives for the environment prepared by the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) and endorsed by the Panel for public consultation at its Plenary meeting on 2 October 2018. The written public consultation for this document was open from 8 October to 19 November 2018. EFSA received a total of 133 comments from 11 interested parties. EFSA and its FEEDAP Panel wish to thank all stakeholders for their contributions. The current report summarises the outcome of the public consultation, and includes the comments received and how the comments were addressed. The FEEDAP Panel prepared an updated version of the guidance on the assessment of the safety of feed additives for the environment taking into account the questions/comments received. This guidance was discussed and adopted at the FEEDAP Plenary meeting on 27 February 2019, and is published in the EFSA Journal.

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Key words: Guidance, assessment of the safety of feed additives for the environment

Requestor: European Food Safety Authority

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1. Introduction

1.1. Background and Terms of Reference as provided by EFSA

The European Food Safety Authority (EFSA) asked the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) to produce a guidance document on the assessment of the safety of feed additives for the environment. The draft guidance was endorsed by the FEEDAP Panel on 2 October 2018.

In line with EFSA's policy on openness and transparency and in order for EFSA to receive comments from the scientific community and stakeholders on its work, EFSA engages in public consultations on key issues.

The FEED Unit is requested to produce a Technical report summarising the outcome of the public consultation on the draft guidance on the assessment of the safety of feed additives for the environment.

2. Methodologies

The draft guidance on the assessment of the safety of feed additives for the environment, which was endorsed by the FEEDAP Panel on 2 October 2018, was released for public consultation from 8 October to 19 November 2018. Stakeholders were informed and invited to submit comments. All comments were subject to evaluation and assessment. Where considered appropriate, the guidance document has been modified to take account of the comments (EFSA FEEDAP Panel, 2019).

3. Assessment

EFSA received 133 comments from 11 interested parties: six public organisations, one industry association, one private company and three consultant organisations. The comments received (after removal of duplicates) are listed in Table 1, together with answers or comments from EFSA. All comments were subject to evaluation and assessment.

EFSA and its FEEDAP Panel wish to thank all stakeholders for their contributions.
**Table 1:** Comments received during the public consultation on the draft guidance on the assessment of the safety of feed additives for the target species.

| # | Organization          | Chapter       | Comment                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Comment by EFSA                  |
|---|-----------------------|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| 1. | Pen&Tec Consulting, S.L.U. | General comments | Pen & Tec Consulting SLU (PenTec) is an EU-based consultancy that has supported over 200 feed and food dossiers through EU evaluations, covering a wide range of food chain and companion animal products, including food and feed enzymes, probiotics and botanicals, and covering all categories and functional groups of feed additives, as well as novel foods. PenTec welcomes this draft EFSA guidance on the assessment of safety of feed additives for the environment. Regulation (EC) Nº 429/2008, together with EFSA guidance documents, are the key documents consulted by applicants when preparing applications for authorisation of feed additives in the EU. PenTec believes that EFSA’s risk assessment must be based on guidance documents that advocate a consistent approach across the food chain and that allow for pragmatic updates, while maintaining excellence in evidence-based science, taking into account documented safe uses and/or best practice from existing or new EU legislation and previous EFSA innovations. Applicants expect EFSA guidance documents to define clearly which data are needed for each assessment and which data may be waived by providing suitable justifications. Via the REFIT procedure, the EU Commission (EC) may review Regulation (EC) Nº 429/2008, and we recommend that EFSA guidance documents are updated as necessary, after any amendments to Regulation 429/2008. Detailed comments will be sent separately, with specific sections and lines indicated. | Noted                            |
| 2. | FEFANA                | General comments | EFSA should fulfil the claim that the guidance can be used as a practical guide. Clearly laid out tables of example test methods immediately after each stage of the phase could effectively improve the practical implementation, so that the guidance meets user expectations and can be used as a helpful tool to meet legal requirements.                                                                                                                                                                                                                     |                                  |
| 3. | FEFANA                | General comments | Especially regarding the re-authorization, a practical guideline and the creation of a usable database for substance evaluation would be useful in order to compile the data effectively and swiftly. If the test methods are clearly listed in tabular form, this data could be used as a start to create a database from the data in which the data sets are collected and accessible to the applicants. Knowledge can be transferred with the help of a database. It is not effective if the test methods are clearly listed in tabular form, this data could be used as a start to create a database from the data in which the data sets are collected and accessible to the applicants. Knowledge can be transferred with the help of a database. |                                  |

Although EFSA agrees that such a database would be helpful to applicants, considering the provisions foreseen in Regulation (EC) 1831/2003 of confidentiality and data protection, it is not feasible at this stage to create such a publicly accessible database.
|   |   |   |
|---|---|---|
| 4. | FEFANA | General comments |
|   |   | It would also be worth considering a higher-level environmental monitoring program to better comply with the precautionary principle and to improve the networking of stakeholders. Aiming to represent the public interest and through an open data flow by continuously measuring environmental data in a representative manner at fixed locations. A trend can only be detected by a long-term documentation. Through a continuous monitoring program of significant measuring sites, studies on ecotoxicological studies on chronic effects and long-term effect studies can be performed. |
|   |   | This is out of the scope of this guidance. |
| 5. | FEFANA | General comments |
|   |   | Editorial comment: Symbols (i.e.: multiplication signs) and subscripts need to be harmonised in all equations of the guidance document. |
|   |   | Editorial comment. The guidance was updated accordingly |
| 6. | FEFANA | General comments |
|   |   | Editorial comment: Regarding the explanation of the symbols following the different formulas, we propose that either symbols or parameters within each sub-chapter (Additive properties, substance independent Input, etc.) are ordered alphabetically or in order of appearance. |
|   |   | The symbols have been reported in alphabetical order under the equations; they are divided into three categories: input (in alphabetical order), Intermediate Output (i.e. PEC\textsubscript{manure}) and Output |
| 7. | Institute of Marine Research | General comments |
|   |   | The Institute of Marine Research is a governmental research institute and a neutral knowledge provider. Our mission is to supply knowledge relating to the sustainable management of the resources in our marine ecosystems and the whole food chain from the sea to the dinner table. The Institute of Marine research calls for a revision of the existing guidelines for assessing the safety of feed additives for the marine environment. Feed additives used in aquaculture can result in contamination of sediment and water. The compartment of concern for the environmental risk assessment for fish farmed in cages is assumed to be the sediment. Accumulation of feed additives in marine sediments will depend on several factors, where most of them will be specific for the site where the additive is released. The distribution of feed additives in the marine environment is linked to the fate of the faeces and to some extent, uneaten feed. The concentration of feed additive in the faeces will depend on the bioavailability of the compound in the fish. Sedimentation rates of organic material (e.g. faeces) are highly variable and the water current at the site will have a large impact on the distribution. When the organic matter has settled on the seafloor it will either be resuspended and transported downstream, incorporated into the sediment |
|   |   | The point of the applicant is acknowledged. In the course of the preparation of the guidance the most recent developments in the field have been investigated. There is work ongoing on this in scientific institutions. The guidance will be updated once the models under development are available and validated. |
by fauna activity (bioturbation) or decomposed by the fauna and bacteria community. The conditions in the sediment will vary due to the decomposition rate of the organic matter, and the oxic state of the sediments will fluctuate (oxic/anoxic). The oxic state often determines the binding capacity of an additive in the sediment together with the lipophilicity of the additive. Together with the level of decomposition and outwashing, these factors will affect the half-life of the additive in the sediment. Other factors such as fish species, resuspension and fallowing periods may also have an effect on the fate of the feed additive in the marine environment. The current model used for assessing the effects of feed additives on the marine environment was published in 2008 (EFSA 2008). As described, many factors affect the concentration of feed additives in sediment. Since 2008 more data has become available regarding the fate of feed additives from fish feed and about fish faeces in the marine environment. This opens for a revision of the model for calculating the predicted environmental concentration of feed additives in sediment as well as of some of the values assigned to parameters. Consequently, the Institute of Marine Research recommends that the current technical guidance for assessing the safety of feed additives for the marine environment is revised.

8. Association of Veterinary Consultants

General comments

The Association of Veterinary Consultants (AVC) was founded in 1995 in Brussels & is a stakeholder organization recognised by the EMA (European Medicines Agency), EFSA, & the European Commission. AVC members number more than 50 international veterinary practitioners, providing expert services to global feed, food, & pharmaceutical industries, frequently involved in advising governments & regulators on key issues relating to human/animal health & nutrition. Among the AVC’s guiding principles are key concepts of evidence-based science, improving animal welfare, & reducing animal experimentation wherever possible. The AVC welcomes the opportunity to comment on his draft EFSA guidance on the assessment of safety of feed additives for the environment. The AVC recognises & supports EFSA’s efforts & progress in risk assessments based on guidance documents that advocate a consistent approach across the food chain, aiming to maintain excellence in, independent, evidence-based science, whilst now taking into account documented safe uses & best practice. EFSA guidance documents must define clearly which data are needed for each assessment, & which data may be waived by providing suitable justifications. Via the REFIT procedure, the EU Commission (EC) is reviewing Regulations 1831/2003 & 429/2008. AVC recommends that EFSA guidance documents are updated as necessary, after any amendments to these regulations.

9. SCC Scientific Consulting

General comments

Ref: Page 4, last line, box on the right and Page 67, line 2096
Comment: This refers to application of FOCUS models in ground water, in particular to
| Company                                      | General comments                                                                 |
|---------------------------------------------|----------------------------------------------------------------------------------|
| Puratos                                     | We support EFSA’s initiative to update the guidance to take into account recent scientific advances. We appreciate that EFSA simplified the wording of the guidance, and set up clearer quality and performance criteria. We also welcome the inclusion of newer technologies and recent publications, as far as they provide added value on relevant safety issues and established protocols to follow. |
| German Environment Agency (UBA)             | We really appreciate the possibility to comment the proposed guidance draft and would like to thank all authors for this substantial and excellent work. Also the appendices are very much appreciated, especially protection goal basics in appendix A. Some specific comments will be provided in the individual chapters. |
| Istituto Superiore di Sanità                | This guidance is overall accurate, up-to-date and clear, although some points for possible improvements are identified (see specific comments below). One general point. The use of feed additives impinges in the more general issue of sustainability of animal farming. The guidance contains no mention of how to assess a given feed additives for its detrimental effects on emissions by animals. Indeed, the FEEDAP Panel has delivered in some instances opinions on the efficacy of feed additives intended to favourably affect the environment, for instance: Vevovitall (benzoic acid) in pigs in regard of ammonia emissions (2007, 2012), products based on 6-phytase in regard of phosphorus emissions in salmonids (2010), sows (2010), laying hens (2013) and others. In principle, the same endpoints can be used to assess both a favourable as well as a detrimental effect on emissions. On the other hand, ecotoxicological tests aim at identifying effects related to cellular/tissue toxicity (e.g., oxidative stress, cell membrane disruption) mechanisms in model organisms for the different environmental comparts. Therefore such tests likely are inadequate for assessing any detrimental effect on emissions. Suggestion: the guidance should mention that, considering the due concern for sustainability of animal production and the current lack of a consistent approach for assessing feed additives under this respect, any effect on emissions (ammonia, carbon dioxide, minerals) would be assessed on a case-by-case basis, when indicated by previous information such as the mode of action and the intended use. |

Poultry manure can be applied to grass land. The default value to start is 5 cm. If the threshold of 0.1 microgram/l is not respected, then the soil depth of 20 cm can be applied. This would represent that the manure containing the additive would have to be applied and ploughed thereafter (application restricted to arable land). A clarification is added to appendix B.

The scope of the guidance is to address the direct impact of additive in the environment, according to the principles described in Regulation (EC) No 429/2008 which focus the assessment on the active substance and its major metabolites. Other effects on the environment related to the use of a feed additive could be assessed following a case by case approach. However, considering the complexity of the effect of e.g. metabolism, diet, feeding rate...on excretion/emission of substances/gasses the FEEDAP Panel did not consider necessary to include this assessment in the present guidance.
(type and number of species, concentration in feeds, etc.) of the feed additive (see also below Phase II C)

| 13. | Puratos | Scope of the guidance |
| --- | --- | --- |
| | | The scope states that for QPS organisms safety for the environment is presumed, therefore no additional information is needed. A GMM micro-organism derived from a QPS microorganism can also be considered QPS, if certain constraints are met (e.g. molecular/genetic characterisation does not give rise to concern). Therefore, for these QPS-considered GMMs is should be logical that safety for the environment is also presumed, therefore no additional information is needed. Please add this addition to the QPS reasoning in the guidance (in line with the reasoning presented in for instance the safety of feed additives for the target species). |
| | | One thing is the safety of a microorganism used as feed additive, and another one is the safety of a food/feed additive obtained using the microorganisms as production strain. The assessment described in the scope of the guidance refers to microorganisms used as feed additives (e.g. probiotics). Feed additives in which viable genetically modified microorganism (GMM) are present, are out of the scope of this document. By law, GMM can only be released to then environment in the EU after authorisation (Directive 2001/18/EC or Regulation (EC) 1829/2003) which include an environmental risk assessment. |

| 14. | Puratos | Scope of the guidance |
| --- | --- | --- |
| | | The scope states that for QPS organisms safety for the environment is presumed, therefore no additional information is needed, which should also logically be extended for GMM-considered QPS strains (if certain constrains are met). If the GMM is considered QPS and safety can be presumed, than using this GMM in confined fermentation production and only using the produced feed additive should also be presumed safe for the environment, without additional evidence. In other words, if the whole GMM can be considered QPS and presumed safe, there is no logic reasoning why removing the GMM would result in a product not presumed safe anymore. Therefore, please add the clarification that a feed additive isolated from a GMM considered QPS should also be presumed safe. |
| | | One thing is the safety of the microorganism used as feed additive, and another one is the safety of the food/feed additive obtained using a microorganism as production strain. The assessment described in the scope of the guidance refers to microorganisms used as feed additives (e.g. probiotics). |

| 15. | Association of Veterinary Consultants | Scope of the guidance |
| --- | --- | --- |
| | | Scope of the guidance Lines 190-210

EFSA says: For those naturally present in soils, plants or gastrointestinal tract of animals, their use as feed additive is considered unlikely to measurably increase numbers in the environment where they are already prevalent. Consequently, the Panel considers that their use as feed additives would not pose a risk for the environment.

- For those not naturally present in soils, plants or gastrointestinal tract of the animals, a case-by-case assessment would be needed. The principles of an OECD Guidance to the environmental safety evaluation of microbial biocontrol agents (SANCO/12117/2012 –rev. 0) may be used as a guide. Furthermore, the European Commission is currently developing a guidance document on the risk assessment of metabolites produced by micro-organism after application as active substances in plant protection products. Such guidance document can be considered in a future update of this guidance.

AVC Comments: The AVC strongly supports the EC initiative to develop a guidance document more appropriate to existing requirements for pesticide products consisting of live micro-organisms. In particular AVC welcomes increased liaison

To indicate further potential resources, the following text was inserted in Line 207 after the parenthesis (SANCO/12117/2012): ‘…or the principles of the EFSA guidance on the risk assessment of genetically microorganisms and their products intended for food and feed use (EFSA GMO Panel, 2011) may be used as a guide.’

Noted
between EFSA & the EU Commission towards adopting the same approaches for micro-organisms used as pesticides to those working well for live micro-organisms used as feed additives. AVC supports that safety requirements for live micro-organisms are aligned, wherever they are used in the food chain. Many micro-organisms added to foods, notably dairy starter cultures & live micro-organisms used in food supplements, are not subject to a formal, pre-market safety assessment through EFSA, unless the strains are novel. Some Member States & a non-EU regulators refer to the current EFSA FEEDAP Guidance on microorganisms used as feed additives or as production organisms (EFSA 2018) when evaluating the safety of live food micro-organisms. The AVC encourages FEEDAP to engage across all EFSA Panels & with the EU Commission to achieve a common safety approach for all live micro-organisms entering the EU food chain. FEEDAP’s recent work on characterisation & safety of micro-organisms is becoming a standard for many stakeholders in EU food & feed industries, particularly food/feed business operators & EU competent authorities. The guidance contributes to significant reductions in safety testing in live animals, while maintaining the highest standards of safety evaluation, based on modern taxonomy, phenotypic testing & bioinformatics analyses of the WGS (Whole Genome Sequence).

In the ERA of feed additives consisting on microorganisms (e.g. probiotics), the natural presence in the environment and potential adverse effects on the environment of the microorganism itself should also be considered.

The FEEDAP Panel considers that natural presence of the microorganisms in the environment is relevant and has to be considered in the environmental risk assessment.

The FEEDAP Panel considers that introducing non-QPS microorganisms in the environment has to be assessed on a case by case basis. Whole genome sequencing (WGS) analysis may be useful but not sufficient to establish the safety of the microorganisms for the environment.

| 16. | Pen&Tec Consulting, S.L.U. | Scope of the guidance | Lines 191-210. As per point 5.1 of EFSA guidance on microorganisms used as feed additives or as production organisms (2018) "for bacterial strains free from acquired antibiotic resistance determinants, shown not to produce relevant antimicrobial substances according to Section 2.3 and shown to be non-pathogenic/toxigenic, no hazards and therefore no risks are identified for target species, consumers and the environment". PenTec suggests that, for consistency, the above approach also applies to this guidance, not solely assess the microorganism risk based on its ubiquity. Thus, the following addition/modification to the text is suggested. (…) - For microorganisms included in the QPS list, any impact on the environment is assessed in the framework of the qualified presumption of safety (QPS) evaluation (EFS BIOHAZ Panel, 2017). When the identity of such a microorganism included in the QPS list is unequivocally established and any qualification (if existing) is met, safety for the environment is presumed. - For bacterial strains not listed in the QPS list but free from acquired antibiotic resistance determinants, shown not to produce relevant antimicrobial substances (according to Section 2.3, EFSA, 2018*) and shown to be non-pathogenic/toxigenic, no hazards and therefore no risks are identified and safety for the environment is presumed. |
- Strains carrying acquired genes for antimicrobial resistance are presumed to pose a risk for human and animal health via the environment.

- For microorganisms not included in the QPS list or considered to be a potential hazard for the environment the following applies: (…)  

*EFSA, 2018. Guidance on microorganisms used as feed additives or as production organisms.

In addition, PenTec supports increased liaison between EFSA and the EU Commission towards adopting the same approaches for microorganisms used as pesticides, in order to bring the safety requirements for live microorganisms into alignment, wherever they are used in the food chain. PenTec notes that many microorganisms added to foods, notably dairy starter cultures and live microorganisms used in food supplements, are not subject to a formal, pre-market safety assessment through EFSA, unless novel. Some Member States and a few non-EU regulators may refer to the current Guidance on microorganisms used as feed additives or as production organisms (EFSA 2018) when evaluating the safety of live food microorganisms. PenTec encourages EFSA FEEDAP to engage across all EFSA Panels and with the EU Commission to achieve a common safety approach for all live microorganisms entering the EU food chain. PenTec believes that FEEDAP’s recent work on characterisation and safety of microorganisms can be a modern standard for many stakeholders in EU food and feed industries, particularly food/feed business operators and competent authorities. The guidance contributes to significant reductions in the need for safety testing in animals, while maintaining the highest standards of safety evaluation, based on modern taxonomy, phenotypic testing and bioinformatics analyses of the WGS (Whole Genome Sequence).

### Scope of the guidance

**Association of Veterinary Consultants**

Scope of the guidance, Lines 191-210, EFSA states:

When assessing the impact of microorganisms used as feed additives to the environment, the following scenarios may apply:

- For microorganisms included in the QPS list, any impact on the environment is assessed in the framework of the qualified presumption of safety (QPS) evaluation (EFSA BIOHAZ Panel, 2017). When the identity of such a microorganism included in the QPS list is unequivocally established and any qualification (if existing) is met, safety for the environment is presumed.

- Strains carrying acquired genes for antimicrobial resistance are presumed to pose a risk for human and animal health via the environment.

- For microorganisms not included in the QPS list the following applies:

  - For those naturally present in soils, plants or gastrointestinal tract of animals, their  

The FEEDAP Panel considers that natural presence of the microorganisms in the environment is relevant and has to be considered in the environmental risk assessment.

The FEEDAP Panel considers that introducing non-QPS microorganisms in the environment has to be assessed on a case by case basis. Whole genome sequencing (WGS) analysis may be useful but not sufficient to establish the safety of the microorganisms for the environment.

To indicate further potential resources, the following text was inserted in Line 207 after the parenthesis (SANCO/12117/2012): ‘…or the principles of the EFSA guidance on the risk assessment of genetically microorganisms and their products intended for food and feed use (EFSA GMO Panel, 2011) may
use as feed additive is considered unlikely to measurably increase numbers in the environment where they are already prevalent. Consequently, the Panel considers that their use as feed additives would not pose a risk for the environment.

- For those not naturally present in soils, plants or gastrointestinal tract of the animals, a case-by-case assessment would be needed. The principles of an OECD Guidance to the environmental safety evaluation of microbial biocontrol agents (SANCO/12117/2012 –rev. 0) may be used as a guide. Furthermore, the European Commission is currently developing a guidance document on the risk assessment of metabolites produced by micro-organism after application as active substances in plant protection products. Such guidance document can be considered in a future update of this guidance.

AVC Comments: As per point 5.1 of EFSA guidance on microorganisms used as feed additives or as production organisms (2018) "for bacterial strains free from acquired antibiotic resistance determinants, shown not to produce relevant antimicrobial substances according to Section 2.3 and shown to be non-pathogenic/toxigenic, no hazards and therefore no risks are identified for target species, consumers and the environment".

AVC suggests that for consistency the above approach can also apply to EFSA’s environmental safety guidance, i.e. not assessing risk based solely on ubiquity of the microorganism. Using modern molecular techniques, analysis of WGS, & phenotypic testing, there is no need to test environmental safety via in vivo testing in animals. Thus, the following addition/modification to the text is suggested.

(…)

- For microorganisms included in the QPS list, any impact on the environment is assessed in the framework of the qualified presumption of safety (QPS) evaluation (EFS BIOHAZ Panel, 2017). When the identity of such a microorganism included in the QPS list is unequivocally established and any qualification (if existing) is met, safety for the environment is presumed.

- For bacterial strains not listed in the QPS list but free from acquired antibiotic resistance determinants, shown not to produce relevant antimicrobial substances (according to Section 2.3, EFSA, 2018*) and shown to be non-pathogenic/toxigenic, no hazards and therefore no risks are identified and safety for the environment is presumed.

- Strains carrying acquired genes for antimicrobial resistance are presumed to pose a risk for human and animal health via the environment.

- For microorganisms not included in the QPS list or considered to be a potential
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| Page | Section | Text |
|------|---------|------|
| **hazard for the environment the following applies: (…)** | | |
| “EFSA, 2018. Guidance on microorganisms used as feed additives or as production organisms.” | | |
| | | |
| 18. Pen&Tec Consulting, S.L.U. | Scope of the guidance | Lines 195-196: “When the identity of such a microorganism included in the QPS list is unequivocally established and any qualification (if existing) is met, safety for the environment is presumed.” PenTec suggests to clarify “qualification” with examples (e.g. absence of AMR, and/or toxins/virulence factors). The qualifications for different types of microorganisms (e.g. antimicrobial resistance, toxin production) are detailed in the Update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA 9: suitability of taxonomic units notified to EFSA until September 2018 (EFSA Journal 2019;17(1):5555) |
| 19. Puratos | 1. Introduction | The scope states that for QPS organisms safety for the environment is presumed, therefore no additional information is needed. Since a QPS organism used as a feed additive can be considered safe for the environment, it should follow logically that any food additive isolated from such a QPS organism (kept in confined production) should equally be considered safe for the environment. Please add this to this section. One thing is the safety of a microorganism used as feed additive, and another one is the safety of a food/feed additive obtained using a microorganisms as production strain. The assessment described in the scope of the guidance refers to microorganisms used as feed additives (e.g. probiotics). Feed additives obtained from fermentation must follow the usual Phase I (and depending on the outcome also Phase II). For instance, the manufacturing process could introduce substances causing adverse effects on the environment. In addition, the food/feed additive obtained from fermentation (e.g. an ionophore) could have intrinsic properties causing adverse effects on the environment. |
| 20. FEFANA asbl | Introduction | Lines 221 - 226: a. How should the methodological substance feasibility take place? b. How can I rate everything together? The present draft guidance lacks a short, practical, coherent application methodology, which is above all manageable. - It would be helpful to have a to-do list, a list of the tests to be completed (OECD), due to the complexity of the guidance. - Short instructions of the implementation steps. c. How can an easily applicable and, above all, clear methodological substance evaluation be carried out? In the introduction a general overview is provided and the details are in the core of the guidance document. |
| 21. FEFANA asbl | Introduction | Lines 253 – 254: “Some feed additives that might otherwise stop in Phase I may require additional environmental information” Is it correct to assume that this concerns to additives later described as PBT or vP/vB? Otherwise, please add examples. Please clarify/give examples The safety concerns may not only relate to PBT or vP/vB. It cannot be excluded that in Phase I an additive is recognised as potential risk for the environment for instance from assessments performed by other scientific assessing bodies. |
| 22. FEFANA asbl | Section 2 | L 267 At the beginning of every phase (Phase I, Phase II, Phase II A and Phase II B) the possible test methods needed to generate data for calculation of the environmental compartments PEC soil, PEC groundwater, PEC sed, PEC surface water etc. The formulas with explanations on the parameters used are indicated in each section. The guidance was reviewed and clarifications have been added when considered necessary. |
|   |   |   |   |
|---|---|---|---|
| 23. | Pen&Tec Consulting, S.L.U. | 2. Phase I assessment | Lines 271-272: “The ERA of major species can be extrapolated to minor species when the same use is proposed.” Would EFSA accept extrapolation criteria outlined in the EFSA Guidance on the assessment of the efficacy of feed additives? |
|   |   |   | The extrapolation criteria outlined in the EFSA guidance on the assessment of efficacy of feed additives cannot be accepted for the ERA because the predicted environmental concentrations depend on the feed intake and the nitrogen excretion of each species. When a major species has a worst-case environmental exposure in Phase I, it can be extrapolated to a minor species. It has been clarified in the guidance document that ‘the same use’ means ‘the same conditions of use’ |
| 24. | Pen&Tec Consulting, S.L.U. | 2. Phase I assessment | Lines 276-279: “The additive is a natural substance, or made of natural substances, the use of which as a feed additive would not exceed its natural occurring concentrations in feed sources, and/or would not substantially alter the concentration and/or distribution of the substance in the receiving environment;” PenTec sees a discrepancy between this section and line 308, since line 277 refers to concentrations of the additive in feed sources, whereas line 308 refers to concentrations of the additives in plants (not necessarily feed sources). As the subject of the guideline is release/presence in the environment, PenTec considers that the generic term “plant” instead of “feed source” should be applied in lines 277, 304 and Figure 1. Not necessarily all times will correspond to the concentration of a substance present in plants. It could be present in feed sources other than plants (e.g. astaxanthin). Plants may become ‘feed sources’, but not all feed sources are based exclusively on plants. |
| 25. | German Environment Agency (UBA) | 2. Phase I assessment | In the lower part of the decision tree between “Q5 Yes” and “Phase II required” it should be make clearer that no cross connection between Q5 and Q6 arrow lines occurs. The current version might be confusing. The figure was reviewed. |
| 26. | FEFANA asbl | Section 2 | L 289 Looking at the decision tree, the following questions arise immediately. It would be helpful to see a direct solution. - Q3: Which test to prove the degradation of the additive in the animal and in the fertilizer? - Q5: Does the substance accumulate in the soil? Are there other effects? Which test should be used? - Q6a and Q6b: What test for PEC in pore water and soil, surface water and sediment? Could EFSA create a small, clear table with example test methods behind the decision tree? Table contents: (Test name + link, data available yes or no, does data already exist?). Please show examples of test methods directly. Please note that: - Explanations on degradation (metabolism or in manure) are provided in Section 2.3; - Explanation to question 5 is provided in Section 2.5; - Regarding questions 6a and 6b questions here are no tests. Just calculations. How to calculate it is reported in Section 2.6.1. |
| 27. | FEFANA asbl | Section 2 | L 290 Figure 1: Quick-check – Environmental Risk Assessment: Phase I Q5: Multi-year application of an additive should be only a concern if the feed is accumulated is a problem when PEC plateau is higher than the PNEC. It is about accumulation in soil, not bioaccumulation in an organism. It refers to |
| No. | Organization | Question | Description |
|-----|--------------|----------|-------------|
| 28. | FEFANA asbl | 2.1 Question 1: Is the additive intended for non-food producing animals only? | Editorial comment, Lines 300 – 301: Please clearly indicate reference to the referred questions. Please replace the sentence by: For those exceptional cases, the ERA would proceed through the questions outlined in chapter 2.2 – 2.6. |
| 29. | German Environment Agency (UBA) | 2.2 Question 2: Is the feed additive a (made up of) natural substance(s), the use of which would not exceed its natural occurring concentration in feed sources and/or would not significantly alter the concentration and/or distribution of the substance? | Line 305 It remains unclear how a “significant” alteration of the concentration and/or distribution of the substance in the receiving environment is defined. It should be considered to delete “significantly” in order to avoid different opinions of assessors if the PECsoil resulting from animal’s intake of food additives is “significantly” higher compared to natural background concentrations. It seems to be more reasonable to refine and maybe accept a calculated PEC than having endless discussions how much the PEC is allowed to exceed natural concentrations. |
| 30. | Puratos | 2.3 Question 3: Is the additive extensively metabolised in the target animal or rapidly and completely degraded in manure? | Is a rationale also sufficient, e.g. there is no reason to assume a normal protein (e.g. an enzyme) is not rapidly degraded. Does specific data need to be shown, or can logic reasoning be sufficient, as has been accepted (and published in the opinions) by EFSA until now. A rationale might be acceptable in specific cases and will be assessed on a case by case basis. |
| 31. | Pen&Tec Consulting, S.L.U. | 2.4 Question 4: Is the feed additive a potential Persistent, Bioaccumulative and Toxic | Line 343: "Annex XIII of the REACH Regulation (EC) No 1907/2006 (5) Footnote: (5) OJ L 396, 30.12.2006, p. 1" It has been updated by adding ‘and subsequent amendments’. |
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### 2.5 Question 5: Has the additive a specific mode of action of concern or may it potentially accumulate in soil due to multi-year application?

Line 379: the issue of endocrine disruption can be mentioned here as it is a major one at EU level, concerning both human health and environmental safety (ECHA-EFSA Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009, EFSA J 2018).

The Panel considers that the example mentioned (reproduction toxicity) is illustrative enough to clarify the meaning of the question.

### 2.6.1 Calculation of PEC in soil (PECsoil)

Please explain why the depth of 20cm has been removed and changed to only 5cm. What has changed why 20cm is no longer acceptable?

The ERA guidance of 2008 considered a soil depth of 20 cm in PECsoil calculations only for poultry manure when applied on arable land. There is evidence that poultry manure is spread on grass land in Europe and it is not incorporated into the soil by ploughing. For this reason, it was decided to reduce it to 5 cm for all animal species.

If there is evidence of active metabolites having toxicity due to their mode of action, the additive should go directly to Phase II. This possibility is already highlighted in question 5 when ‘other substances’ are considered: ‘Other substances, on the basis of toxicological studies on laboratory animals or other evidence, may show toxicological properties in vivo that are of potential concern for environmental biota at sub-lethal concentrations, e.g., reproductive toxicity.’

If both equations the input parameter RHSoil is used, but the respective tables below indicate that both are different values, one referring to dry and the other to wet.
|   | Agency (UBA) | (PECsoil) | wet soil. In order to avoid confusion, two different abbreviations should be used for “RHOsoil”. |
|---|-------------|-----------|------------------------------------------------------------------------------------------------|
| 36. | FEFANA      | 2.6.1 Calculation of PEC in soil (PECsoil) | Line 442:  
Why has the default mixing depth of 20 cm been removed?  
Please clarify why the 20 cm limit has been removed. Is it due to farming practices? Are these farming practices common in Europe?  See the reply to comment 33. |
| 37. | Puratos     | 2.6.2 Estimation of PEC groundwater | For certain feed additives it might impossible to calculate PECgroundwater, as certain parameters (eg Vapour pressure or water solubility) cannot be determined. Is it in this case, as accepted by the EFSA until now, still sufficient to show only the estimation of PECsoil giving no risk? Vapour pressure and solubility can be estimated. If the compound is not volatile or soluble, calculations could be done with very small values, e.g. 0.0001 mg/l for solubility and 10^{-13} Pa for vapor pressure. |
| 38. | Pen&Tec Consulting, S.L.U. | 2.6.2 Estimation of PEC groundwater | Line 447:  
"2.6.2. Estimation of PECgroundwater”  
For consistency with previous sections (2.6.1), PenTec suggests changing wording to:  
2.6.2. Estimation of PEC in groundwater (PECgw) Text modified to take account of the comment |
| 39. | FEFANA      | 2.6.2 Estimation of PEC groundwater | Editorial comment, Line 468:  
Please include the brackets where appropriate in the equation.  
Ksoil-water = (Fairsoil x Kair-water) +Fwater-soil +(Fsolidsoil x Kpsiol x RHOsolid/1000) Text modified to take account of the comment |
| 40. | Pen&Tec Consulting, S.L.U. | 2.6.2 Estimation of PEC groundwater | Page 17, Line 468  
For consistency with the glossary of symbol/parameters and the other formulas PenTec suggests:  
- to add the ‘x’ symbol instead of ‘*’ to represent multiplication,  
- to use ‘PECpw’ instead of ‘PECportewater’,  
- to use ‘Ksoil-water’ instead of ‘Ksoil water’,  
- to consistently use subscripts throughout formulas and glossaries in the document. Text modified to take account of the comment |
| 41. | Pen&Tec Consulting, S.L.U. | 2.7 Question 6b: Is the predicted | Page 18, lines 481-484:  
"In aquaculture operations involving the use of sea cages, benthic organisms (living Text modified to take account of the comment |
| Page 18, lines 493-496: |
| If PEC for sediment: |
| - (PECsed) (default: 5 cm depth assuming 2±0.5% organic carbon (OC)) is less than 10 μg/kg dry weight; and |
| - PEC for surface water (PECsw) is less than 0.1 μg/l |

Bullet points re-arrangement suggested:

"If:
- PEC for sediment (PECsed) (default: 5 cm depth assuming 2±0.5% organic carbon (OC)) is less than 10 μg/kg dry weight; and
- PEC for surface water (PECsw) is less than 0.1 μg/l"
|   |   |   |   |
|---|---|---|---|
| **Consulting, S.L.U.** | PEC in the sediment (PECsed) for sea cages | The multiplication dot (·) before \(k_{dep}\) is redundant considering the presence of \(x\), therefore PenTec suggests removing the multiplication dot for consistency with the rest of the formulas: In general, PenTec suggests using the same multiplication sign throughout the dossier, instead of alternating “\(x\)”, “\(*\)” and “\(\cdot\)”. |   |
| 45. | FEFANA | 2.7.1 Calculation of PEC in the sediment (PECsed) for sea cages | Line 507: We note that PECsed is based on dry weight, as in the current guidance it is based on wet weight. Please clarify | In sediment ERA for e.g. pesticides it is common practise to express the PECsed in terms of mg/kg dry weight sediment (or in terms of μg/g organic carbon in dry sediment). Also, sediment toxicity estimates according to OECD guidelines with artificial sediment usually are expressed in terms of mg/kg dry weight. Key is that the PEC should be expressed in terms of the same metric than the toxicity estimate to appropriately link exposure to effects. A PEC expressed in terms of mg/kg wet weight will of course be lower but can only be used in ERA if the toxicity estimated are expressed in mg/kg wet weight as well and the water content (and OC content) of the sediment is similar for both the PEC and NOEC/ECx estimates. |
| 46. | FEFANA | 2.7.1 Calculation of PEC in the sediment (PECsed) for sea cages | Line 507: Why has the default depth of 20 cm been changed to 5 cm despite in Regulation (EC) 429/2008 is set at 20 cm? Please clarify where this number comes from. | The PEC in sediment for sea cages is brought in line with that for soil. The predicted environmental concentration in soil is calculated with a default depth of 5 cm when manure is spread on the surface. Debris contaminated with feed additives from sea cages will accumulate at the sediment surface and exposure concentrations will be highest there. In addition, in the upper centimetres of sediment the biological activity of benthic organisms is larger than in deeper layers. There is no ploughing of sediment. Therefore, there is no logic to have different depth default values for PECsoil and PECsed. |
| 47. | FEFANA | Section 3 | L 534 and L980 A short tabular list of example tests for the detection of persistent, bioaccumulate and toxic substances should be included. Please show examples of test methods directly | Each part of the guidance explains what study is necessary. A long list at the beginning may be confusing since not all the studies suggested are always necessary for compounds that deserve a Phase II assessment. |
| 48. | FEFANA | Section 3 | L 561 – 568 and Fig 3 When doing Phase IIB and IIC in parallel, a calculation of PECB/PNECR is not necessary if PECB/PNECI AND PECA/PNECR < 1. What happens if one of the two ratios is below and the other is above 1? Is any of the two tiers worth more than the other? Please clarify: Are Phase IIB and Phase IIC actually parallel or sequential tiers? If they are parallel, does ANY ratio ≥ 1 trigger the PECB/PNECR-calculation? | The figure shows different possibilities. What matters is to have a PEC/PNEC ratio below 1, whatever the approach taken. |
### 49. FEFANA
- **Section 3**
- **L 566 and Figure 3**
  - Does the risk ratio have to be ≥ 1 (as suggested in Figure 3) or > 1 (as suggested in line 566) to warrant a PNECR? Please harmonise figure and text
  - It has been harmonised with the sign ‘≥’

### 50. German Environment Agency (UBA)
- **3 Phase II assessment**
- **Line 566**
  - Please replace „(ratio > 1)” with “(ratio ≥ 1)”. As correctly described in figure 3 and on other passages of text, a RQ of 1 already reflects a potential risk.
  - Text modified to take account of the comment

### 51. FEFANA
- **Section 3**
- **L 593 – 602**
  - For many existing/available chronic sediment/terrestrial studies, monitoring of substance concentration during the study is not available.
  - It is often not possible to clarify whether a decline of exposure concentration takes place in the course of the experiment. How to handle all these studies? For these studies it seems sufficiently conservative to use initial exposure concentration for deriving effect values and compare the derived PNECs with PEC max.
  - In a proper OECD study the concentration of the additive (exposure) should be measured through the study. Chronic studies with only nominal concentration of the additive are not acceptable.

### 52. FEFANA
- **3.2 Environmental fate studies**
- **Table 4 – Line 651:**
  - Under 3.2.2. the aquaculture study OECD TG 308 is mentioned. It would make sense to mention it in the overview table (Table 4) too.
  - Please also state in the table that the photodegradation study refers to ‘photodegradation in water’
  - Text modified to take account of the comment.

### 53. German Environment Agency (UBA)
- **3.2.1. Soil adsorption/desorption**
- **Line 655**
  - Please replace „dissociation constant (Kd)” with “distribution constant (Kd)”.
  - Text modified to take account of the comment.

### 54. Pen&Tec Consulting, S.L.U.
- **3.2.1. Soil adsorption/desorption**
- **Page 23, Line 668:**
  - “In most cases the Koc can be used to estimate the sorption of the feed additive to soil or sediment,”
  - The text refers to the “additive”, while lines 699 – 700 refer to the active substance/metabolites. PenTec suggests clarifying whether the studies have to be
  - The assessment is based on the safety of the additive for the environment and the evaluation is based on the active ingredient. The Koc will refer to the active ingredient. It has been clarified. In line 668, ‘active substance’ has been inserted in brackets.
|   |   |   |
|---|---|---|
| 55. | SCC Scientific Consulting Company | 3.2.2. Soil biodegradation and degradation in aquatic compartment |
|   | Ref: | Page 23, line 651f |
|   | Comment: | In Table 4 (line 651) a study according to OECD 308 should also be listed as optional study. It is stated in the text that this study type may be more relevant when feed additives are used in aquaculture (line 677). A line with “Water/sediment study (route and rate)”“OECD 308” and in line 652 “Recommended only for aquaculture use” should be added. |
|   | Text modified to take account of the comment |   |
| 56. | German Environment Agency (UBA) | 3.2.2. Soil biodegradation and degradation in aquatic compartment |
|   | lines 676-677 |   |
|   | Weak wording regarding recommendation of the OECD 308. Please do tighten the sentence "When feed additives are used in aquaculture a water/sediment degradation simulation study (OECD TG 308) is more relevant.” to e.g. “For feed additives used in aquaculture an OECD 307 should be replaced by a water/sediment degradation simulation study (OECD TG 308).” |
|   | Text modified to take account of the comment |   |
| 57. | FEFANA | 3.2.3. Photodegradation and hydrolysis |
|   | Lines 679 to 684: |   |
|   | We suggest clarifying that photodegradation refers to aquatic photodegradation (and not to photodegradation in air). Please also reference the appropriate test guideline (both OECD 316 and 111), similar to the other chapters. | Text modified to take account of the comment and clarify that it will be referred to the photodegradation in aquatic compartment. |
| 58. | SCC Scientific Consulting Company | 3.3.1. Phase II A PECsoil calculation |
|   | Page 4, last line, box on the right and Page 67, line 2096 |   |
|   | Comment: | It seems that the terms PECsoiltot and PECsoilpw are related to the first decision tree where PECpore water is the surrogate for PECgw. It seems that the depths are more related to the spreading of slurry on soil surface for grassland with 5 cm depth and spreading of slurry via incorporation for arable soils with 20 cm depth (realistic worst case)? Suggestion for line 2096: “… default 5 cm for grassland and 20 cm for arable soils (realistic worst case)”. This would be in line with the approach presented under 3.3.1 concerning the ploughing depth and would clarify the depth in relation to the application type mentioned in line 2093. |
|   | There is evidence that poultry manure is in some cases applied directly on grass land. The default value to start the PEC soil calculation is 5 cm. If the threshold of 0.1 microgram/l is not respected, then the soil depth of 20 cm can be applied. This would represent that the manure containing the additive would have to be applied on arable land and ploughed thereafter (application restricted to arable land). |   |
| 59. | Istituto Superiore di Sanità | 3.3.1. Phase II A PECsoil calculation |
|   | Lines 696-7 |   |
|   | “In addition, the biological activity of metabolites compared to the parent compound should be considered.” Besides differences in quantitative potency, metabolites might show on occasion qualitative differences (i.e., different and more worrying effects) compared to the parent compound, as shown by the experience gained on pesticides. In silico | The paragraph refers to metabolism. When metabolites are <10% of the dose, they may be excluded during the evaluation if they are not characterised by a biological activity. Line 2096 refers to application rate for FOCUS models; it has been amended for better clarity. The possibility to consider relevant metabolites is already included in the guidance (e.g. Phase II B) |
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| 60 | Pen&Tec Consulting, S.L.U. | 3.3.1. Phase II A PECsoil calculation | Page 24, Lines 699-700:  
"The adsorption/desorption of the active substance/metabolites of concern onto soil is preferentially determined by studies in soil."  
The text states "preferentially". Are other methods allowed? If so, it would be useful to have examples of other acceptable methods. This possibility should also be mentioned in 3.2.1 Soil adsorption/desorption. | The FEEDAP Panel considers that studies in soil are needed. Therefore, the text has been amended by deleting ‘preferentially’. |
| 61 | Pen&Tec Consulting, S.L.U. | 3.3.1.1. Recalculation based on metabolism | Page 24, Lines 720-723  
"When metabolism data are considered, the PECsoil A is calculated based on the methodology described in Phase I and recalculated as shown […]  
Fa* Fraction of the dose considered to be active”  
For clarity it would be useful that the document provides a definition of “fraction of the dose considered to be active”. e.g. we understand that this refers to the % of the parent active substance that is excreted. | The guidance was updated. The note % of the parent active substance that is excreted’ was added |
| 62 | FEFANA | 3.3.1.1. Recalculation based on metabolism | Line 722 (Section 3.3.1.1)  
Line 762 (Section 3.3.1.3)  
We suggest that the refined PECsoil after considering metabolism (line 722) or degradation (line 761) should use different acronyms  
e.g. 722 = PEC soil A ref metabol and 762 = PEC soil A ref degradation soil (see comment for Line 1169) | All different refinement of PECsoil in Phase A can be used in risk assessment.  
Since in the explanation of risk assessment (schemes and paragraph) refers in general to PECs, it is considered that changing the names would create just confusion. |
| 63 | FEFANA | 3.3.1.2. Recalculation based on | Lines 740 – 744:  
We would like to note, that the EFSA Panel has not allowed the use of PEC soil degradation in soil for Phase IIA refined, with the argument that earthworms / plants | This part is related to refinement of PECsoil for persistent compound.  
Generally, persistence is evaluated through soil degradation studies performed in the laboratory. When a high persistence is evaluated, the PECplateau should be calculated and the equations of Section 3.3.1.2. |
| Page  | German Environment Agency (UBA) | Istituto Superiore di Sanità | FEFANA | Istituto Superiore di Sanità | Istituto Superiore di Sanità | FEFANA |
|-------|---------------------------------|-----------------------------|--------|-----------------------------|-----------------------------|--------|
| 64.   | 3.3.1.3. Recalculation based on degradation in soil under multiple applications | 3.3.2. Phase II A PEC groundwater calculation | 3.3.2. Phase II A PEC groundwater calculation | 3.3.3. Phase II A PEC surface water calculation | 3.3.4. Phase II A PEC sediment calculation | 3.3.6.1. Terrestrial compartment |
|       | line 762 The input parameter PECsoil single event needs the further definition, which is given with eq. 13 in EMEA/CVMP/ERA/418282/2005-Rev.1-Corr. | Lines 768 and followings The exposure to relevant metabolites should be considered also in this compartment (see above 3.3.1) | Line 768: It is not clear why pore water can be used Insert same explanation for using pore water as in chapter 2.6.2 | Lines 780 and followings The exposure to relevant metabolites should be considered also in this compartment (see above 3.3.1) | Lines 791 and followings The exposure to relevant metabolites should be considered also in this compartment (see above 3.3.1) | Lines 823 – 840: |

Provide a worst-case assessment. When a risk is identified, there are two possibilities for further refinement: one through a chronic toxicity study; and the other through a refinement in exposure calculation. When a degradation study in manure is available, the DT50 from this study may be used for refinement. If not, a DT50 from a dissipation study performed in field treated with manure containing the additive may be provided. Both DT50 are considered suitable to derive a more realistic PECplateau.

Considering chronic toxicity studies, the guidance clarifies which studies should be presented; for earthworms, 2 studies are required: one study according OECD 220/222 together with a study on a second soil invertebrate. Although in the guidance (Section 3.5.1.2) it is noted that OECD guideline 222 is not designed to study exposure via manure (because the test requires the substance to be mixed into the soil and that clean manure is added to promote the reproduction of the earthworms), it is recognised that these OECD tests are the only available. In addition, the procedure for the assessment is in line with CVMP guidelines.

64. German Environment Agency (UBA)

65. Istituto Superiore di Sanità

66. FEFANA

67. Istituto Superiore di Sanità

68. Istituto Superiore di Sanità

69. FEFANA

Text modified to take account of the comment

The possibility to consider relevant metabolites is already included in the guidance (e.g. Phase II B)

In section 3.3.2, line 768 has been amended and it reads ‘…the concentration in groundwater (expressed as porewater)…’

The possibility to consider relevant metabolites is already included in the guidance (e.g. Phase II B).

The possibility to consider relevant metabolites is already included in the guidance (e.g. Phase II B).

The environment risk assessment is based on a tiered assessment, starting...
|   |   |   |
|---|---|---|
| 70. | FEFANA | 3.3.6.1. Terrestrial compartment |
|   |   | Lines 824 – 826: |
|   |   | According to Regulation (EC) 429/2008, chapter 3.4 of Annex II, “Studies for the terrestrial environment shall include: toxicity to earthworms; three terrestrial plants; and soil micro-organisms (e.g. effects on nitrogen fixation)”.
|   |   | However the Guidance document requests to perform the growth test in six different terrestrial plant species (at least two monocotyledonous and two dicotyledonous species). The requirements of the guidance document should not go beyond the criteria defined in the regulation.
|   |   | Please align the requirements with to Reg. (EC) 429/2008. |
| 71. | Pen&Tec Consulting, S.L.U. | 3.3.6.1. Terrestrial compartment |
|   | Page 28, Line 832: |
|   | “Table 5: Ecotoxicity studies required in Phase IIA to derive PNEC; soil Nitrogen Transformation (28 days); Terrestrial plants (14-21 d) Earthworm acute (14 d) ” |
|   | ‘Ecotoxicity’ is misspelled. Text in brackets is not consistent. PenTec suggests to use either ‘days’ or ‘d’. |
| 72. | Pen&Tec Consulting, S.L.U. | 3.3.6.1. Terrestrial compartment |
|   | Page 29, Lines 837-840: |
|   | “When a sufficient number of appropriate chronic toxicity values (EC10 or NOEC values from long-term tests) for rooted plants (i.e. six plant species) and soil invertebrates are available, the Phase IIA PNECI (which is assumed to be sufficiently conservative) may be superseded by a Phase IIC PNECR (see Section 3.5.1).” |
|   | The term “sufficient” is ambiguous. PenTec suggests clarifying what “a sufficient |

Here we have a mixture of both acute (EC50) and chronic values; we suggest to separate between acute and chronic tests and its appropriate assessment factors. Especially the OECD 208 is considered as a chronic terrestrial plant test and the derivation of a NOEC is more applicable than an EC50 value. Similar to the REACH guidance, substances with high logPow/log Koc and poor biodegradation may end up in soil and sediments. Therefore long-term studies may be even more appropriate compared to short-term toxicity tests. Considering these aspects, OECD 222, 216 and 208 is considered as appropriate.

Please amend section accordingly from acute and then moving to chronic studies that allow a reduction of the assessment factor. For plants the study is the same. Depending on the approach taken by the applicant, the PNECi or the PNECr will be considered.

Requesting 6 tests from the beginning may reduce the burden and time needed for the assessment since the acquired experience indicates that almost in all cases a study on 3 additional plants is requested. This is also in line with the EMA guidance of CVMP (Reflection paper on testing strategy and risk assessment for plants, EMA/CVMP/ERA/147844/2011).

Amended. Days are expressed as ‘d’ along the document.

An example is already included for plants.
number of chronic toxicity studies would be.

73. German Environment Agency (UBA)
3.3.6.2. Freshwater compartment (including sediment)

line 842
The „and“ between … livestock animals … and … freshwater aquaculture … should be replaced by an „or“. Reason: feed additives used only in livestock and distributed on field in liquid manure may also reach the water bodies e.g. by run-off.

Text modified to take account of the comment

74. FEFANA
3.3.6.2. Freshwater compartment (including sediment)

Table 6 – line 849:
We suggest referring to 72 h data, rather than 96 h data, for algal growth inhibition. Rationale: even for 96 h studies, appropriate ECx/NOEC values can be derived based on 72 h.
For any new studies a 96 h test would not be considered appropriate, as this may lead to a plateau growth towards the end of exposure and consequently to a failure of the validity criteria of the study.
Furthermore, we suggest including also Lemna (OECD 221) as an alternative to algae, in case technical issues prevent the applicant from performing an appropriate algae test. Those limitations might be colouration of substances or rapid degradation in a static system.

Please amend accordingly

75. German Environment Agency (UBA)
3.3.6.2. Freshwater compartment (including sediment)

lines 859-860
The intention to avoid unnecessary vertebrate testing is very welcomed. But the objective of this guideline is to assess any environmental risk of feed additives in an appropriate way. Therefore, the higher tier aquatic testing should not focus only on aquatic invertebrates.
The sentence “The long-term toxicity test should normally be a test …” should be rewritten and the passage should be extended.
Reason: if in the “acute phase” algae or fish would be the most sensitive organism group, it makes no sense to test Daphnia in a chronic assay because of specific mode of action reasons.
Please rewrite e.g. as follows: “The long-term toxicity test should normally include tests on an invertebrate and algae species. To avoid unnecessary vertebrate testing, it is sufficient to perform a chronic fish test only if fish is the most sensitive organism group of the acute assessment tier. For more details please see chapter 3.5.2.2.”

Guidance amended with the suggested text: “The long-term toxicity test should normally include tests on an invertebrate and algae species. To avoid unnecessary vertebrate testing, it is sufficient to perform a chronic fish test only if fish is the most sensitive organism group of the acute assessment tier. For more details please see chapter 3.5.2.2.”

76. Pen&Tec Consulting, S.L.U.
3.3.6.2. Freshwater compartment (including)

Page 29, Line 861:
“According to REACH (ECHA, 2008) a log Koc or log Kow ≥ 3 for an organic chemical…”

A hyperlink to ECHA 2008, chapter R10 has been added
For consistency with other in-text citations, PenTec suggests hyperlinking ECHA, 2008, as done in line 1213 with the same reference.

For consistency with other footnotes, PenTec suggests using capital letter at the start of the sentence.

Section 3.3.6.3. refers to semi-acute sediment toxicity tests with sediment-dwelling marine species (Phase IIA ERA). The following three tests concern water toxicity tests:
- Toxicity towards Skeletonema costatum (Algae), ISO/DIS 10253
- Toxicity towards Acartia tonsa (Crustacea), ISO TC 147/SC5/WG2
- Toxicity towards Scophthalmus maximus (Fish), PARCOM Protocol 1995 part B
- Toxicity towards Corophium volutator (Sediment-dwelling organism), PARCOM Protocol 1995 Pt A

The following test ‘- Toxicity towards Corophium volutator (Sediment-dwelling organism), PARCOM Protocol 1995 Pt A (OSPAR 2006, Part A).’ has been included in the table because it also concerns a 10d sediment toxicity test.

For surface water data from the trophic levels are always available whereas for marine environment no data are available. For this reason, the EqP was not included in the marine environment.
| No. | Commentor | Page Line | Text | Changes |
|-----|-----------|-----------|------|---------|
| 82. | Pen&Tec Consulting, S.L.U. | 3.3.6.3. Marine compartment | Page 30, Line 895: "In the Phase IIA effect assessment the PNEC;sed can be derived from sediment-spiked 10d toxicity" For consistency throughout the text, PenTec suggests to either use 10d or 10-d when accompanying the words ‘toxicity tests’ or any other words. | It has been harmonised to ’10-d’. |
| 83. | FEFANA | 3.3.6.3. Marine compartment | Table 8 – line 903: The guideline ASTM E1367-03 / PARCOM, Protocol 2006 Pt A (Test available for 10-d acute and 28-d chronic stage) is currently used by external laboratories for Corophium volutator. We suggest including this test in Table 8. | Text modified to take account of the comment. |
| 84. | FEFANA | 3.3.6.3. Marine compartment | Table 9 – line 916 Table 10 – line 922 We suggest referring to standardised chronic OECD tests only, which are also regularly carried out in European laboratories (i.e. OECD 218 and OECD 225). See also Table 17. Semi chronic tests are hardly to be used for a regulatory purpose especially as they are carried out in European Labs as frequently (see also comments above). Please add reference to OECD 218 and OECD 225. | Tables 9 and 10 refer to acute (short term) ecotoxicity test in Phase IIA. The (phase IIC) ERA based on chronic sediment toxicity tests with sediment-dwelling marine and freshwater species is presented in section 3.5.3 of the ERA guidance document. In Table 17 the references to OECD 218 and OECD 225 are already available. As indicated in Figure 3, the applicant may decide to perform chronic toxicity tests directly (Phase IIC), avoiding Phase IIA. |
| 85. | Pen&Tec Consulting, S.L.U. | 3.3.6.3. Marine compartment | Page 31, Line 920: "following Table 10 by selecting the lowest toxicity value for the three benthic species" A full-stop is missing. | Text modified to take account of the comment |
| 86. | Pen&Tec Consulting, S.L.U. | 3.3.6.3. Marine compartment | Page 32, Line 922: "Table 10: Ecotoxicity studies required in Phase IIA to derive PNEC;sed for invertebrates in marine " ‘Ecotoxicity’ is misspelled. ‘sed’ in PNEC;sed should be a subscript. | Text modified to take account of the comment |
| 87. | SCC Scientific | 3.3.6.3. Marine compartment | Ref: | Text modified to take account of the comment: ‘If in the near future ISO
| Consulting Company | compartment | Page, line, comment | Comment: |
|---------------------|-------------|---------------------|-----------------|
| FEFANA              | 3.3.6.3. Marine compartment | Lines 926 – 927:   | and/or OECD guidelines for short-term toxicity tests with marine/estuarine bentic species become available, these protocol tests are preferred. |

**88.**

Consulting Company

compartment

Page 32, line 924

Comment:

Please add for better clarity “marine/estuarine” in the footnote of Table 10: “If in the near future ISO and/or OECD guidelines for short-term toxicity tests with marine/estuarine species become available, these protocol tests are preferred.”

**89.**

Pen&Tec Consulting, S.L.U.

3.3.6.3. Marine compartment

Page 32, Line 929:

In the formula, a space is missing ‘orEC10experiment’.

**90.**

Pen&Tec Consulting, S.L.U.

3.3.6.3. Marine compartment

Page 32, Line 934:

"value used for the PEC calculation. If so, then the PNEC could be further normalised using the" PenTec believes the term ‘than’ should be replaced by ‘then’.

**91.**

German Environment Agency (UBA)

3.3.8. Phase II A Risk characterisation

line 952

Please replace „is > 0.1 µg/L“ with “is ≥ 0.1 µg/L”; this is in accordance with the current “Guideline on assessing the environmental and human health risks of veterinary medicinal products in groundwater, April 2018”.

**92.**

Istituto Superiore di Sanità

3.3.9. Assessment of persistent, bioaccumulative and toxic substances

Lines 955-79

This sub-chapter should make clear that the identification of VPVB/PBT substances is relevant to both parent substances and metabolites (see above 3.3.1)

**93.**

Pen&Tec Consulting, S.L.U.

3.4.1.1. Refinement based on degradation in manure

Page 33, Line 993:

"As the storage capacity shows a large variation amonog the different EU Member States”

Typo: “among” instead of “amonog”

Text modified to take account of the comment
| #  | Organization/Consulting Company | Section | Line/Page/Ref | Comment | Decision |
|----|---------------------------------|---------|---------------|---------|----------|
| 94. | FEFANA                          | 3.4.1.1. | 1008          | Refinement based on degradation in manure:  
Previous refinement due to metabolism (PECsoil x FA) is not considered in this formula to calculate PEC manure.  
Please amend accordingly. | It is not the case. Refinement for manure already includes the metabolism. Therefore, the text was not modified. |
| 95. | SCC Scientific Consulting Company | 3.4.1.1. | Page 34, line 1011ff | Ref:  
Comment:  
For DEPTHfield it is recommended to make a distinction between application/spreading on grassland or on arable soils. 5 cm for grassland and 20 cm for arable soils would be in line with the approach presented under 3.3.1. for Phase II A concerning the ploughing depth and should therefore also be applicable for the higher tier Phase II B. | The possibility to use the ploughing soil depth of 20 cm will be only for Phase IIB, not for Phase IIA. |
| 96. | Pen&Tec Consulting, S.L.U.       | 3.4.2.1. | 1032          | “geographic settings with various combinations of crops, soils and climate. Groundwater concentrations”  
PenTec believes the word ‘climate’ should be in the plural form. | It has been amended with singular form for all names |
| 97. | German Environment Agency (UBA) | 3.4.2.1. | Page 35, line 1041 | Please cite the current up to date model version “FOCUS PEARL v4.4.4”. | The calculations were performed for the first guidance of 2008. Calculations were not repeated. Therefore, the reference to the old model is appropriate. |
| 98. | Pen&Tec Consulting, S.L.U.       | 3.4.2.1. | 1058          | “ensure the leaching concentrations is < 0.1 μg/L).”  
PenTec believes the verb ‘is’ should be replaced by ‘are’. | Text modified to take account of the comment |
| 99. | Pen&Tec Consulting, S.L.U.       | 3.4.2.1. | Page 36, line 1064 | “FOCUS GW”  
PenTec suggests to include “GW” in abbreviations (page 48). | Text modified to take account of the comment |
| 100. | SCC Scientific Consulting Company | 3.4.2.1. | Ref: page 36, line 1069 | For the application on grassland a refinement with the crop “grass + alfalfa” should be possible as this crop is implemented in the FOCUS groundwater model for all FOCUS models were developed for pesticide products, which are characterized by a label and a GAP defining the exact time of application and the exact crop. Manure application has neither a label nor a specific crop; therefore, the proposal of different scenarios seems not appropriate.  
The first step of the leaching assessment for feed additives is based on an application date some weeks before the emergence of winter wheat (i.e. 3 October). For standardisation purposes, the exposure assessments timing of... |
Report public consultation on guidance on the safety of feed additives for the target species

|   |   |   |   |
|---|---|---|---|
| 101 | SCC Scientific Consulting Company | 3.4.2.1. Groundwater | Ref: Page 36, line 1073 and page 37, line 1110  
Comment: For the application on grassland a refinement with multiple applications according to good agricultural practice instead of one spreading event should be possible. |
|   |   |   |   |
| 102 | SCC Scientific Consulting Company | 3.4.2.2. Surface water | Ref: Page 36, line 1073 and page 37, line 1110  
Comment: For the application on grassland a refinement with multiple applications according to good agricultural practice instead of one spreading event should be possible. |
|   |   |   |   |
| 103 | SCC Scientific Consulting Company | 3.4.2.2. Surface water | Ref: Page 37, line 1105  
Comment: For the application on grassland a refinement with the crop “grass + alfalfa” should be possible for the scenarios D3, D4 and R3 as this crop is implemented in the FOCUS surface water model. |
|   |   |   |   |
| 104 | Istituto Superiore di Sanità | 3.5. Phase II C to estimate refined PNEC (PNEC R) values | Lines 1134-1147  
The toxicological profile of the substance in mammals (e.g., the presence of endocrine disrupting effects) and the intended mode(s) of action should be added as pieces of information to be used in the selection of tests for refining assessment of effects and PNECs (see also Scientific Opinion on good modelling practice in the context of mechanistic effect models for risk assessment of plant protection products, EFSA J, 2014, already referenced in the draft Guidance) |
|   |   |   |   |
| 105 | Istituto Superiore di Sanità | 3.5. Phase II C to estimate refined PNEC (PNEC R) values | After line 1139  
Suggestion for an additional statement; considering the due concern for sustainability of animal production and the current lack of a consistent approach for assessing feed additives under this respect, any effect on emissions (ammonia, carbon dioxide, minerals) would be assessed on a case-by-case basis, when indicated by previous information such as the mode of application to soil is assumed to coincide with the drilling of winter cereals (in the absence of pure grassland scenario; in FOCUS grassland is associated to alfa-alfa), as these crops are typically grown throughout Europe and represent a significant input of manures on a total mass basis across Europe. Moreover, these crops represent a “worst case” among FOCUS crops. Application in autumn is appropriate for a conservative first step because it results usually in higher leaching concentrations than application in any other season. The dose has to be considered applied onto soil (depth 5 cm) as a first step; the incorporation at 20 cm, a more realistic scenario, is considered a refinement.  
It is very difficult to find adequate interval times between applications to fit in the FOCUS models. Single application is simpler and easy to use.  
See comment 101  
If during the assessment the assessors consider that additional information is needed it will be requested following a case-by-case approach.  
See the reply to comment 12 |
| No. | Commentor | Section and Comment |
|-----|-----------|---------------------|
| 106. | Pen&Tec Consulting, S.L.U. | 3.5. Phase II C to estimate refined PNEC (PNEC R) values: Page 37, Line 1144: “test, see sections 3.3.6.1or 3.5.2.1) as influenced by the experimental design of the study, those that” A space is missing in ‘3.3.6.1or 3.5.2.1’ Text modified to take account of the comment |
| 107. | Istituto Superiore di Sanità | 3.5. Phase II C to estimate refined PNEC (PNEC R) values: Lines 1198 and followings the tests listed in Tables 14, 15, 17, 19 should be better presented as preferred options, that might be modified based on available information. These are the studies that the Panel considers necessary. Nevertheless, the scope of the guidance already foresees that the applicant may deviate from any requirements of the guidance and provide an adequate justification. |
| 108. | FEFANA | 3.5.1.4. PNEC R derivation for soil organisms Lines 1207 – 1208 (Section 3.5.1.4) Lines 1268 – 1269, Lines 1287 – 1288 (Section 3.5.2.2) Does the recommendation intend to suggest that the study should be discussed a priori with the EFSA staff or FEEDAP experts? In case positive, please correct the sentence, since the EFSA is not a regulatory authority. This service is not currently foreseen in the EFSA’s Catalogue of support initiatives during the life-cycle of applications for regulated products. It will be removed from the guidance document. See the reply to comment 108 |
| 109. | Pen&Tec Consulting, S.L.U. | 3.5.1.4. PNEC R derivation for soil organisms: Page 39, Line 1207: “It is advisable a priori to discuss the design of such advanced studies with the responsible regulatory authority.” Does this mean that EFSA are now open to discuss study design in detail a priori? |
| 110. | German Environment Agency (UBA) | 3.5.1.4. PNEC R derivation for soil organisms: line 1212 Please include after “… potential risk” following addition “due to the non-specific mechanism of action of the active substance”. Reason: in case of specific mechanism of action of the active substances it seems to be not appropriate to include several taxonomic groups in the SSD. This REACH-based approach might be useful just for “narcotic” industrial chemicals with non-specific mechanism. This section is related to very rare cases where high risk is identified for more than 1 taxonomic group. A general proposal is made on how to address the risk. Since we cannot anticipate which kind of additive may encounter this situation, it is preferred to suggest a general approach for a case by case situation. |
| 111. | SCC Scientific Consulting Company | 3.5.2.2. Refined PNEC derivation for freshwater pelagic (PNECR;sw) Ref: Page 40, Table 16 Comment: If no ErC10 or NOEC can be derived from the algae study in Phase IIA, there It is not accepted. When algae are not the most sensitive species, it is preferred to have two chronic studies. |
| Line  | Author | Comment | Page | Lines | Description | Resolution |
|-------|--------|---------|------|-------|-------------|------------|
| 1259  | German Environment Agency (UBA) | 3.5.2.2. Refined PNEC derivation for freshwater pelagic (PNECR;sw) and sediment (PNECR;sed) organisms | 43   | 1341-1345 | “The EFSA guidance Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011) provides instructions on how to identify and select “scientific peer-reviewed open literature” and how to report it in a dossier. Even if the guidance was prepared to answer a specific question of the Regulation 1107/2009 for pesticide, the criteria described for the literature selection can be considered common to all chemicals.” What about reference to EFSA guidance on systematic reviews, 2010 & guidance on how to appraise study designs, systematic reviews and literature searches, 2015? | EFSA guidance on safety assessment of feed additives for the target species includes an extensive literature search and describes the procedure. A similar approach will be used for the safety of feed additives for the environment. Section 4 has been updated accordingly. |
| 1323  | German Environment Agency (UBA) | 3.5.4. Phase II C Risk assessment for secondary poisoning | 45   | 1576 | Koc has been defined as ‘organic carbon-water partitioning coefficient’ and used along the document | |
| 1259  | German Environment Agency (UBA) | 3.5.4. Phase II C Risk assessment for secondary poisoning | 45   | 1576 | Koc Sorption/desorption coefficient, normalized to organic carbon content.” Koc is known as ‘organic carbon-water partitioning coefficient’ since it is calculated based on the amount of chemical absorbed onto soil with respect to water. Similarly, Kow is also based on the relation between the concentration of the chemical in n-octanol vs water. For consistency, PenTec suggests referring to Koc as “Organic carbon-water partitioning coefficient” throughout the guidance when the abbreviation is not used. Also, PenTec suggests using the same name to refer to Koc throughout the guidance (e.g. see line 2162, where Koc is referred to as “the organic carbon-water partitioning coefficient”). | |
| 1259  | Pen&Tec Consulting, S.L.U. | 4. Literature reviews | 45   | 1576 | Koc Sorption/desorption coefficient, normalized to organic carbon content.” Koc is known as ‘organic carbon-water partitioning coefficient’ since it is calculated based on the amount of chemical absorbed onto soil with respect to water. Similarly, Kow is also based on the relation between the concentration of the chemical in n-octanol vs water. For consistency, PenTec suggests referring to Koc as “Organic carbon-water partitioning coefficient” throughout the guidance when the abbreviation is not used. Also, PenTec suggests using the same name to refer to Koc throughout the guidance (e.g. see line 2162, where Koc is referred to as “the organic carbon-water partitioning coefficient”). | |
| 1259  | Pen&Tec Consulting, S.L.U. | Abbreviations | 45   | 1576 | Koc Sorption/desorption coefficient, normalized to organic carbon content.” Koc is known as ‘organic carbon-water partitioning coefficient’ since it is calculated based on the amount of chemical absorbed onto soil with respect to water. Similarly, Kow is also based on the relation between the concentration of the chemical in n-octanol vs water. For consistency, PenTec suggests referring to Koc as “Organic carbon-water partitioning coefficient” throughout the guidance when the abbreviation is not used. Also, PenTec suggests using the same name to refer to Koc throughout the guidance (e.g. see line 2162, where Koc is referred to as “the organic carbon-water partitioning coefficient”). | |
| No. | Commentator | Section | Comments |
|-----|-------------|---------|----------|
| 116. | Pen&Tec Consulting, S.L.U. | Abbreviations | Page 49, Line 1576: “PECporewater”  
PenTec suggests changing for PECpw for simplicity and consistency with other parts of the guidance (e.g. line 469). | Text modified to take account of the comment |
| 117. | Pen&Tec Consulting, S.L.U. | Abbreviations | Page 49, Line 1576: “PECsoil”  
PenTec suggests including abbreviations PECsoil-dw and PECsoil-ww used in lines 441 & 465. In general, abbreviations dw & ww should be included as they are used as subscripts throughout the dossier (e.g. soildw in line 2090). |
| 118. | Pen&Tec Consulting, S.L.U. | Abbreviations | Page 48, line 1576: PenTec suggests including GW (groundwater) as abbreviation and consistently using it throughout the dossier (e.g.in line 447 PECgroundwater is used, whereas in line 1064 GW is used). | Text modified to take account of the comment |
| 119. | German Environment Agency (UBA) | Appendix A – Specific protection goal options and associated exposure assessment goal options for environmental risk assessments of feed additives | Appendix A is very much appreciated! | Noted |
| 120. | FEFANA | Appendix B – Application of FOCUS models in Ground water | Line 2089:  
Conversion factor 100: In the same formula, given in the ERA-guidance of 2008 (page 27), the conversion factor is 100.000, while the only other assumption that has changed is the mixing depth with soil (was 20 cm, is now 5 cm). This does not seem to warrant a factor 1000 difference in the conversion factor.  
Please describe the justification for the difference between the old and the new | It is related to the measure unit of the input data. In the former guidance cm and m were used and in the new guidance it has been standardised to m. |
| 121. | SCC Scientific Consulting Company | Appendix B – Application of FOCUS models in Ground water | Ref: Page 4, last line, box on the right and Page 67, line 2096  
Comment: It seems that the terms PECsoil;tot and PECsoil;pw are related to the first decision tree where PECpore water is the surrogate for PECgw. It seems that the depths are more related to the spreading of slurry on soil surface for grassland with 5 cm depth and spreading of slurry via incorporation for arable soils with 20 cm depth (realistic worst case)? Suggestion for line 2096: “… default 5 cm for grassland and 20 cm for arable soils (realistic worst case)” | There is evidence that poultry manure is in some cases applied directly on grass land. The default value to start the PEC soil calculation is 5 cm. If the threshold of 0.1 microgram/l is not respected, then the soil depth of 20 cm can be applied. This would represent that the manure containing the additive would have to be applied on arable land and ploughed thereafter (application restricted to arable land).  
See Comment 58 |
| 122. | Spanish Medicines Agency (AEMPS) | Appendix C – Application of FOCUS models in surface water | The AEMPS would like to thank EFSA the opportunity of making comments.  
It would be helpful to include the incorporation depth that should be used in the calculations for run-off scenarios and the CAM value that should be considered.  
Is there any difference in the incorporation depth or CAM if the manure is applied to grassland or arable land? If so, it should be specified in the guideline. | FOCUS models were developed for pesticide products, which are characterized by a label and a GAP defining the exact time of application and the exact crop. Manure application has neither a label nor a specific crop; therefore, the proposal of different scenarios seems not appropriate. The timing of application has a significant impact on predicted losses. In general, losses will be greater with autumn applications, slightly lower in spring and the lowest with summer applications. The application of manure to arable and grass land is considered to coincide with the drilling of cereals in autumn (in the absence of a pure grassland scenario). In order to select the most appropriate date, the Pesticide Application Timer should be used. Furthermore, it is proposed to select soil incorporation as the application type in SWASH model, CAM 1 is the default value and is referred to soil application with a linear degradation in the first 4 cm. It is a worst case for runoff, therefore suitable for addressing contamination through this route. |
| 123. | Istituto Superiore di Sanità | Appendix D – Quantitative structure-activity relationships calculations | Appendix D  
As minimum, this Appendix should at least mention the read-across approach, which has remarkable and increasing applications, especially in the ECHA Domain (see e.g., https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/774f9be1-b76d-40ab-8513-4f3a533b6ac9 https://echa.europa.eu/documents/10162/13628/raaf_en.pdf/614e5d61-891d-4154-8a47-87efeb1851a)  
Read-across uses relevant information from analogous ('source') substances to predict the properties of 'target' substances, providing a major alternative approach for filling data gaps. In the context of this Guidance read-across is expected to support the assessment of the ecotoxicological activities of metabolites (see above 3.3.1). | New text has been included in Appendix D considering this option. |
| 124. | FEFANA | Appendix D – Quantitative structure-activity relationships calculations | Line 2147: The possibility of applying QSAR methods should already be mentioned in line 267 as a proof test, as it is named in line 2147 as a valid methodology for Phase I. The short tabular listing with possible test methods could also include QSAR evidence. | Appendix D is presenting the QSAR approach for a restricted number of cases (flavours compounds evaluation) and it is not applicable to the rest of feed additives. |
| 125. | FEFANA | Appendix D – Quantitative structure-activity relationships calculations | Line 2198: PNECSed EqP is mentioned in the main part of the guidance, and PNEC soil (EqP) in the annex. What does this mean for the ERA assessment process? PNEC marine-sed (EqP) is not mentioned at all. Does this mean, this will be not considered anymore? Please clarify | The question relates to parameters of Appendix D with reference to the text guidance. Appendix D is presenting the QSAR approach for a restricted number of cases (flavours compounds evaluation) and it is not applicable to the rest of feed additives. |
| 126. | FEFANA | Appendix F – Concentration of a feed additive (mg/kg feed) that would correspond to a PEC below the trigger value for the different species | Editorial comment, Table F1 – line 2279: Header row cannot be properly read | Text modified to take account of the comment |
| 127. | Pen&Tec Consulting, S.L.U. | Appendix F – Concentration of a feed additive (mg/kg feed) that would correspond to a PEC below the trigger value for the different species | Page 76, Lines 2279-2280, Table headings cannot be well read in columns 2-4 (too close together). PenTec suggests adding visible column divisions or using wider columns. | Text modified to take account of the comment |
| 128. | Spanish Medicines Agency (AEMPS) | Appendix G – Rationale for the proposal to increase the nitrogen load to agricultural land form manure | We thank EFSA for the opportunity of commenting this guideline. I our opinion the use of 250 kg N/ha per year would be an unrealistic scenario that would lead to worst case assumptions difficult to handle in later stages. EFSA should take into account the following: - 250 kg N/ha are the total needs of corn throughout its production cycle. - Once the manure is spread, nitrogen losses can be very important due to the high | Appendix G may be used in case of concern of particular Member States. The FEEDAP Panel, however, will consider the default value of 170 Kg N/ha and year. A sentence has been added in the guidance to clarify this point. |
- Therefore the 250 kg N have to be applied in several occasions during the plant cycle. In Spain it is recommended that the total nitrogen needs for corn are applied as follows: 1/3 of the total N applied before sowing as basal dressing (mixing fertilizer with soil – ploughing). 1/3 of the total N applied as top dressing when the plant is 40 cm high. 1/3 of the total N as top dressing when the plant is 1 meter high.
- Manure can be used as basal dressing before sowing but for the top-dressing application, an inorganic fertilizer that can be applied with the irrigation will be probably preferred (in the case of Spain) as the application of manure with a tractor and a 5000 l tank might damage the plants. Besides, the use of formulated product improves the uptake of N by the plant and reduces losses.
- Besides this, it should be taken into account that when running FOCUS, only a single application is considered, i.e. we would be telling FOCUS that the 250 kg N are applied in one single application, which would not be the real case. This would lead to an over estimation of the exposure to surface and ground waters.
- The same situation is expected in other environmental compartments: PECsoil will be calculated considering that there is one intensive exposure of an amount that in reality will be reaching the environment in successive applications.

In conclusion, in our opinion basing the PEC calculation in 250 kg N/ha would be unrealistic in most of the scenarios because:

- The total needs of nitrogen will be probably covered with a mixture of manure and inorganic fertilizers.
- The total needs of the crop will be split in several applications throughout the production cycle. Nevertheless, the risk assessment will consider the effect of 250 kg N/ha applied in a single occasion. The risk will be overestimated.

| 129. | FEFANA | Appendix G – Rationale for the proposal to increase the nitrogen load to agricultural land form manure application from 170 to 250 kg N/ha per year | Line 2300 – 2303:
It seems that the “nitrogen standard load” of 170 kg N/ ha per year has been used both in the old ERA guidance and in the new draft guidance. However, the appendix G presents a rationale to use 250 kg N/ha per year instead. Does this have any practical implication for the applicant?
Please clarify practical implications of Appendix G for applicants. | Appendix G may be used in case of concern of particular Member States. The FEEDAP Panel, however, will consider the default value of 170 Kg N/ha and year in the assessment.
A sentence was added in the text of the guidance to clarify this point. |
| 130. | Institute of the Republic Slovenia for Nature | Appendix G – Rationale for the proposal to increase the | We have reviewed the material in public debate. In particular, we would like to highlight Appendix G: “Rationale for proposal to increase the nitrogen load to agriculture land for manure application from 170 to 250 kg n/ha per year”. | Appendix G may be used in case of concern of particular Member States. The FEEDAP Panel, however, will consider the default value of 170 kg N/ha and year. 170 kg N/ha is the default value set in the nitrate’s directive (Council Directive of 12 December 1991 concerning the protection of waters. |
| **Conservation nitrogen load to agricultural land form manure application from 170 to 250 kg N/ha per year** | We believe that the rise of standard value for calculation of the PECsoil, in Appendix G is justified well enough. Therefore, we propose that Appendix G is not a recommendation only but rather a compulsory standard for determination of doses of compounds added to forage.

As the national institution responsible for the conservation status of nature, we are deeply concerned about the unfavourable status of karst underground water ecosystems. With 230 water species, Slovenian karst represents the richest underground fauna worldwide. A major part of the area is included in the Natura 2000 network. It is extremely rich in endangered species, with the olm (*Proteus anguinus*) at the top, which is also a Natura 2000 umbrella species, and one of the most remarkable representatives of stygofauna in Slovenia and probably in Europe.

We have arrived at a conclusion that the nitrates from agricultural sources are one of the key factors influencing deterioration of the quality of the underground water. The state monitoring of groundwater and other available data indicate that recently, the values of NO3 in several olm habitats have been increased up to 20 to 30 mg NO3/l. This is a clear evidence that by fertilizers of animal origin, the livestock production induces a largely increased load to the environment. Taking in account that for olm, the proposed limit groundwater nitrate value (including the natural background concentration) shall be 9.2 mg NO3/L, its conservation status is declared as unfavourable. A substantial contribution to the high nitrate value in the considered olm habitat underground waters (even above 240 kg N/ha) is due to high inputs of bovine and swine slurry as well as chicken manure, spread by farmers over prevalingly karst meadows.

According to nitrate directive, Slovenia is on the critical list of countries with the entire state territory identified as a nitrates vulnerable zone. We strongly believe that for sensitive groundwater-dependent ecosystems in karst areas, the limit value for nitrate intake should be more rigorous (i.e. lower), while the standard values for calculation of PECsoil should be increased in accordance with Appendix G. | against pollution caused by nitrate’s from agricultural sources (91/676/EEC) and used by European Medicine Agency for veterinary medicines. In addition, there are several worst-case assumptions in the model. Increasing this default value to higher nitrogen loads would need to include further refinements on storage and application of the manure (e.g. frequency of application). A sentence was added in the text of the guidance to clarify this point. |

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| 131. Puratos | Appendix G – Rationale for the proposal to increase the nitrogen load to agricultural land form manure application from 170 to 250 kg N/ha | The amount of nitrogen used per hectare utilised agricultural area was 64 kg in 2015 (https://ec.europa.eu/eurostat/statistics-explained/index.php/Agri-environmental_indicator_-_mineral_fertiliser_consumption). Instead of elevating the 170 kg N/Ha, should it therefore not be lowered to more realistic values? Appendix G may be used in case of concern of particular Member States. The FEEDAP Panel, however, will consider the default value of 170 Kg N/ha and year. 170 kg N/ha is the default value set in the nitrate’s directive (91/676/EEC) and used by EMA for veterinary medicines. |
| Per year | The purpose of this letter is to express the support the proposed increase of the nitrogen load to agricultural land from manure application from 170 to 250 kg N/ha per year suggested in the Appendix G and to illuminate some additional reasons for consideration of suggested (i.e. higher) PEC values for nitrogen and nitrogen-related substances (including feed additives).

Firstly, the determination of maximum nitrogen loads to agricultural land is based on potential effects nitrogen compounds on human health and development (WHO, 2011), although even higher susceptibility to nitrogen compounds have been shown in other vertebrates, primarily amphibians (e.g. Marco et al 1999, Rouse et al 1999, Ortiz et al. 2004) and water invertebrates (Camargo et al, 2005).

Another aspect supporting the use of suggested value of 250 kg N/ha per year load as a more realistic nitrogen load comparing to currently used 170 kg N/ha per year includes a high water permeability of the karst as well as alluvial soils. In the case of the Dinaric Karst in the western Balkans also overlays an important water source and unique underground ecosystem. This highly fragile and endangered underground environment hosts one of the largest biodiversity of underground invertebrates worldwide (Sket 2005) and the only known habitat for the largest cave animal - charismatic and unique European blind salamander (Proteus anguinus). In order to protect groundwater species and limit the impact to springs and surface water, the higher and more realistic nitrogen loads shall be considered in a calculation of predicted environmental concentration of feed additives from agricultural activities. Such approach might ensure the sufficient protection of exposed organisms and populations.

In that view, me and my colleagues strongly support the arguments given in Appendix G and suggest the consideration of 250 kg N/ha per year in the main text of the “Guidance” as a more realistic value of a nitrogen load and its application in all PEC-related based predictions of nitrogen load (e.g. chapters 2.6.1.).

References:
Marco, A., Quilichano, C. & Blaustein, A. R. 1999. Sensitivity to nitrate and nitrite in pond-breeding amphibians from the Pacific Northwest, USA. Environmental Toxicology and Chemistry, 18,12:, 2836–2839. http://doi.org/10.1002/etc.5620181225
Ortiz, M.E., Marco, A., Saiz, N., Lizana, M. 2004. Impact of Ammonium Nitrate on Growth and Survival of Six European Amphibians. Acta. Environ. Contam. Toxicol. 47: 234-239.
Rouse, J. D., Bishop, C. A. & Struger, J. 1999. Nitrogen pollution: An assessment of its threat to amphibian survival. Environmental Health Perspectives, 107,10:, 799–803. http://doi.org/10.1289/ehp.9910779
Sket, B. (2005) Dinaric karst, diversity. Encyclopaedia of caves (ed. by D.C. Culver and W.B. White), pp. 158–165. Elsevier Academic Press, Oxford. | Appendix G may be used in case of concern of particular Member States. The FEEDAP Panel, however, will consider the default value of 170 Kg N/ha and year. 170 kg N/ha is the default value set in the nitrate’s directive (91/676/EEC) and used by EMA for veterinary medicines. In addition, there are several worst-case assumptions in the model. Increasing this default value to higher nitrogen loads would need to include further refinements on storage and application of the manure (e.g. frequency of application). |
| 133. | Pen&Tec Consulting, S.L.U. | Appendix H – Calculations and assumptions made to update the values of feed intake and nitrogen excretion of different animal species/categories | Page 85, Line 2515: “Yearly egg production of 321 eggs (ITAVI, 2014)”

The yearly egg production reference was taken from ITAVI (2014). However, for laying hens, the assumptions refer to Brown layer hen HY line breed (line 2510). Since a specific genetic line is indicated, why not using the yearly egg production provided by the breeder, instead of taking it from the generic ITAVI survey? | The data on egg production of ITAVI is considered to represent the general egg production of different breeds of laying hens. No similar data were found for the zootechnical parameters as feed intake or body weight gain, which are in most cases related to specific breed lines. The assumptions made for the Brown layer hen HY line breed regarding feed intake or body weight gain can be considered representative for brown layers. ‘Brown layer hen HY line breed’ has been changed by ‘Brown layer hen’ |
References
The EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed),
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